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Telemedicine in the treatment of headache

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A dissertation for the degree of Philosophiae Doctor – June 2017

TO FUTURE TELEHEADACHE PATIENTS

The future is already here -It's just not evenly distributed. William Gibson, 2003

TABLE OF CONTENTS

PREFACE

Before I got involved in research, a friend of a friend of mine had told me that taking a PhD is a piece of cake: "*You only need to write three articles and that's it.*" Little was I aware of the extensive work with planning, organizing, coordinating, reporting, funding, data collection, registrations, investigating, writing and analyzing, being interdependent, disputing with people that had different agendas, etc. The following project was planned in 2008, and the researchers started recruiting patients from a small rural hospital in Mosjøen, Northern Norway in 2009. Due to different complications, the pilot study was stopped and put on ice for a while. In 2012 it was reorganized into the project that I have worked on. I started to work on it in parallel with my clinical work as a neurologist at the Department of Neurology at Tromsø University Hospital. From September 2014 I got a grant from Helse Nord RHF, but kept on working my shifts at the Department of Neurology.

At times, unforeseen events and major obstacles appeared. Despite the difficulties we had to overcome, I am very grateful to have been given the opportunity to work together with so many people. I feel honored and privileged to be a part of this project.
First, I want to thank the 402 headache patients who participated in the trial. Your willingness to be consulted in a nontraditional manner and answering questionnaires made this work possible. Thank you very much!

I would like to thank Svein Ivar Bekkelund, of whom I am indebted to for being the great supervisor who was in tune with my personality. You introduced me to the world of science, gave me the opportunity to learn, and taught me the importance of teamwork, interdependency, and not to forget to get the most out of the available resources.
Special thanks goes to my co-supervisor Karl Bjørnar Alstadhaug. You have been great. Even when you were short of time, you always helped. I am especially grateful for your support, willingness and advice during my main supervisor's absence.

Claus Albretsen, thank you for arranging a hybrid model that made it possible to combine the research with clinical work. My colleagues at the Department of Neurology and

Neurophysiology, I would like to convey my special appreciation for your support and flexibility in a busy, but pleasurable work atmosphere.

My warm thanks goes to Jorun Willumsen and Anna-Kirsti Kvitnes who skillfully coordinated the project, and joined me to test the different functions of the equipment (Figure 1). I do want to express my gratitude to Irene Lund and the National Neuromuscular Centre (NMK) for providing us with such excellent study coordinators. The secretaries at the Department of Neurology also helped coordinating patients. Lilly Ann Klaussen was excellent in managing administrative tasks. Marlen Lauritsen and Nora Bekkelund, your data collection and plotting have been very helpful.

Figure 1 Conversation between me and the study coordinator to test the telemedicine equipment. A computer screen with the electronic patient record is seen on the right.

Karin Flatekval Eines, Torill Erdahl, Marianne Røst, and Grethe Berg Johnsen from the Department of Neurology in Tromsø managed the participants very skillfully. Thank you!

Staff at the research department made valuable contributions with randomization and study advice. I especially want to mention Bjørn Straume, who gave valuable statistical advice. At Tromsø University Hospital, I am in debt to economist Thomas Krogh, who contributed with data collection and cost analyses in article 1. Thanks to my fellow PhD students and staff at EPINOR, in which it was a pleasure to be a part of.

I am also indebted to the following organizations:

- The Northern Norway Regional Health Authority (Helse Nord RHF) that funded the study.
- The University of Tromsø (UIT) that gave me the opportunity to become a PhD student and finally dispute.

To my wife Margrethe, and our children Jakob and Jahn for enriching these days.

The present PhD project began as an innocent commitment, and ended with a separation that gave me new paradigms, and hopefully will open new doors. To all who were involved, I give my sincere thanks and appreciation, for giving me inspiration and challenges as well as experiences with enrichments and friendships I would not have otherwise known.

1. June 2017, Tromsø, Kai Ivar Müller

ABBREVIATIONS

ANOVA	ANalysis Of VAriance
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CONSORT	CONsolidated Standards Of Reporting Trials
CT	Computer Tomography
DIPS	The Distributed Information and Patient System for hospitals (DIPS ASA, Bodø, Norway)
EPR	Electronic Patient Record
FAS	The Norwegian Research and Management database
HIT-6	Headache Impact Test-6
ICER	Incremental Cost Effectiveness Ratio
ICHD	International Classification of Headache Disorders
ICMJE	International Committee of Medical Journal Editors
IHS	International Headache Society
IT	Information Technology
MOH	Medication Overuse Headache
MRI	Magnetic Resonance imaging
PC	Personal Computer
RCT	Randomized Controlled Trial
REC	Norwegian National Committee for Medical and Health Research Ethics
SPSS	Statistical Package for Social Science
SUNCT	Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing
SUNA	Short-lasting Unilateral Neuralgiform headache attacks with cranial Autonomic symptoms
TAC	Trigeminal Autonomic Cephalalgia
VAS	Visual Analogue pain Scale
WHO	World Health Organization

NORWEGIAN SUMMARY

Hodepine er en av de vanligste plager hos mennesket, og er også den hyppigste årsaken til at pasienter oppsøker helsevesenet. På grunn av det store geografiske dekningsområdet for to nevrologiske avdelinger i Nord-Norge, mangler mange hodepinepasienter tilgjengelighet til god spesialisthelsetjeneste. Mangel på hodepinespesialister og tungvinn tilgang til omsorg kan gi grobunn for feildiagnostisering, ikke optimal behandling og vansker med oppfølging av hodepinepasienter.

Vi ønsker å kompensere for disse uheldige forholdene, og laget en randomisert kontrollert ikke-underlegenhetsstudie i et forsøk på å vise om telemedisin og tradisjonelle hodepinekonsultasjoner på kontoret hos nevrolog gir ulike resultater. For å utføre dette, sammenlignet vi telemedisin med tradisjonelle konsultasjoner i pasienttilfredshet, behandling, sikkerhet og egnethet. I tillegg vurderte vi aksepten av telemedisin fra hodepinepasienten, og estimerte kostnadsbesparelser.

Resultatene viste at de fleste hodepinepasienter aksepterer telemedisin, og er fornøyd med konsultasjonsmetoden. Så og si alle endepunktene i studien viste at hodepinekonsultasjoner via telemedisin ikke er underlegen tradisjonelle nevrologiske konsultasjoner. Vi anser derfor telemedisin som et godt alternativ for de fleste pasienter med ikke akutt hodepine. Denne studien vil være et fundament til å fremme videre forskning på ehelsetjenester, og for etablering av telemedisinske konsultasjoner for pasienter med hodepine i klinisk praksis.

ENGLISH SUMMARY

Headaches are one of the most common complaints among humans as well as the most frequent reason for patients seeking health-care. Due to the huge geographical area of coverage for the two Departments of Neurology in Northern Norway, headache patients have variable accessibility and availability to proper specialist care. Few headache specialists and poor access to care may lead to misdiagnosis, suboptimal treatment and inconvenience with follow-up plans for headache patients.

We want to compensate for these unfortunate conditions, and designed a non-inferiority randomized controlled trial in an attempt to demonstrate whether there are differences in outcome of neurologic consultations depending on assessment method; telemedicine versus traditional in-person headache visits. To accomplish this, we investigated endpoints of different aspects, and compared telemedicine to traditional visits in patient satisfaction, treatment efficacy, safety and feasibility. Additionally, we assessed headache patients' acceptability of telemedicine, and evaluated the cost savings.

The results showed that most headache patients accept telemedicine, and are satisfied with the consultation type. Virtually all endpoints in the trial indicated that specialist headache visits via telemedicine is non-inferior to traditional in-patient visits. We thus consider telemedicine as a good alternative for most patients with nonacute headache referred to a secondary neurology department. This trial will serve as a base for further research on ehealth services, and for the establishment of telemedicine consultations for headache patients in clinical practice.

PUBLICATIONS

This thesis is based on the following articles:

I. **Acceptability, Feasibility, and Cost of Telemedicine for Nonacute Headaches: A Randomized Study Comparing Video and Traditional Consultations.**
Müller KI, Alstadhaug KB, Bekkelund SI.
J Med Internet Res. 2016 **18:** e140.

II. **Telemedicine in the management of non-acute headaches:**
A prospective, open-labelled non-inferiority, randomised clinical trial.
Müller KI, Alstadhaug KB, Bekkelund SI.
Cephalalgia. 2016: 0333102416654885.

III. **Headache patients' satisfaction with telemedicine**
A 12-months follow-up randomized non-inferiority trial
Müller KI, Alstadhaug KB, Bekkelund SI.
European Journal of Neurology. *2017 Apr 21. doi: 10.1111/ene.13294. [Epub ahead of print].*

IV. **A randomized trial of telemedicine efficacy and safety for nonacute headaches**
Müller KI, Alstadhaug KB, Bekkelund SI.
Neurology (in press).

1. INTRODUCTION

Data acquired from several epidemiological studies show that within one year, the global prevalence of an active headache was 47%; migraine 10%, tension type headache 38% and chronic daily headache 3% [1]. During a lifetime, headaches will be experienced by more than 9 out of 10 individuals [2]. Tension-type headache and migraine are respectively the second and fourth most prevalent disorders in the world [3]. Together with Medication Overuse Headache (MOH) they are the first, second and third most prevalent neurologic disorders [3, 4]. Since these nonacute headaches are extremely common, they represent the most frequent neurologic reason for patients visiting primary care doctors as well as neurologists [5-8]. Migraineurs are those who most frequently seek primary, secondary and tertiary health-care [6, 8]. During our trial, that lasted 2.5 years, 557 out of 6193 (9%) patients were referred to our neurologic department in Tromsø city due to nonacute headache. A total of 6040 consultations were made, including the 402 (6.7%) that participated in our trial.

In the Global Burden of Disease study, migraine was the seventh leading cause of years lived with disability, while medication overuse headache was the 20tieth [3, 9]. It is reason to believe that the influence of headaches on daily life is high in the population of northern Norway as well [10].

Due to the high prevalence and burden of these headaches, general practitioners and neurologists must have proper knowledge to be able to adequately handle nonacute headache disorders. Unfortunately, physicians often find these conditions challenging to diagnose and treat [11-14]. Cumbersome access to care and lack of availability of neurologists and headache specialists add to the known under-diagnoses, misdiagnoses and suboptimal treatment of headache sufferers, and leads to patients being less satisfied with their health care [15].

The cost of headaches is tremendous, and it illustrates the high burden in monetary units. A study in 27 countries of the European Union (the United Kingdom included), from November 2008 until August 2009, estimated the total annual direct and indirect cost of adult

headache patients to €173000 million [16]. In 2010, another study estimated a total headache cost of €43514 million in the EU countries, the UK, Iceland, Norway and Switzerland [17]. Migraine, which accounts for an annual cost of €111000 million [16], is the third most costly neurologic disorder, only exceeded by dementia and stroke [8].

Northern Norway has a widespread geography with many sparsely populated areas (Figure 2). The poor weather conditions, and many valleys and fjords make travelling burdensome and expensive. During the study, the estimated annual travel cost, based on the cheapest means of public transport from the Norwegian Patient Travel Agency, of patients to our neurologic outpatient department was €381320 (11486 patients*83 median/2,5).

The main motivations for this trial were the high frequency and burden of headaches in the society, the poor access and availability to headache specialist competence, and the expensive and time consuming travel conditions in our region. Although telemedicine has the potential to be interdependent of location, information and communication technologies are too often implemented without proper analysis of the health care that is delivered [18-20]. The intention of this trial is not to wire all of our neurologic headache consultations, but to enable a change to meet headache patients and their needs. We have investigated different perspectives of telemedicine visits for nonacute headaches before planning to adopt it into clinical practice. This thesis aims at answering whether telemedicine is a good alternative for patients with nonacute headaches.

Figure 2 The Department of Neurology at the University Hospital of North Norway is located at 69◦N in the city of Tromsø (red dot). Patients were recruited from almost all of Northern Norway. Inserted in the figure is the archipelago of Svalbard. Norway Statistics 31.12.2014. Printed with permission from © Kari C. Toverud.

2. BACKGROUND

2.1 Headache diagnosis and classification

Headaches can be caused by a wide spectrum of disorders. The diversity of causes ranges from trivial to more complex conditions, from short-lived remitting to unremitting, and from benign to life threatening disorders. Due to the high prevalence of headaches, and the different underlying causes, a classification is required to enable valid diagnosis for research purposes, but is also a valuable tool to differentiate headache disorders in clinical practice.

The International Headache Society (IHS) has developed such a framework in the International Classification of Headache Disorders (ICHD). Since the first paper based edition of ICHD in 1988, the characteristics of these headaches have gradually evolved, and are based on both empirical evidence and expert consensus [21]. Today, the classification system is in use in both clinical practice and research. The ICHD classification is considered indispensable, and every headache patient entered into a research project, be it a study of telemedicine, a drug trial or a study of pathophysiology or biochemistry, must fulfill a set of diagnostic criteria [21]. The latest version of the headache classification is the ICHD-3, which was published in 2013 [21]. Patients in our study were diagnosed according to the second version (ICHD-2) [22].

According to the ICHD, headaches can be divided into two main categories; primary and secondary headaches [21].

2.1.1 Primary headaches

To avoid misdiagnosis, mistreatment and overlooking secondary causes, every primary headache is considered a diagnosis of exclusion [21, 23, 24]. This is reflected in a standard ICHD phrase, i.e. it should be "*Not better accounted for by another ICHD- 3 diagnosis*". When no underlying cause is found, the headache is categorized as primary [21].

There are 60 different primary headache diagnoses when subgroups of migraines and tension-type headaches are taken into account [21]. Only the main groups are mentioned here (Figure 3).

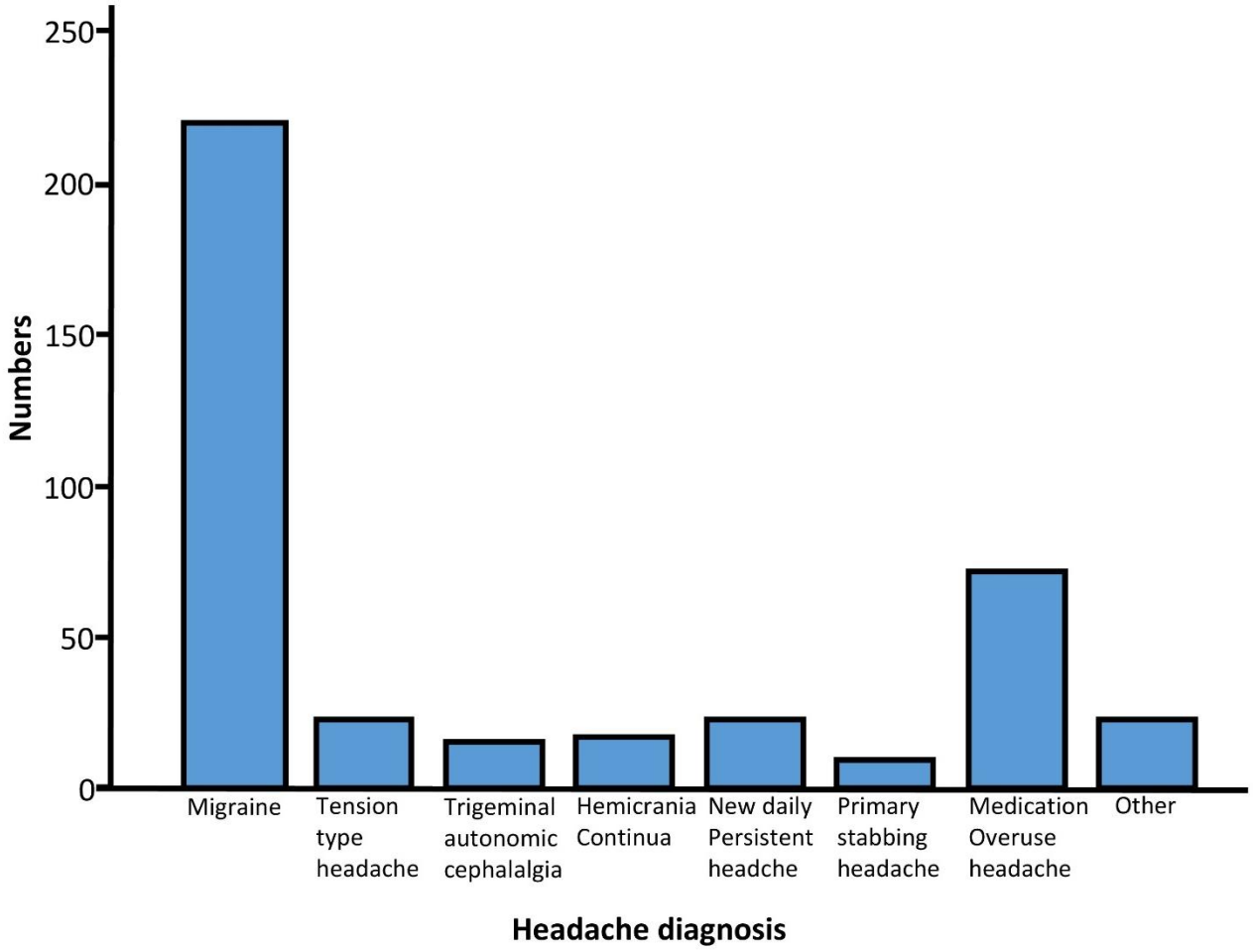


Figure 3 Nonacute headaches referred to our Department of Neurology [25].

Migraine is the most common headache syndrome seen by doctors [6, 8], and it affects 10% of the worldwide population [1]. In adults, the female:male ratio is 3:1 [2, 26, 27], and the 1 year prevalence is approximately 15-18% in women and 6 % in men [2, 26, 28]. There are five subtypes of migraine. Migraine without aura and migraine with aura constitute the vast majority. The ICHD-3 criteria for migraine without aura and chronic migraine are summarized in Table 1.

Aura, which occurs in 15-30% of all migraineurs, is a transient focal neurologic omen strongly associated to migraine [29]. The most frequent aura is a visual disturbance prior to the headache that is experienced by more than nine of ten patients [21, 30]. Next in frequency are sensory phenomena in 30-50 %, and speech disturbances in 20-30% [21, 30, 31]. The

mentioned aura types most often follow in a temporal order, spreading gradually over ≥ 5 minutes and lasting 5-60 minutes [21]. Usually the aura precedes a migraine headache, but not infrequently aura is followed by non-migraineous headache or no headache at all [21].

Table 1 Diagnostic criteria for migraine without aura and chronic migraine.

ICHD-3 diagnostic criteria for 1.1 migraine without aura and 1.3 chronic migraine
A. ≥ five attacks fulfilling B-D
B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
C. Headache has at least two of the following four characteristics:
1. Unilateral location
2. Pulsating quality
3. Moderate or severe pain intensity
4. Aggravation by or causing avoidance of routine physical activity
D. During headache at least one of the following:
1. Nausea and/or vomiting
2. Photophobia and phonophobia
E. Not better accounted for by another ICHD-3 diagnosis.
Chronic migraine is diagnosed when headache occurs ≥ 15 days per month for more than 3 months, where ≥ 8 of days have the features of a migraine headache. Adapted from ICHD-3

Tension type headache is not as disabling as migraine, but has great influence on socioeconomic and health care resources due to its high prevalence [9]. The headache lasts from 30 minutes to 7 days, is mild to moderate, and usually, but not mandatory it is located bilaterally [21]. It is a featureless headache with no more than one of photo- or phonophobia, but mild nausea is accepted in the chronic form [21]. Based on the attack frequency, it is divided into infrequent, frequent and chronic subtypes with or without

pericranial tenderness [21]. The headache of the chronic tension type should have occurred for ≥ 15 days per month for ≥ 3 months [21].

Trigeminal Autonomic Cephalalgias (TACs) constitute a group of primary headaches characterized by unilateral pain accompanied by cranial autonomic symptoms [21]. The following conditions belong to this group: Episodic and chronic cluster headache, episodic and chronic paroxysmal hemicrania, episodic and chronic Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing (SUNCT), episodic and chronic Short-lasting Unilateral Neuralgiform headache attacks with cranial Autonomic symptoms (SUNA) and hemicrania continua [21]. Of these, the latter (hemicrania continua) was added to the TACs in the third edition of ICHD [21, 22]. The other headache syndromes in the group are short-lasting. Both the paroxysmal hemicranias and hemicrania continua are considered as Indomethacin-responsive headaches, i.e. they should respond absolutely to Indomethacin [21, 32].

A less common Indomethacin-responsive syndrome is the primary stabbing headache [32]. The condition is characterized by short stabbing pain (usually up to three seconds) from one to many stabs a day, and without cranial autonomic symptoms [21, 32]. Although considered Indomethacin-responsive, approximately 1/3 of these headaches do not respond to Indomethacin [33].

Another headache syndrome is the new daily persistent headache. This is a continuous headache without remission, and often with characteristics of migraine and/or tension type headache [21]. However, the pathognomonic feature is that the headache has a distinct onset that is clearly remembered by the patient, without good response to preventive headache treatment [21, 34]. It may start out of the blue, but often appear in the wake of an infection or another stressful event [34].
Table 2 and 3 provide typical clinical characteristics and common treatment options for the most common primary headaches in this trial.

Table 2 Typical clinical characteristics of some primary headaches [21, 35]

Headache	Duration	Other features	Intensity	Localisation
Migraine	4 – 72 hours	Aura, nausea, photo-/ phonophobia, Aggravated by physical exercise	Moderate – severe	Unilateral or bilateral
Tension-type headahce	Episodic: 30 min. - 1 week Chronic: ≥ 15 days for ≥ 3 months	No more than one of photo- or phonophobia. Mild nausea is accepted in chronic	Mild – moderate	Bilateral
Cluster headache	15-180 minutes	Cranial autonomic symptoms*****	Severe	Unilateral within each cluster
Chronic paroxysmal hemicrania (CPH)	2-30 minutes	Cranial autonomic symptoms*****	Severe	Unilateral and sidelocked
Hemicrania continua	Chronic	Cranial autonomic symptoms*****	Varying	Unilateral and sidelocked
Primary stabbing headache	≤ 3 seconds (80% of stabs)	None	Varying	Unilateral with sideshift
New daily persistent headache	Chronic	Photo-/ phonophobia or nausea	Varying	Unilateral or bilateral

*****Conjunctival injection/lacrimation, nasal congestion/rhinorrhea, eyelid oedema, forehead and facial sweating, forehead and facial flushing, miosis and ptosis.

Table 3 Documented pharmacological treatments of some primary headaches in the trial listed with reasonable doses [34-40]

Headache	Abortive treatment	Preventive treatment
Migraine	Aspirin (1000 mg)	Propranolol (40- 160 mg daily)
	Paracetamol (1000 mg)	Metoprolol (50-200 mg daily)
	Diclofenac (50 -100 mg)	Flunarizine (5-10 mg daily)
	Ibuprofen (200 -800 mg)	Topiramate (25-200 mg daily)
	Naproxen (500 -1000 mg)	Sodium valproic acid (500-1800 mg daily)
	Metoclopramide* (20 mg)	Botulinumtoxin A for chronic migraine
	Triptans	(PREEMPT protocol)
Tension Type	Aspirin (500-1000 mg)	Amitriptyline (10-75 mg nocte)
headache	Ibuprofen (200 -800 mg)	
Cluster headache	100% oxygen (15 l/ min)	Verapamil (240-960 mg daily)
	Sumatriptan (6 mg s.c. or 20	Steroids (e.g. prednisolon 60 mg daily for 5
	mg nasal)	days, then reduce the dose with 10 mg daily.)
	Zolmitriptan* (10 mg nasal)	
Chronic	-	Indomethacin (up to 225 mg daily)
paroxysmal		
hemicrania		
Hemicrania	-	Indomethacin (up to 225 mg daily)
Continua		
Primary stabbing	-	Indomethacin (up to 150 mg daily)
headache		
New daily	-	According to phenotype
persistent		
headache		

*Metoclopramid = Level B, Zolmitriptan = Level A/B. Except for primary stabbing headache and new daily persistent headache, the remaining medications are categorized as evidence level A.

2.1.2 Secondary headaches

When the underlying cause is identified, or if a presumed causal factor with close temporal relationship to the headache is present, the headache is categorized as secondary [21]. More than 90% of all headaches are considered primary [41], but the share of secondary headaches tends to be higher in the elderly [42]. Most of these, however, are attributed to headache caused by trauma/injury to the head and/or neck, and headache attributed to intake or withdrawal of substances [42]. To achieve correct treatment, it is important to differentiate primary headaches from secondary headaches.

The far most common secondary headache that seeks medical attention is MOH. The prevalence of MOH varies between 0.5%-7% in population studies [43], and the headache condition is found in more than 30% of patients in headache clinics [44]. Overuse of pain relieving drugs (Paracetamol, NSAIDS, opioids, triptans, barbiturates, etc.) may give a paradoxical effect that increases headache frequency and causes chronic headache (MOH) [4, 44]. MOH pathophysiology is not well understood [45], but a preexisting headache is required [44]. In practice, migraine or tension type headache is the underlying primary headache condition. Table 4 presents the ICHD-3 criteria for medication overuse headache [21]. The recommended treatment is patient information and education, abrupt or tapering withdrawal of the headache overused medication(s), and eventually prophylaxis [44-47]. A meta-analysis published in 2016 concluded that there is little evidence regarding effective preventive medications for MOH, and that the withdrawal of the overused medications therefore remains the best documented advice [48]. Additionally, another recent published study reported effective treatment by a brief intervention method administered by general practitioners [46, 47].

Table 4 ICHD-3 diagnostic criteria for 8.2 Medication Overuse Headache

A. Headache occurring on ≥ 15 days per month.
B. Regular overuse for > 3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache (1-7).
C. Not better accounted for by another ICHD-3 diagnosis.

1. Regular intake of ergotamine on ≥ 10 days per month for > 3 months.
2. Regular intake of one or more triptans on ≥ 10 days per month for > 3 months.
3. Regular intake of simple analgesic (Paracetamol and/or NSAIDS) on ≥ 15 days per month for > 3 months.
4. Regular intake of one or more opioids1 on ≥ 10 days per month for > 3 months.
5. Regular intake of one or more combination-analgesic medications on ≥ 10 days/month for > 3 months.
6. Regular intake of any combination of ergotamine, triptans, simple analgesics, NSAIDs and/or opioids on a total of ≥ 10 days per month for > 3 months without overuse of any single drug alone.
7. Regular overuse, on ≥ 10 days per month for > 3 months, of one or more medications other than those described above, taken for acute or symptomatic treatment of headache.

Malignant secondary causes of nonacute headaches are rare [41, 42], and the frequency of secondary intracranial pathologies is less than 2% in most studies [49-57]. During a headache consultation, physicians should aim at identifying red flags. These flags are alarming signs that indicate a secondary headache cause, and warrant further investigation. Worrisome red flags are listed in table 5.

Table 5 Common red flags. Based on Detsky, Sandrini and De Luca [58-60].

RED FLAGS
- Focal neurologic signs (e.g. papilledema, cranial nerve palsy, paresis, hypoesthesia)
- Neurologic symptoms (e.g. altered mental status, syncope, seizures, focal signs)
- Sudden onset of headache (e.g. subarachnoid hemorrhage)
- New onset headache > 50 years (e.g. tumor, giant cell arteritis)
- Atypical headache (Headache not clearly belonging to any category of ICHD-3)
- Headache progression, change in intensity, frequency or feature (e.g. tumor, hemorrhage and vasculitis)
- Systemic symptoms (fever, stiff neck, rash, weight loss, chills, night sweats)
- Risk factors (e.g. cancer, HIV)
- Dynamic in nature (triggered/worsened by cough, other Valsalva maneuvers, exertion and sexual activity)

2.2 Headache consultation methods

The gold standard for a specialist headache visit is an in-person face-to-face consultation between the specialist doctor and the patient. The in-person visits have gradually changed as technology has evolved. When the Personal Computer (PC), the Mac, and the Linux entered the mainstream in the late 80ties, it started a transformation to a more digitalized health-care [61, 62]. In this century, health-care has gradually gone from paper based medical records to electronic patient records in Europe and the US [61, 63-65]. Although, this shift gave doctors better access to the patients' medical records, it also changed the traditional in-person consultations, and doctors often seemed to be more focus oriented on the computer screen than on the patient [61]. Today, giving medical help by ordinary letter mail has also changed, and is often replaced by e-mail, but privacy rules and regulations prevents health care personnel to use unencrypted email.

Another consultation type that has existed for over a century is the telephone consultation. The first telephone consultation was reported in Lancet in 1897, 21 years after Alexander Graham Bell invented the telephone [66]. As the telephone access increased, so did its use in health care. Today it is used to handle a wide variety of chronic and acute conditions, but absence of nonverbal communication is of course a major limitation [67]. In specialist headache care, telephone consultations have been recognized as an extensive part of daily work [68]. However, its feasibility as a headache behavioral modifying and motivational tool has been assessed with diverging results [69-71]. It is recommended that telephone consultations ought to follow a certain pattern, and that they are made by health care personnel who are trained in such delivery [67].

When the Internet evolved during the 90ties, new consultation possibilities accompanied [62]. By the increased broadband access, use of telemedicine consultations through fixed and mobile devices such as PC, laptops, tablets, smartphones and even smartwatches became evident. Regardless of the consultation method, well developed communication and interpersonal skills are fundamental to the care of patients who suffer from headaches [72].

2.2.1 Traditional in-person headache consultations

This consultation form has an in-person relationship between the patient and the neurologist. For decades, the cornerstone of the traditional headache consultation has been a thorough headache interview combined with a neurologic examination. In addition, present and past medical history, family history, social and psychological factors should be known. The interview is considered as the most important part of the traditional headache consultation [41].

To stimulate the patient to talk freely, it is common to start the interview with an open ended question [72, 73]. Two examples of open-ended questions are:
"Do you have a headache? Tell me about it, and how it affects your life."
"Can you describe your headache, and how you cope with it?"
The open-ended questions are then followed by specific, close-ended headache questionings. These questions cover age at headache onset, location, character, intensity, duration, frequency and time of the headache attack. Additionally, the doctor ought to know about associated headache symptoms, premonitory and aura symptoms, postdrome symptoms, as well as relieving and worsening factors [72, 73].
Before continuing to a physical and neurologic examination, warning signs that may indicate the presence of a secondary headache (Table 5) must be identified [41]. Presence of a warning sign mandate further investigation with neuroimaging [41, 58]. Many consider a complete neurologic work-up and examination of every patient presenting with a headache unnecessary, and the interview with examinations could be tailored to every patient [57, 72].

After the examination, the traditional headache consultation continues with prospective additional investigations, headache diagnoses, and non-pharmacological and pharmacological treatment [41, 72]. Figure 4 shows a flow chart of a normal in-person headache consultation.

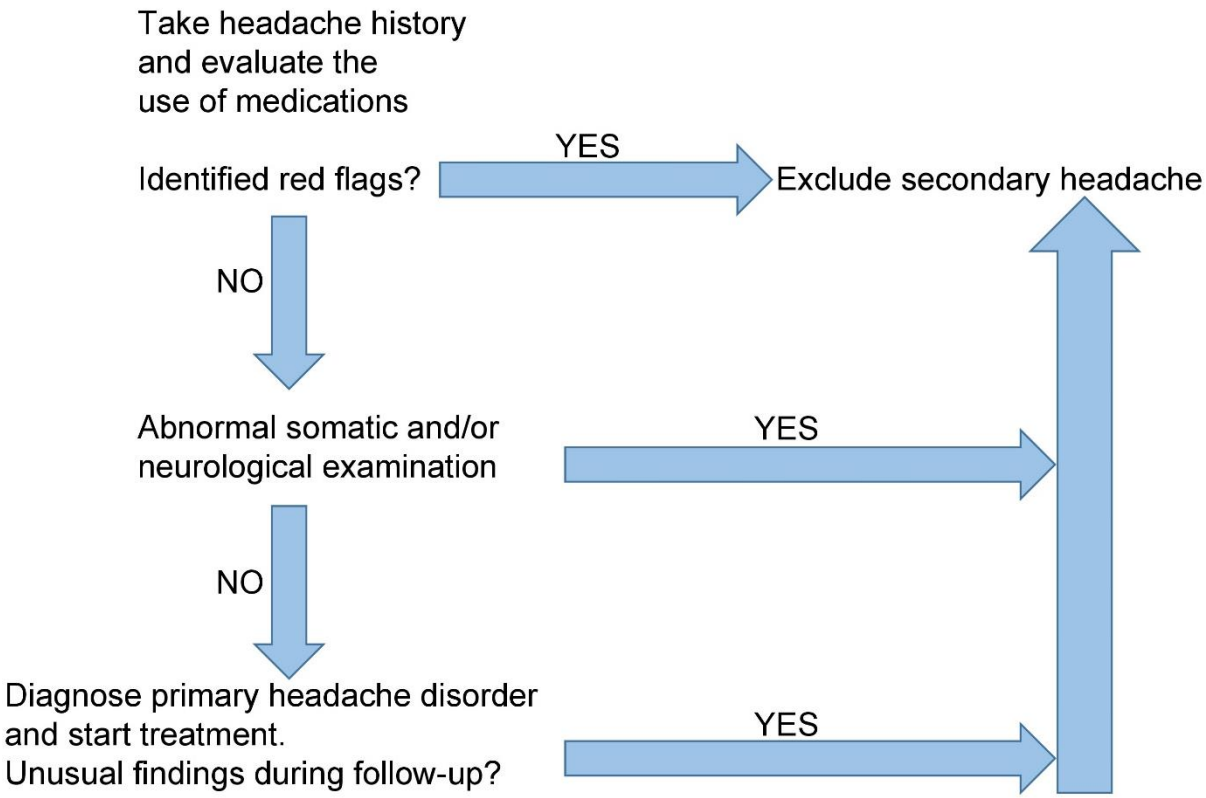


Figure 4 An algorithm for a traditional in-person headache consultation [72].

2.2.2 Telemedicine headache consultations

To consider telemedicine we need to know what it is, and what it is not. Although, telemedicine is not a new concept, the evolving technology has made it better and more available over time. The first definition of telemedicine was made by Bird in 1971 [74]. He defined telemedicine as "*the practice of medicine without the usual physician-patient confrontation via an interactive audio-video communication system.*" In a review of the literature from 1970-2006, the authors found 104 definitions of telemedicine [75]. These reflected different perspectives; the medical, the technological, the spatial and the benefit perspective [75]. In my own experience, telemedicine is basically like a traditional consultation, but without the patient being physically present. Use of information and communication technologies in research is comprehensive, and a PubMed research revealed 23536 hits for "telemedicine" pr. April 26, 2017.

In this trial, we defined telemedicine as consultations that had a two-way video- and audio communication between the neurologist and the patient. Such headache consultations have an indirect online relationship rather than a direct in-person relationship.

Having online patient-doctor relationships have both advantages and disadvantages. The indirect contact between the doctor and the patient creates both a physical and a psychological distance (the virtual space) [76], which neurologists can use to the benefit of their patients. The physical distance provides a feeling of safety, a more objective observation, a more direct, straight forward conversation and feedback from the patient [76]. The psychological distance is considered as the most important part of the virtual space. The less doctor authority in telemedicine gives the patient more control, and in case of any inconvenience the patient can simply "hang up" to end the consultation [76]. Additional benefits of telemedicine, such as less travel, less expenses, easier access to headache specialist, less geographical disparity and high family and patient satisfaction make telemedicine more patient centered as compared to in-person traditional consultations [77]. One major downside of telemedicine is the difficulties in performing a full neurologic examination. A study of 17 patients with neurologic disorders showed that a tailored neurologic examination via telemedicine is possible when more than one observer is present, but this finding needs further investigation by including more patients and performing full neurologic examinations [78].

2.3 Basic theory of economic evaluation

Health economics play an important part in documenting value for money, in decision making processes, as a starting point for health business models, and in payment for health services when new technology is implemented into clinical practice [8, 79]. To understand the role of economics in the management of different health conditions, neurologists need to have basic knowledge about economic evaluation [8]. To make health economic research more homogenous and easier to follow, it should follow a certain pattern, and be based on reporting statements, such as the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement [80].

Economic health evaluations analyze the costs and health benefits/efficiency of a new technology or treatment compared with one or more older treatments [81]. Its basic components are costs and health related outcomes. Costs can further be divided into different categories:

- Direct costs, such as medication and hospital costs, are related to management of a disease or disorder. Indirect costs are related to the reduced work capacity due to morbidity and/or mortality.
- Tangible costs are those that straightforward can be expressed in monetary units, while intangible costs are those, which are difficult to quantify in monetary values (for example costs related to quality of life) [8, 82].

Additionally, it is common to divide costs into medical and nonmedical categories. Likewise, there are many types of cost evaluations. The most common types that are used in health economics are cost minimization analysis, cost-effectiveness analysis, and cost-benefit analysis [82].

Cost minimization analysis evaluates only the costs of two or more interventions. This kind of analysis is used when the studied interventions are otherwise considered equally efficient [8, 79, 82].

Cost-effectiveness analysis compares clinical outcomes and costs of different interventions. Its goal is to identify equal or more benefits of an intervention at lower costs for a certain given disorder (e.g. migraine) [79]. The costs are divided by the effect, which is measured in one dimensional units (e.g. headache days) [79]. This is done by calculating an Incremental Cost Effectiveness Ratio (ICER) [81, 83]. ICER is the cost/effect of one intervention divided by the cost/effect of another (ΔCost/ΔEffect) [81, 83]. It is common to show a graphical illustration of the difference in cost effectiveness between an intervention and the control (Figure 5) [81, 83]. In figure 5, the existing control intervention is preferred in quadrant 4, and the new intervention dominates in quadrant 2. Since the new intervention is less costly and less effective in quadrant 3, and both more costly and effective in quadrant 1, an ICER needs to be calculated. The accepted ICER threshold depends on the intervention and health outcome that is studied.

Cost-utility analysis is a kind of cost-effectiveness analysis that applies natural units to benefits. This enables comparisons between treatments of different diseases [8, 79, 82].

Quality Adjusted Life Year is the most commonly used parameter. It ranges from 0 (worst state) to 1 (best state) per year after the intervention/treatment [79, 82].

In cost-benefit analysis, benefits are transposed into monetary units, and aims to find positive net benefits (benefit minus cost) [79].

The methods of economic evaluations are being debated, and there is often uncertainties regarding the data [84]. Sensitivity analysis could be performed to cope with some uncertainties in the variables and the conclusions that are made, but maintaining transparency is also important [79, 84].

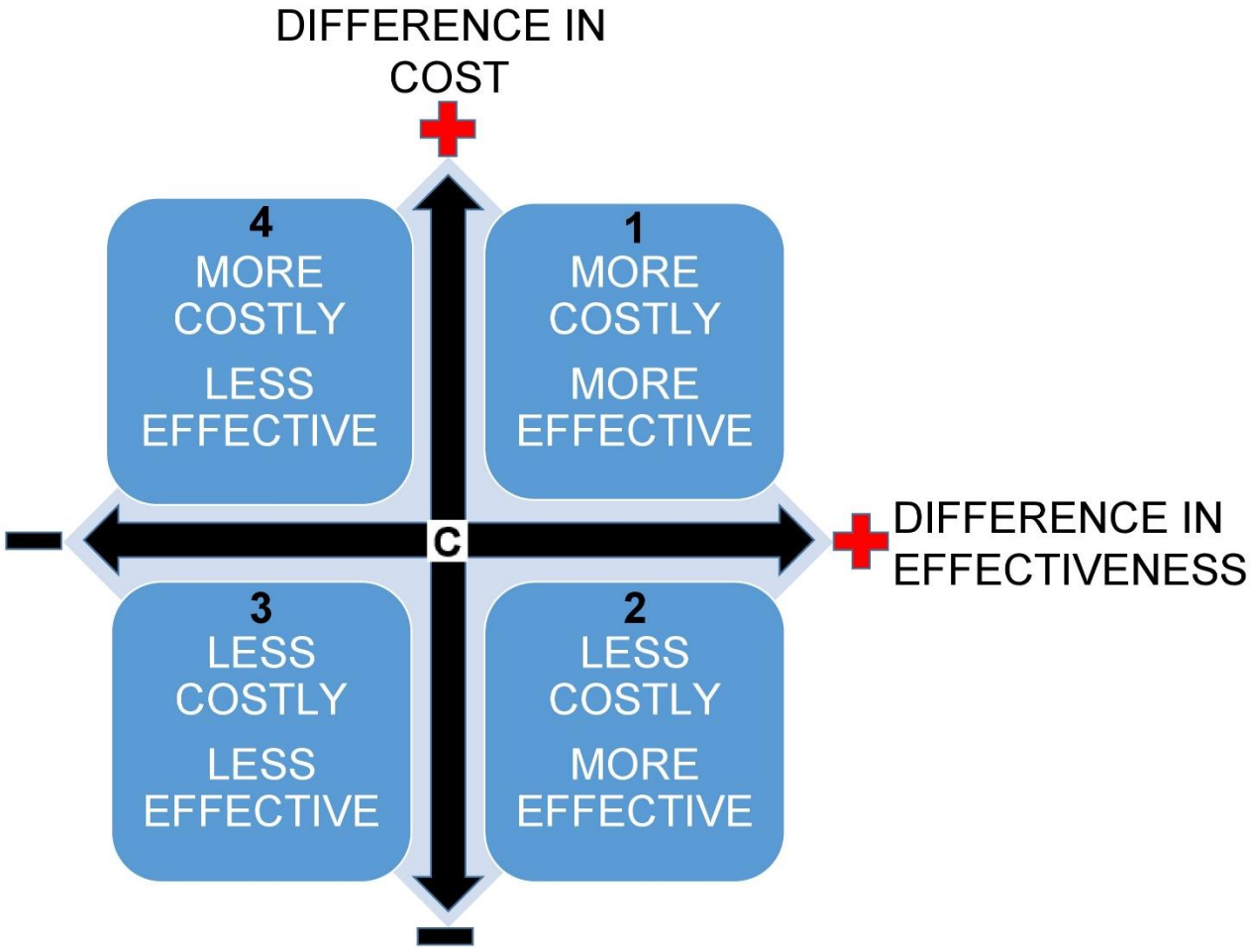


Figure 5 The cost-effectiveness plane based on Petrou and Gray [81]. C is the comparator intervention or treatment.

2.4 Basic actor-network theory

Since implementation of telemedicine for headache patients can be viewed as an informational infrastructure that is in use in our department, I would argue that actor-network theory makes a good fit to analyze different aspects of the information and communication infrastructure. In the general discussion of this thesis (7.6 Telemedicine dynamics and 7.7 Future perspectives), actor-network theory will be used to analyze the present situation and possible future implementation of telemedicine for headache patients in clinical practice. Actor-network theory may help us analyze the borders between the technological and social aspects [85]. It can help to analyze and describe how previous and current status of both the interactions in the networks between paper based patient records, electronic patient records, telemedicine technology and the travelling patients and neurologists work and adopt to each other; to get a better understanding of what kind of negotiation is going on in the "eco-system". Furthermore, it can help to analyze how implementation of a shared electronic patient record and telemedicine consultation would influence the environment of a neurologic outpatient practice.

Actor-network theory, which is born out of science and technology studies, is regarded as both a theory and a methodology used to analyze and describe informational infrastructures, i.e. the connections (network) between technological and non-technological elements and the dynamics in how these elements work together [86]. All networks contain both humans and technology. Actor-network theory provides a vocabulary we can use to describe informational infrastructures: the borders and boundaries between the social and technology, its interactions and the negotiation that is going on in these networks.

Some key concepts in actor-network theory are: actor or actants, inscription and translation, program and anti-program, irreversibility, black-boxing or black-box, delegates, enrollment, momentum and alignment [86, 87]. Actors can be both humans and non-humans. Non-humans are referred to as technological artefacts or equipment. Sometimes non-humans are named actors, but a more proper term could be actants [86, 87]. Actants could also be used to differentiate non-humans from humans. Inscription and translation are considered as key concepts in actor-network theory [86]. Inscription refers to how a technical artefact makes an action; i.e. how it generates a pattern of use. The stronger the inscription, the more likely

a user will follow a given pattern of use and vice versa. Translation may be viewed as the process of how an inscription is made, how we intend to align a technical artefact. To follow a program means to use a system or equipment in an anticipated way. If something is used in an unanticipated way, we follow an anti-program.

Four important aspects of inscription and translation in actor-network theory are, "*Standardization, id. of all anticipations (scenarios) held by the various actors, materials of the inscriptions; how anticipations are translated and inscribed into standards, who inscribes them and strength and weaknesses of the inscriptions; what it takes to work around them or oppose them*" [86].

In a description of the biologists' network in the scallop industry of St Brieuc Bay, translation was divided into four parts: problematization, interessement, enrollment and mobilization [88]. Problematization defines the problem, identifies the actors and the program made to solve the problem. By interessement the actors tries to engage other actors, giving them different roles and tasks in the network. In the enrollment phase, roles are defined and given to actors. In mobilization, primary actors use different methods to represent other actors in the network. The author concludes: "*Translation is a process before it is a result*", and the result is that some actors end up controlling others and translation may fail. The paper demonstrates that actor-network theory is a well suited method to identify and analyze power relationships [88].

Enrollment Components in an Actor-network theory are in alignment when they cooperate to achieve a common goal, and a network that is aligned is also stable. Alignment happens through enrollment. Delegates mean actors or actants with special viewpoints inscribed [87]. Irreversibility shows how difficult it is to change an actor network element and how prone it is to changes from other translations [86]. In other words, it gives a scale for the elements, and shows a level where it is not possible to choose a different path or direction [87]. The black-box refers to all the invisible elements of an actor network that works properly [87, 89]. When a system works properly, we only see the inputs and outputs of the "black-box", and not how the input and outputs actually are created (we do not see the often complex system within) [87, 89]. The complex system within only appears for users upon a system

failure or breakdown, i.e. when there is inadequate input and/or output [90]. The momentum shows how problematic it is to stop a process. When a process/program gains momentum it may become almost impossible to stop it, and only a catastrophic or historical event may stop it [86]. Internet is a common example of a software that has gained momentum [62].

The actor-network theory does not distinguish between humans and non-humans, neither does it distinguish between microphenomena and macrophenomena [85, 86]. I would therefore argue that it is not a well-adapted method to analyze ethical issues [85, 86]. Although the actor-network theory does not differentiate between humans and non-humans, it recognizes each individual as different, as well as each technology as different [85].

Because of the tight relationships and negotiations between the actors and actants in actor-network theory, introduction of a new actor or actant often leads to realignment or influence on the other actors/actants [91]. The same applies if an actor or actant is replaced or disappears from the network [91].

3. AIMS OF THE STUDY

My aim in this thesis is to determine whether telemedicine in the treatment of nonacute headache patients is a good alternative to traditional in-patient consultations. In order to achieve this, different perspectives of telemedicine consultations were investigated:

- Whether telemedicine is accepted among patients with headaches (Paper I).
- Whether telemedicine consultations for headaches are cost-saving (Paper I).
- Whether the management of headache patients via telemedicine is technically feasible (Paper I).
- Whether headache patients are satisfied with a telemedicine consultation (Paper II and III).
- Whether the treatment of headache patients via telemedicine is efficacious (Paper II and IV).
- Whether the management of nonacute headache patients via telemedicine is safe (Paper IV).
- Whether the management of nonacute headache patients via telemedicine is cost-effective (Thesis).
- Whether the management of headache patients via telemedicine is feasible (Thesis).

4. PATIENTS AND METHODS

4.1 Trial design

To evaluate different aspects of telemedicine consultations for nonacute headaches, we conducted a prospective, single center, unblinded, randomized and controlled non-inferiority trial. Telemedicine consultations were compared to traditional in-person specialist consultations.

4.2 Eligibility criteria

The participants were Norwegian-speaking patients, aged 16-65 years, who were referred to our neurologic outpatient department for diagnosis and/or treatment of a nonacute headache. In Norway the age of consent is 16. Nonacute headache was defined as a headache that had occurred at least four weeks before referral, and without clinical or radiological signs of structural intracranial pathology causing the headache as reported by the referring general practitioner [92]. This definition, together with recruiting from a working population not older than 65, was considered as sufficient to exclude the presence of secondary headaches (except MOH). To prevent recruiting already consulted and diagnosed patients, those who were evaluated for headache by a neurologist two years prior to the referral letter were not included. To avoid outdated information, the waiting time was set to no more than four months from the date of the referral letter. When in doubt for inclusion, the patient was discussed in a meeting between two neurologists (KIM and SIB).

4.3 Study population and patient administration

From September 30 2012 to March 30 2015 we included, randomized and consulted 402 out of 557 nonacute headache patients referred to our neurologic outpatient department (Figure 6). The participants were patients from the three northernmost counties in Norway; Finnmark, Troms and upper Nordland, as well as from Svalbard. The area of inclusion corresponds to the area of coverage for the Department of Neurology at the University Hospital of North Norway in Tromsø city, and is shown in figure 2. Apart from one neurologist in Harstad city, the department in Tromsø is the only neurologic service in Finnmark, Troms and upper Nordland County, and the travel distances to other neurologic departments are extensive.

During the inclusion period, a neurologist (KIM) daily screened referral letters to the Department of Neurology in Tromsø University Hospital for eligible candidates. The referral letters were located in the Distributed Information and Patient System for hospitals (DIPS ASA, Bodø, Norway) [65, 93, 94]. If a patient met the inclusion criteria, a study coordinator sent an information letter to the patient. Then, she called the patient to check whether the patient met the inclusion criteria, and whether the patient accepted telemedicine and wanted to participate. If the patient agreed to participate (orally), the study coordinator sent an invitation letter, a consent form, and a questionnaire (Appendix III). These patients got included in the project. If the patient did not give consent, the referral letter was returned to the neurologist (KIM) who evaluated the application for an ordinary in-patient visit at the department.

All participants met at the neurologic outpatient department in Tromsø city, and were taken care of by a study nurse at the neurologic treatment unit. The nurse checked the participants' pre-filled questionnaire (Appendix III), measured height, weight and blood pressure, and randomized the participant by calling the external randomization office at the research department at the hospital in Tromsø. Every phone call was made between 9:00 am and 15:00 pm. After randomization, a nurse followed each participant to the appropriate consultation room. Patients were either followed to a video-conference room located just outside the Department of Neurology, or to an examination office located in the department. The pre-filled questionnaire consisted of questions about social and family history, medications, alcohol, smoking, physical exercise and headache influence on daily life.

The neurologists (KIM and SIB) consulted patients from the telemedicine- and traditional in-patient group from the same examination offices at the Department of Neurology. All consultation fees were waived for patients who participated in the study.
To ensure no physical contact between the neurologists and the patients in the telemedicine group, these patients were kept out of sight of the neurologist. The consultations took place on weekdays from 9 am to 3 pm.

All patients had a one-time consultation, which in both groups consisted of a structured interview without neurologic examination (IV). The telemedicine consultations were performed in the same manner as the traditional in-patient consultations. They all started with open-ended questions before the structured questions.

The structured questions (Appendix IV) consisted of

- Age at onset and headache duration,
- Location and character of the headache(s),
- Duration, frequency and timing of the headache attacks,
- Pain intensity and headache influence on daily life,
- Precipitating and aggravating factors,
- Premonitory and aura symptoms,
- Associated headache features.

Secondary headaches were rechecked and differentiated from primary headaches by rechecking red flags (Table 5) and neuroimaging. The consultations ended with diagnosing the specific headache disorders according to ICHD-2, ordering investigations, starting treatment (education, advice, medication) and scheduling follow-up.
At three and 12 months, the study coordinator sent a questionnaire to every participant. The questionnaires were sent out by patient preference, either in an ordinary letter mail, or through an internet survey system (Questback [95]). The coordinator sent a reminder to participants who did not answer within two weeks. A flow chart is provided in figure 6.

4.4 Randomization

Randomization was performed by the randomization office in the research department at Tromsø University Hospital, which was an external party not otherwise involved in the study. The concealed block randomization was computer generated by the use of an Rnd function in Microsoft access (Redmond, WA) [96]. The block sizes ranged between four, six and eight. Stratification was made on each neurologist.

4.5 Interventions and infrastructure

The telemedicine consultation was a two-way encrypted video- and audio communication between the neurologist in the examination room at the Department of Neurology and the participant in the videoconference room located just outside the department.

The information and communication equipment consisted of the following technology: Cisco (Moorestown, NJ) C40 Integrator Package, Cisco C40 Integrator Multisite, Cisco Precision HD 1080p 12xcamera, an NEC X551s 55-inch light-emitting diode (LED) monitor, Audio-Technica ceiling microphones and JBL LSR2325P active speakers, Integrator Package C40 Dual Display option and a Cisco Touch-Control Device for C Series. This equipment is installed in one office (Figure 7). The neurologist consulted the patients from two other examination rooms via a Cisco EX60 unit with an InTouch panel (Figure 1 and 8).

4.6 Data collection and questionnaires (Papers I – IV)

Data was collected from the referral letters (Appendix II), from telephone interviews prior to the inclusion (Appendix I), from a questionnaire prior to the consultation (Appendix III), from the consultation (Appendix IV), from follow-up questionnaires at three and 12 months (Appendix V and VI, respectively), and from the electronic patient hospital records in Northern Norway. Additionally, a hospital economist collected data on travel expenses from the Norwegian patient travel agency (Pasientreiser) (Appendix VII) [97]. Estimated patients' salary was based on data from Statistics Norway (Paper I).

In all papers, baseline characteristics were collected from the referral letter, from the telephone interview, from the questionnaire prior to the consultation, from the consultation and from the electronic patient records in Northern Norway [93].

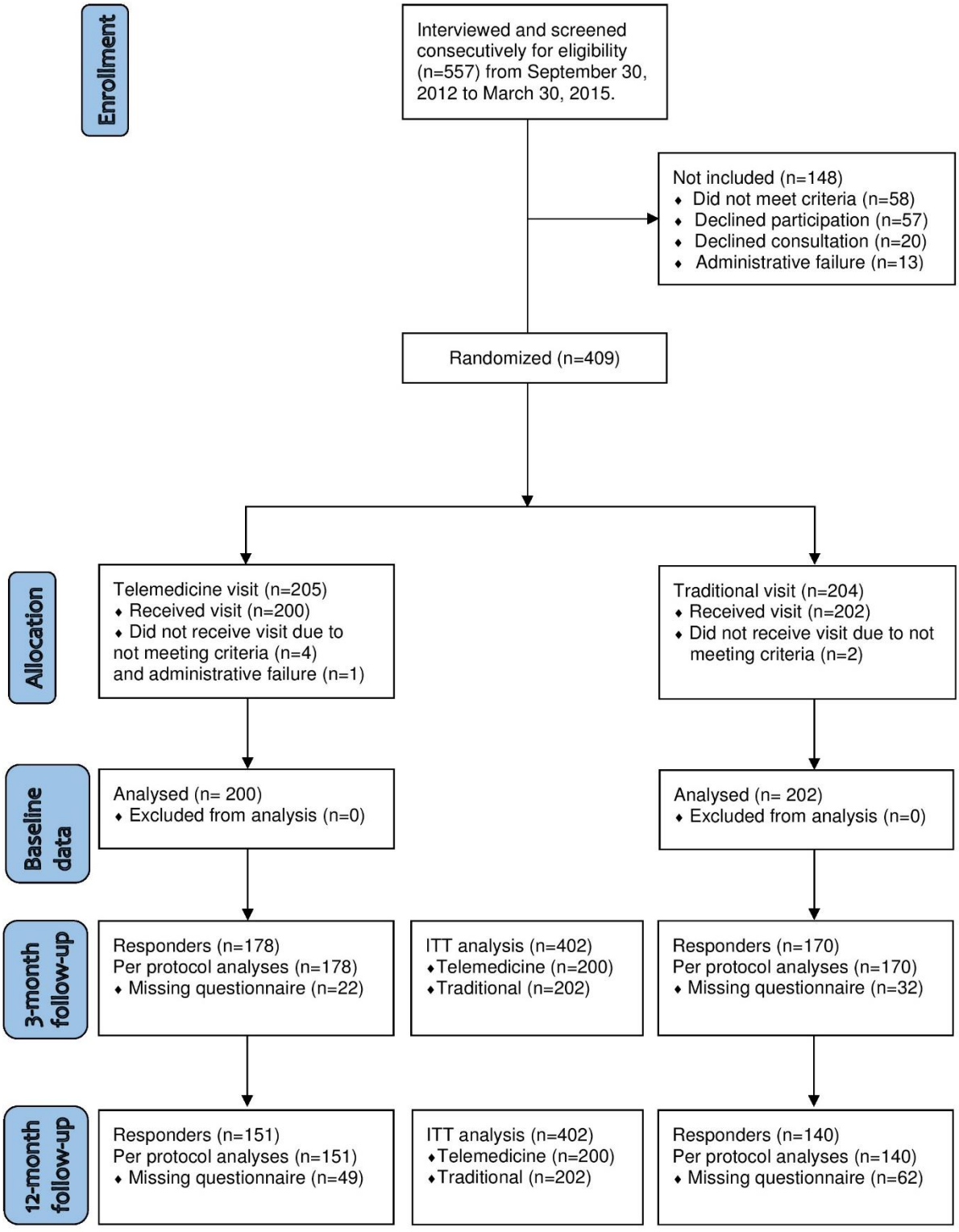


Figure 6 Patient recruitment and flow through the trial.

Figure 7 Telemedicine Infrastructural Setup at the Department of Neurology in Tromsø University Hospital from the patient's perspective.

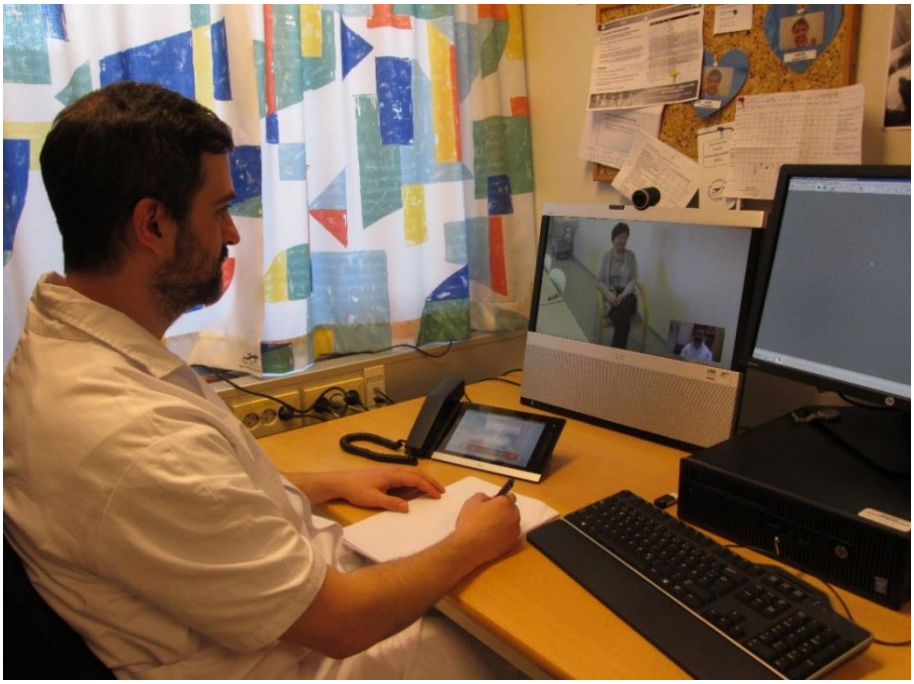


Figure 8 Telemedicine Infrastructural Setup at the Department of Neurology in Tromsø University Hospital from the neurologist's perspective.

4.7 Measurements

4.7.1 Headache diagnosis and measurements

Diagnosis of headache was made by a structural clinical interview at the consultation (Appendix IV). Patients were diagnosed according to the International Classification of Headache Disorders-2 (ICHD-2) [22]. In case of more than one headache disorder in a patient, data for this study were primarily evaluated for the most prominent headache. The most prominent headache was defined as the headache that had the most significant influence on the patients' daily life.

The Headache Impact Test-6 (HIT-6) questionnaire was developed from 54 preexisting headache impact test questions and 35 questions from clinicians in 2003 [98]. It is a headache specific patient outcome measure designed for use in both clinical practice and research to quantify the severity of headache influence on patients' daily life [98]. The questionnaire is made of 6 items regarding the intensity of the headache, its influence on work and social activities, and the association with fatigue, irritation and concentration. Each question has five answers ("*Never*", "*Rarely*", "*Sometimes*", "*Very Often*" and "*Always*"), and each answer scores 6, 8, 10, 11 or 13, respectively. A score of 50 or higher is considered high, and suggests contact with a physician.

In this trial, Baseline HIT-6 measures were used in all papers. In paper II, we used HIT-6 three months after the consultation and calculated change from baseline. In paper III, we constructed a variable that showed the between-group minimally important difference in HIT-6 (2.3 points) change 12 months after the baseline consultation [99]. In paper IV, we used mixed between-within participants ANalysis of Variance (ANOVA) to assess change in HIT-6 across three time periods (at baseline, three and 12 months). Additionally, in paper IV we constructed a variable that showed change in HIT-6 from baseline to 12 months, and calculated HIT-6 from the 12-month questionnaire.

To measure headache intensity, we used a Visual Analogue pain Scale (VAS) together with its numerical counterpart at baseline. Only the numerical scale was used in the questionnaires at three and 12 months. The scale range is from 0 (no headache) to 10 (worst possible headache).

We used VAS at baseline in all papers. In paper II, we used VAS as a headache intensity measure three months after the consultation and calculated change from baseline. In paper III, we constructed a variable that showed the minimally important difference in VAS (we chose 1.3 points based on previous literature) change 12 months after the baseline consultation [100-102]. In paper IV, we used mixed between-within participants analysis of variance to assess change in VAS across baseline, three and 12 months. Additionally, in paper IV we constructed a variable that showed change in VAS from baseline to 12 months, and collected VAS from the 12-month questionnaire.

We divided headache frequency into three groups: < 7 days, 7-14, and ≥ 15 days per month within the last 3 months [22] before the baseline consultation. Headaches occurring < 7 days per month were defined as low frequency episodic headaches, 7-14 days per month as high frequency episodic headaches, and chronic headaches as having ≥ 15 headache days per month in the three months before the baseline consultation and questionnaires. Headaches occurring 7-14 days per month have previously been shown to have increased risk of medication overuse headache [103]. These three categories were used in paper I, II and IV. In paper III, headache frequency was divided into < 15 days and ≥ 15 days.

Additionally, at baseline patients were asked if the headache had changed while waiting for the specialist consultation, and at three and 12 months they were asked if the headache had changed in the wake of the consultation: "*Is the headache better, unchanged, or worse?*", "*Is the headache frequency reduced, unchanged, or increased?*", and "*Is the headache intensity reduced, unchanged, or increased?*". From the questionnaires at three and 12 month, we constructed a categorical variable to show if patients were subjectively better, unchanged or worse from their headache.

4.7.2 Satisfaction measurements

Acceptability of telemedicine was evaluated by a telephone interview of eligible candidates made by a study coordinator (Appendix I). The candidates were asked if they accepted telemedicine visits or not. Answers were coded as a categorical binary variable denoting feasibility of telemedicine ("*Yes*" or "*No*") as reported in paper I.

At each telemedicine consultation, the neurologist asked participants if they were satisfied with the video- and audio quality. These answers were categorized into two binary variables ("*Yes*" or "*No*") as reported in paper I.

All participants received a questionnaire at three months. They were asked if they were satisfied with the consultation three months earlier ("*Yes*" or "*No, why not*?"). All participants received another questionnaire at 12 months. Participants were asked if they were satisfied with the consultation 12 months earlier ("*Yes*" or "*No*"). Additionally, participants were asked if they were satisfied with the communication, information, diagnosis, advice and medication at the specialist consultation 12 months earlier ("*Yes*" or "*No*"), and what kind of consultation form they preferred in light of the consultation 12 months earlier ("*traditional*", "*telemedicine*" or no "*preference*".

Satisfaction with consultation was evaluated as a categorical binary outcome measure at 3 months (Paper II) and at 12 months (Paper III). To ensure a more dynamic long-term evaluation of satisfaction, we additionally constructed a variable of patients who were satisfied at both three and 12 months (Paper III). Participants satisfied with communication, information, diagnosis, advice and medication were evaluated as categorical binary outcome variables ("*Yes*" or "*No*") at 12 months (Paper III).
All satisfaction variables are listed in table 6.

4.7.3 Cost and travel measurements

In paper I, data from the Norwegian Patient Travel Agency regarding patient travel expenses, and the agencies probabilistic method of calculating the least expensive means of travel, were obtained and used for travel cost evaluations [97] (Appendix VII). A hospital economist provided these data (Appendix VII). Patients' incomes were calculated from the Norwegian full-time employee's average salary (€4.681 per month in 2014) [104]. We defined economical loss for patients from urban areas (in Tromsø), having travelled plus being consulted < 3.5 hours, as half a day's salary. The loss for patients from rural areas (outside Tromsø), spending > 3.5 hours on travel and consultation, was defined as one day's salary. All costs were adjusted to the consumer price index (CPI) per January 1, 2015 from Statistics Norway, and Norwegian kroner were converted into euros by using the exchange from the

Norwegian Bank on December 31, 2014. Traveling distance in kilometers, and traveling time in hours, were estimated by Google Maps and controlled with maps available from the Norwegian yellow pages [105]. When these programs failed to calculate a distance, we measured it manually on Google Maps. Cost and travel variables are summarized in table 6.

4.7.4 Feasibility measurements

These variables were constructed from a telephone interview (acceptability), and from data registered during the consultation (Paper I). Additional feasibility variables that concern quality and safety were retrieved at three and 12 months. Feasibility variables are listed in table 6.

4.7.5 Safety aspects and measurements

As reported in paper IV, the electronic patient records from all hospitals in Northern Norway were thoroughly reviewed for safety outcomes, from the first document to one year after the specialist headache consultation, and these were compared to information given by the participants in both the three and 12-month questionnaire (for the presence of secondary headaches, neuroimaging, lumbar puncture results and other test results). The variables we constructed are presented in table 6.

Table 6 Variables from the interview, the pre-consultation, consultation, 3 and 12-month questionnaires and patient medical records to assess telemedicine feasibility for nonacute headaches*.

Cost/Travel	Satisfaction	Clinical characteristics	Technical
Waiting time Travel cost Lost pay Travel distance (km) Travel distance (hours)	Acceptability Satisfied with video and audio quality Satisfaction at 3 and 12 month At 12 month satisfied with: -communication -information -diagnosis -advice -medication Preferred consultation type	Change in diagnosis Additional diagnosis Additional MRI/CT Nonpharmacological advice Prescriptions New GP appointment New neurologist appointment Number of GP visits at 3 and 12 months. Number of neurologist visits at 12 months. Presence of secondary headache at 12 months. Major MRI/CT abnormalities at 12 months. CSF pathology at 12 months.	Dropout, medical reasons Dropout, technical failure Technical issues Preparation to visit (min) Visit time (min)

*Apart from Cost/Travel values, which were presented as median (range), the other values were presented as n (%) for categorical or mean (SD) for continuous variables.

4.8 Statistical analysis

A pre-study power analysis was performed to calculate a 15% non-inferiority margin (Δ) of binary satisfaction variables. This limit was chosen based on literature [106].
To calculate sample size we used 1% significance level (alpha) and 95% power (1-beta). According to a questionnaire-based study, approximately 50% of participants in northern Norway were satisfied with their headache specialist consultation [107]. Based on this, and if there is no difference between the in-person consultations and telemedicine, we would need 351 headache patients in each group to achieve enough participants to exclude a difference of more than 15%. Because the share of satisfied patients in previous telemedicine studies are reported above 90% [108], we made an interim analysis for the first 40 participants regardless of group setting. The share of satisfied participants was 92.5%. Based on this, we expected satisfaction as being 90% in each group. If there is truly no difference between the standard in-person traditional consultations and telemedicine, then "*127 headache patients are required to be 95% sure that the upper limit of a two-sided confidence interval (or equivalently a 99% one-sided confidence interval) will be sufficient to exclude a difference in favor of the traditional group of more than 15%"* [109]. By anticipating dropout, and to ensure enough participants throughout the study, we enrolled 402 headache patients.

Data was analyzed with version 21 of the Statistical Package for Social Science (SPSS) in paper I and II, and version 23 was used for paper III and IV.

We checked continuous variables for normal distribution with the Shapiro-Wilk test, skewness, kurtosis as well as visual inspection of histograms, Q-Q plots, and box plots. The independent samples T test and Mann–Whitney U test conclusions agreed for all continuous variables in all papers. For a normal distribution, we defined the Shapiro-Wilk test P value above 0.05, skewness and kurtosis as being somewhere between -1.96 to 1.96, and histograms, Q-Q plots and box-plots should visually indicate a normal distribution. Continuous variables with normal distribution were primary compared with independent samples T test.

In paper I, normally distributed variables were given in mean with standard deviation (SD), and non-normally distributed as median with range. For consistency reasons, all continuous variables were given in mean (SD) in paper II, III and IV. Additionally, in large samples the statistics that we used are considered tolerant for violation of the normality assumption. Categorical variables were compared with Chi square test, and are presented as numbers and percentages in all papers. Yates continuity correction was used for 2 ×2 tables. All tests were two-sided. Statistical significance was defined as $p < 0.05$.

Variables in the papers are labelled prespecified or non-prespecified. At three and 12 months, we performed both per-protocol and intention-to-treat analyses. Last observations carried forward (LOCF) for continuous variables and chi-square cross-tabulation with missing values for categorical variables were used for performing the intention-to-treat analyses.

The seven patients who were excluded after randomization did not take part in the intention-to-treat analyses. These patients were included in the other excluded patients, and accounted for by comparing participants with those who were not found eligible for the study.

In paper I, we made two hierarchical multiple regression models to assess the ability to predict VAS and waiting time for rural patients when adjusted for age, sex and other variables. All variables in the models were first tested in univariate analysis. Apart from sex and age, only variables associated with changes in pain scores in the first model, or could be associated with changes in waiting time in the second model, were used. The nonparametric variable waiting time was log transformed. To check for outliers, variables were controlled with normal probability plots (P-P) of the regression standardized residuals, histograms, and scatterplots for normality, linearity, and residual independence. Multicollinearity was checked by tolerance and variance inflation factor (VIF) in both models

In Paper I, study participants' age and sex were compared to patients who were not eligible for the study. In paper III, we compared demographics and clinical characteristics of participants who answered the three and 12-month questionnaire with participants who did

not answer. Baseline and clinical characteristics of participants were also compared with the same data from non-respondents in paper III.

4.9 Ethics

The patients' privacy, physical and mental integrity have been safeguarded in accordance to the ethical principles in the Helsinki Declaration [110] and to the principles outlined in the Norwegian Code of Ethics for Doctors [111].

All of the participants' informed consents were obtained before data collection began. Participants could withdraw from the study at any time, and without any specific reason given. Withdrawal would not affect the patients' further treatment or follow up. The Norwegian National Committee for Medical and Health Research Ethics (REC), number 2009/1430/REK approved the study.

The trial was first registered, and its progress was yearly reported, at the Norwegian Research and Management database (FAS, ID3897/HST959-10 and HST1216-14) [112, 113].

As explained earlier, the trial overlaps with a project in a small rural hospital in Northern Norway from 2009. Due to reorganizations, lack of time to research, and difficulties in patient recruitment in the smaller hospital, the study was stopped and reorganized. At that time, the researchers considered telemedicine consultations as research on health services, and did not regard it as being a study that required registration according to International Committee of Medical Journal Editor's (ICMJE) definition in 2008 [114]. Therefore, it was registered retrospectively at ClinicalTrials.gov (ID. NCT02270177).

5. SUMMARY OF RESULTS

5.1 Paper I

In this study we demonstrated the acceptance, cost-savings and technical feasibility of telemedicine for consulting nonacute headache patients. Out of 479 eligible patients, we found that 402 (83.9%) accepted telemedicine consultations (Figure 6). By using the Norwegian patient travel agencies probabilistic method of finding the least expensive public travel, and Norway Statistics average salary, we estimated that consultations were most expensive for patients living in rural areas (median travel cost €249 (range 409) and loss of a day's salary (€234).

To evaluate the technical feasibility, the 402 patients that accepted telemedicine took part in an intervention study, and were randomized to receive either a telemedicine or a traditional in-person visit. All telemedicine patients were satisfied with the video quality and 198/200 (99%) were satisfied with the sound. There were some minor technical errors (21/200, 10.5%), which did not influence the consultations significantly. However, one drop out was caused by a technical error. The telemedicine consultations were 5 minutes (11%) shorter than the traditional visits ($P < 0.001$). We found no differences in the consultation parameters (investigations, advice, prescriptions and GP and neurologist follow-up appointments) ($P > 0.05$) between the randomized groups.

Fewer women were referred from rural areas as compared to urban ($P = 0.04$), and women from rural areas had higher VAS intensity score than those from the urban areas ($P = 0.01$). Patients from the rural group waited longer for specialist consultations than those in the urban group ($P = 0.001$).

In summary, we documented that telemedicine is highly acceptable, provides significant cost saving benefits and is a technically feasible consultation for nonacute headaches

5.2 Paper II

Based on the cohort described in paper I, we wanted to determine whether telemedicine is non-inferior to traditional consultations in patient satisfaction and treatment efficacy at three months. We postulated that the share of satisfied patients in the telemedicine group at three months should be not less than ≤ 15% of the share in the traditional group.

The satisfaction rate was 158/178 (88.8%) in the telemedicine group and 156/169 (92.3%) in the traditional group (-3.5% difference with standard error). Figure 9 shows the share of satisfied patients in the two randomized groups. A two sided 98% confidence interval for the difference of these two proportions is -0.11 to 0.04 = -11% - 4% [115, 116]. The lower boundary of the confidence interval for the difference is above the prespecified -15% limit of non-inferiority.

By using per-protocol and intention-to-treat analysis, we found no statistical difference in treatment outcomes (HIT-6, VAS, subjective headache change, headache days per month for the last three months, use of painkillers and triptans, diagnostic recall, compliance and work status) between telemedicine and traditional consultations at 3 months ($P > 0.05$).

A non-prespecified per-protocol subgroup analysis of rural patients showed that fewer shares of participants who underwent telemedicine visited their general practitioner within three months after the baseline consultation ($P = 0.002$), and those who underwent telemedicine had less general practitioner headache visits ($P = 0.003$). The conclusions of these per-protocol analysis coincided with the intention-to-treat analysis.
At baseline, and in patients who answered at three-months, women were younger than males ($p = 0.001$ and 0.001), and had more years of education ($p = 0.02$ and 0.02).

In conclusion, this study demonstrates that a telemedicine consultation is non-inferior to an in-person consultation in patient satisfaction and treatment at three months.

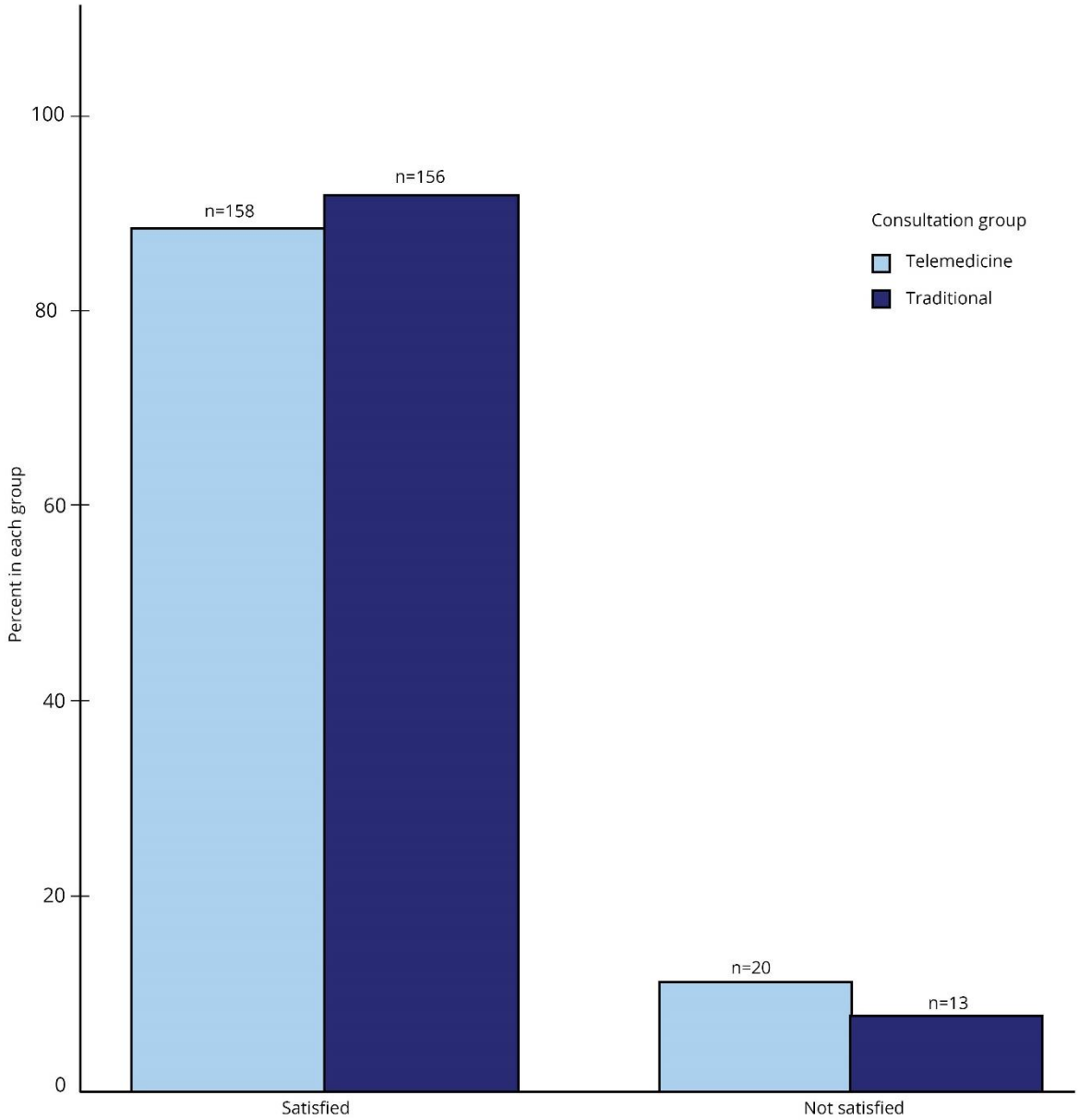


Figure 9 A Per-protocol analysis showing the share of satisfied patients in telemedicine and traditional in-patient consultations, P = 0.35.

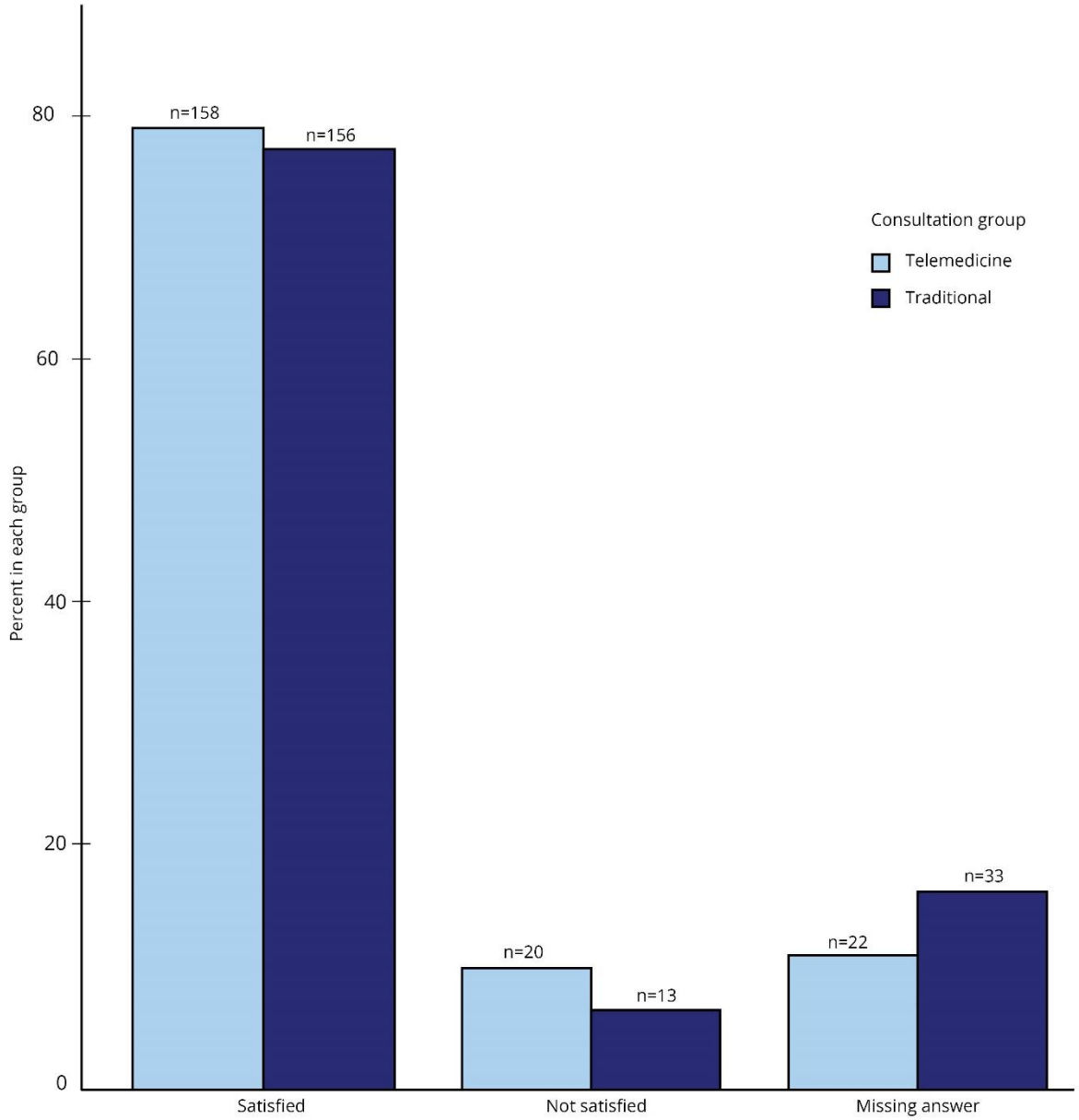


Figure 9 B Intention-to-Treat analysis showing the share of satisfied patients in telemedicine and traditional in-patient consultations, P = 0.16.

5.3 Paper III

In this 12 month questionnaire based follow-up our aim was to confirm the three months satisfaction results from paper II. Additionally, we wanted to investigate different aspects of telemedicine satisfaction and patients' consultation preferences.

The share of patients who were satisfied at both three and twelve months was 124/145 (85.5%) in the telemedicine group and 118/134 (88.1%) in the traditional group (Figure 10). This is a -2.6% difference with standard error. The 98% confidence interval is -0.12 to 0.07 = --12% to 7% [115, 116], which is above the prespecified non-inferiority limit set at -15%.

The share of patients who were satisfied at twelve months was 134/151 (88.7%) in the telemedicine group and 127/140 (90.7%) in the traditional group (-2.0% difference with standard error). The 98% confidence interval for the differences is from -0.1 to 0.07 = -10% to 7% [115, 116]. The lower boundary confidence interval is -10%. This is above the prespecified non-inferiority limit set at -15%.

We found no difference in patients' satisfaction with communication, information, diagnosis, advice and prescriptions between the telemedicine and traditional group ($P > 0.05$).

In the telemedicine group, 99/147 (67.3%) headache patients were indifferent to the consultation form as compared to 42/138 (30.4%) in the traditional group ($P = 0.001$ for per-protocol and intention-to-treat analysis).

There was a higher share of women satisfied with communication in the telemedicine group ($P = 0.027$ and 0.001 for per-protocol and intention-to-treat, respectively). In the intention-to-treat analyses, a higher proportion of women were satisfied with information, diagnosis, advice and medication and a higher share were overall satisfied in the telemedicine group ($P < 0.05$), but the per-protocol analyses did not concur with these results ($P > 0.05$).

In conclusion, the long-term satisfaction with a telemedicine consultation is not inferior to a traditional in-person consultation.

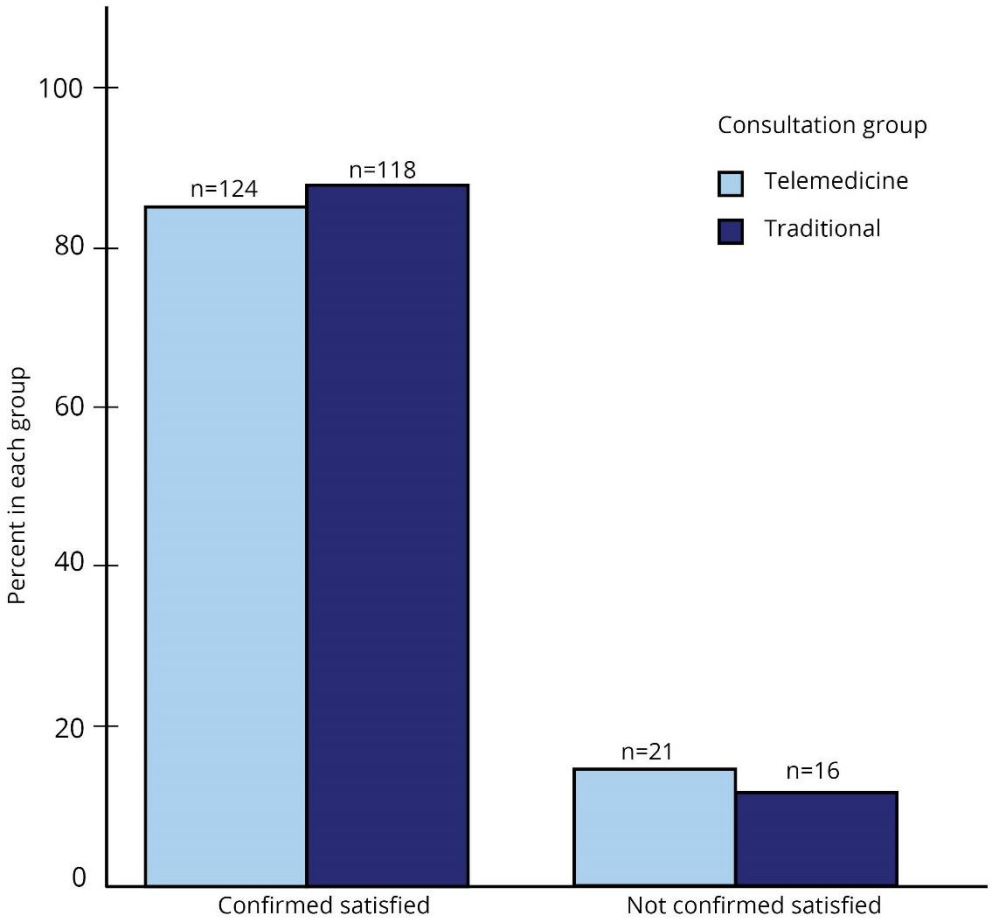


Figure 10 A Per protocol comparison between telemedicine and traditional headache consultations of patients who were satisfied at both 3 and 12 months (confirmed satisfied) and those who were unsatisfied at both 3 and 12 months (not confirmed satisfied), P = 0.65.

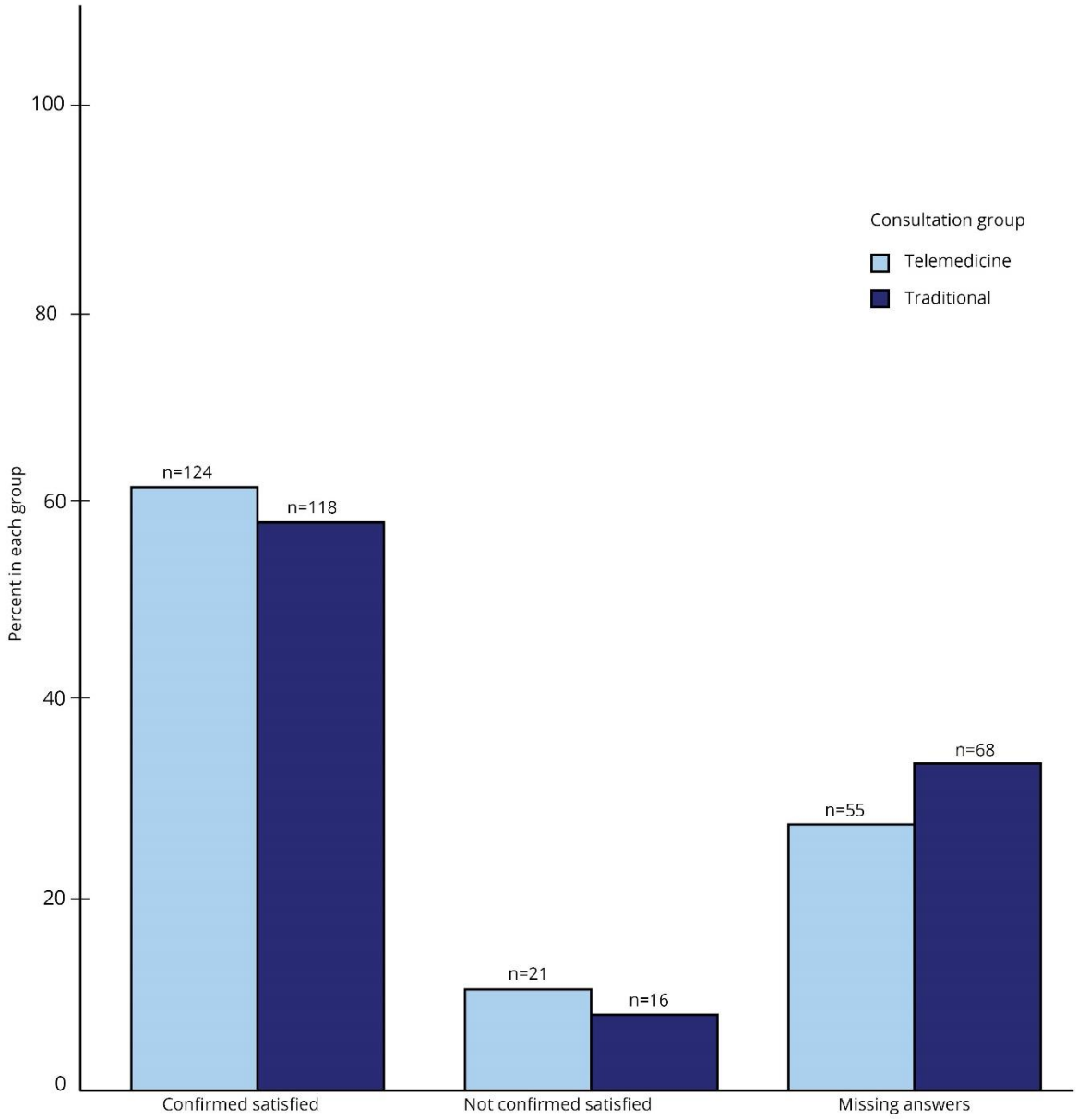


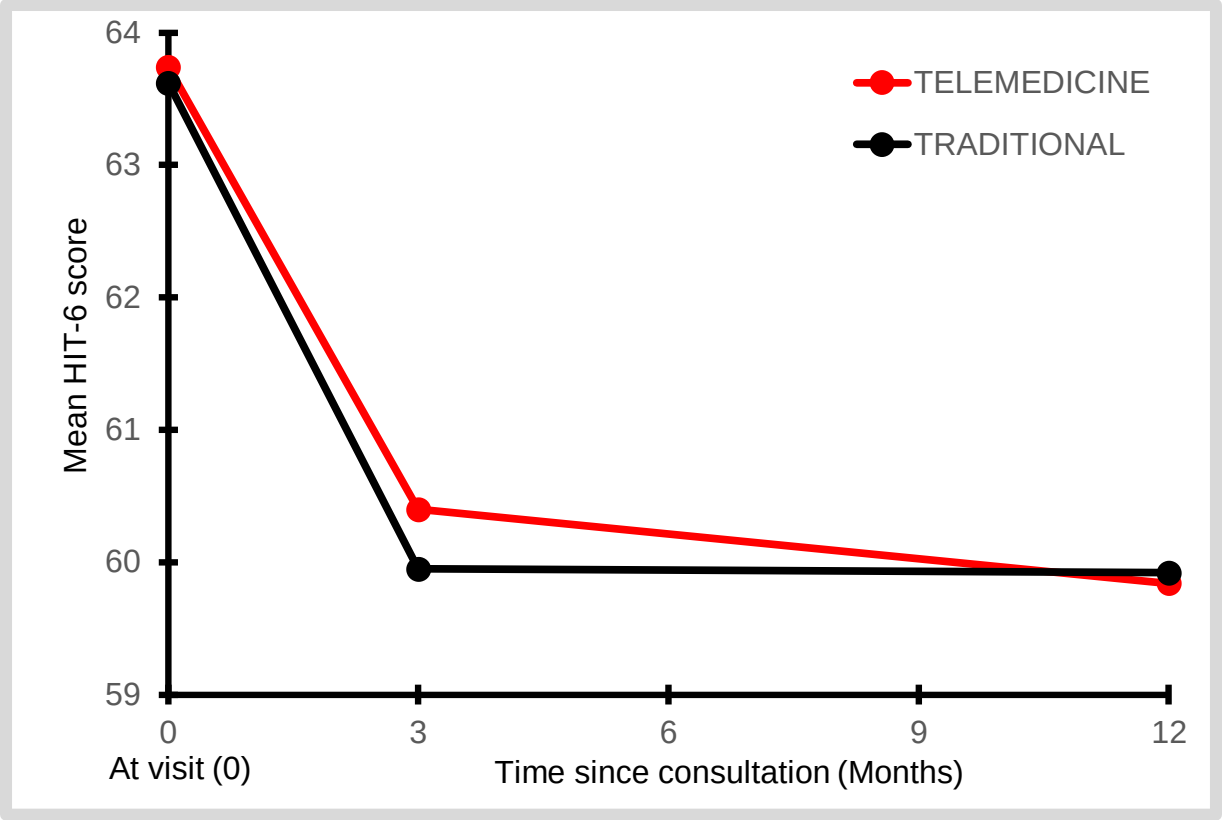
Figure 10 B Intention-To-Treat analysis comparison between telemedicine and traditional headache consultations of patients who were satisfied at both 3 and 12 months (confirmed satisfied) and those who were unsatisfied at both 3 and 12 months (not confirmed satisfied), P = 0.34.

5.4 Paper IV

In this paper, we further elaborated on the efficacy and quality, to evaluate the treatment efficacy and safety of telemedicine within one year after the specialist consultation. We used a mixed between-within patients analysis of variance for assessing differences in headache influence on daily life (Figure 11) and headache intensity between telemedicine and in-person consultations. With a significance level of 0.05 and 95% confidence intervals we found no differences in HIT-6 or VAS between the two groups assessed over three time periods (at consultation, at three months and at 12 months), $F(1, 271) = 0.043$, $p = 0.84$ and $F(1, 255) = 0.22$, $p = 0.64$ for HIT-6 and VAS, respectively. At 12 months, the telemedicine and traditional visits were not different in patients subjective headache change, headache days per month, frequency in the use of pain-killers, triptans and prophylactic headache medications, diagnostic recall and frequency of general practitioner visits due to headache ($P > 0.05$).

By reviewing the questionnaires and every participant's electronic patient record in all hospitals of Northern Norway, we identified one secondary headache in each randomized group. Patients in both groups showed no differences in pathological findings on neuroimagings and cerebrospinal fluid analysis, or in compliance to treatment and frequency of specialist visits and hospitalizations ($P > 0.05$).

After one year of follow-up, telemedicine treatment efficacy and safety is non-inferior to traditional in-patient consultations.



	Telemedicine visit			Traditional visit		
Time period	n	Mean	SD	n	Mean	SD
At consultation	142	63.7	6.5	131	63.6	6.1
At 3 months	142	60.4	8.6	131	60.0	7.4
At 12 months	142	59.8	9.2	131	59.9	8.2

Abbreviations, SD; Standard Deviation

Figure 11 A prespecified mixed between-within patients ANOVA of HIT-6 (P=0.84) at 3 time periods (at baseline, at 3 months and at 12 months).

6. METHODOLOGICAL CONSIDERATIONS

6.1 Study design

The randomized controlled trial (RCT) is like a classic experiment, in which patients are allocated at random to either an experimental or a control intervention, and in which the independent variables are manipulated on. RCT is considered as the gold standard method for investigating effects of presumed preceded causes (causality) [117, 118]. Proper concealed randomization minimizes the risk of systematic errors, which will be discussed in the next section.

In the present trial, eligible participants gave informed consent before randomization. To include more patients, we could have asked for consent after randomization, and only get consent from patients who underwent the telemedicine intervention, arguing that the other group would get a traditional consultation anyway (as in Zelen designs) [119]. A downside would be the possibility of telemedicine patients crossing over to traditional consultations, which would dilute the endpoints and bias the intention-to-treat analysis. Since only 10% of the eligible patients declined telemedicine and participation in this trial, the consent prior to randomization does not minimize the generalizability. Another way to increase generalizability, was to include a usual care "real life" control group. Due to the number of patients needed, this would be more time consuming and hard to achieve.

A *non-inferiority trial* aims at determining if an intervention is no worse (non-inferior) to a control intervention based on a predefined non-inferiority margin [120]. This design was chosen due to the many potential advantages and convenient aspects of telemedicine as compared to traditional in-person visits (eliminate unnecessary travel, give patients more time, reduce both direct and indirect costs and increase access to care, especially in areas without headache specialists) [106, 120].

The 15% non-inferiority margin was based on previous literature and clinical considerations. In non-inferiority studies of telemedicine, a non-inferiority margin of 10% is often considered as strict and 20% as liberal [106]. This margin is similar to Food and Drug Administration's threshold for establishing bioequivalence [121]. To achieve an adequate amount of

participants, we performed a power analysis, which was followed by an interim analysis. This was done in order to ascertain enough enrolled participants, and to prevent unnecessary study prolongation if participants were unsatisfied with telemedicine. The reason for choosing satisfaction variables for power analysis is explained in paper II.

6.2 Bias and confounding

Bias is defined as a systematic error that occurs due to unprejudiced favoring one answer over another. An illustration of biases in the randomized controlled trial is shown in figure 12. A confounder is defined as an underlying factor that affects the outcome, the mediator or the predictor in a causal path.

The telephone interview on telemedicine acceptance and participation, and the cost analysis in this study (paper I) have not been derived from randomization, and should be regarded as equivalent to a nonrandomized cohort. Hence, the assessment of the variables from these methods is more prone to observation bias. To compensate for this, two well-trained study coordinators performed the telephone interview according to a standard work protocol (Appendix I). The travel cost analysis was performed by an independent experienced hospital economist, who obtained data from the Norwegian Patient travel Agency and calculated travel expenses based on their standard probabilistic method (Paper I, appendix VII). Having these clear, standardized procedures minimize the risk for observer bias. Other limitations of the cost-saving analysis have been discussed in paper I.

In paper I, we controlled nonrandomized subgroups for confounders by using hierarchical linear regression to assess rural location as a predictor of VAS and to assess the ability to predict the waiting time of patients from rural locations. Travel distance and time was calculated by Google Maps and controlled with a function in the Norwegian yellow pages, which will bias the results because all patients do not travel by car. In paper II, the subgroup analysis of patients from urban and rural areas was non-prespecified and not randomized, which is more likely to give a false positive result by chance [122]. Likewise, the gender comparisons and telemedicine subgroup analysis of patient preference in paper III are more prone to spurious findings, and ought to be interpreted with caution.

To conceal allocation as long as possible for patients and neurologists, the randomization was always made as the last step before patients were followed to the allocated consultation type. To further assure good allocation concealment, a telephone to an external independent party (the hospitals randomization office) was made. On that site, block randomization was generated in a locked unreadable computer program. A concealed randomization compensates for selection bias. In addition, the patients were consecutively recruited from those referred to our neurologic outpatient department. On the other hand, we only recruited eligible patients who accepted telemedicine and study participation from this group, but most of the interviewed eligible patients accepted both (Figure 6).

Having the randomization process as the last step before consultation also compensated performance bias. This bias may still occur if one neurologist favors one consultation type over the other, being aware of the fact that studies with positive results are more likely to be published (citation bias) [123]. Performance bias could have disturbed the causality when comparing the two consultation types. To avoid any neurologist effect, we stratified on neurologist at randomization. Blinding can compensate for performance and also interviewer bias (observation bias), but would be very challenging to achieve in this trial. However, both positive and negative results in this trial would be valuable findings. The neurologists' experience could also have effect on the outcome. On the other hand, the neurologists were experienced with evaluating patients with headache, and patient satisfaction and treatment effect were balanced and did not increase substantially over time in the study groups.

In most studies, some patients declines participation, and others are lost to follow up. Such attrition is important since it may cause bias, which is not eliminated by randomization. In this study, most of the eligible patients accepted participation, and only 7 were excluded after randomization. These 7 patients were excluded on the basis of information recorded before the randomization. To reduce drop-outs one reminder was sent to those who did not answer the questionnaires. Additionally, participants chose between answering the questionnaires on paper or electronic. Two methods of collecting questionnaires could cause the questions to be interpreted differently by respondents. However, a recent review and meta-analysis concluded that paper and electronic administration of patients related

outcome measures are quantitatively comparable [124]. The majority of participants in our trial answered the questionnaires via the Internet, and relatively few were lost to follow up at 3 and 12 months (Figure 6). We found no statistical differences between patients who were included and those who were excluded regarding gender and age (Paper I). Apart from 3.5 years older respondents as compared to non-respondents at 12 months (P = 0.020), we found no differences in the dropout analyses at 3 and 12 months (Paper III). To avoid further issues with attrition we also analyzed the 3 and 12-month material with intention-to-treat.

Two neurologists (the first and last author of all four papers) performed all consultations, and took part in both data collection and analyzing the data, which could have complicated the study outcomes. To increase the internal consistency of the study, the first author was primarily responsible for data collection and analysis, but methods and findings were discussed and consulted with the two other authors. Detection bias is often handled by blinding personnel and/or patients. Because the two studied consultation types are quite different, blinding would require more resources and make the logistics more complicated by adding another researcher.

By sending the questionnaires three and 12 months after the consultation, we wanted to ensure enough time for reflection, but simultaneously not wait too long and risk too much recall bias. Nevertheless, recall bias is a limitation of the study, especially the results from the 12-month questionnaire. To reduce this at consultation, the waiting time was set to not more than 4 months from the date of the referral letter. In paper IV, we compensated for the recall bias by thoroughly rereading every participants electronic patient record in Northern Norway.

To avoid effects on causality, confounders have to be identified and conditioned on in the analysis (if possible). By having the telemedicine and the traditional consultation at the same hospital, we ruled out the confounding effects of travel, the use of different personnel and the use of different locational settings prior to randomization. Additionally, all included patients were referred from primary care in Northern Norway, and their age was limited to that of a working population. In this way, patient conditions were similar to the point of

randomization, and the inclusion criteria was identical as well. Other confounding effects in this trial were ruled out by the concealed randomization.

We reduced plausible confounders, used a strict and structured protocol, and compensated for bias by concealed randomization. This made it relatively easy to interpret differences between telemedicine and traditional consultations. Hence, this trial has a high internal validity for the comparisons of the two randomized groups. However, just being part of a study, and having the consultation fees waved may have biased the results.

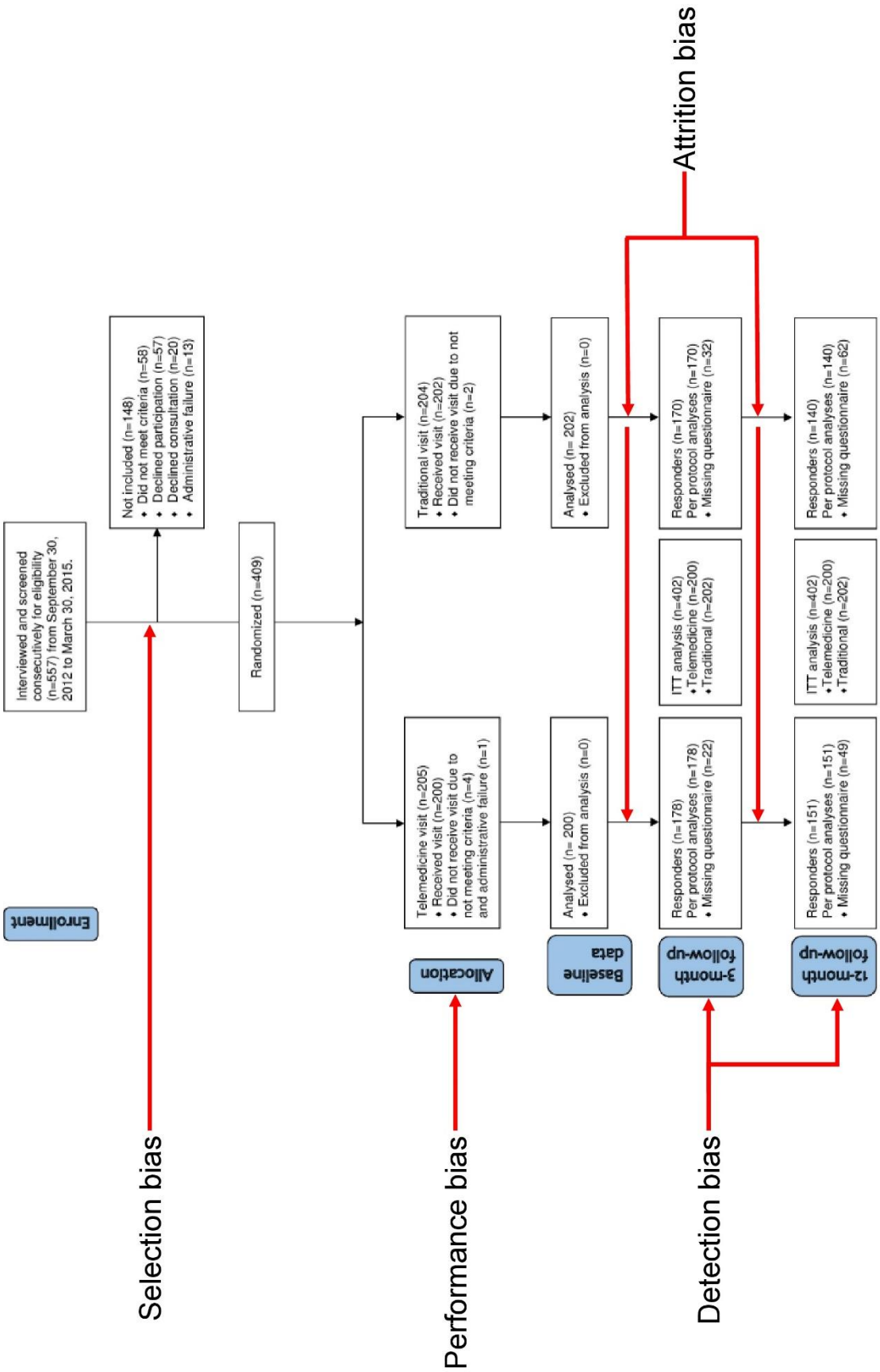


Figure 12 Illustration of bias in the randomized controlled trial.

6.3 Random error

Every significant finding can occur by chance (random error). In superiority trials, a type 1 error (α) means reporting a false outcome difference by erroneously rejecting the null hypothesis (H_0). The analyses of the primary hypothesis may be robust, but the chance to get a false-positive result is increased in the secondary analysis due to multiple testing, especially in the non-prespecified and post hoc hypothesis. This is especially a limitation of the significant results claiming telemedicine superiority in paper 2. A type 2 error (β) would be failure to reject the H_0 when there is a true difference in outcome.

In contrast to a superiority trial, the null hypothesis (H_0) in a non-inferiority trial states that a treatment is inferior to a control:
H_0: Share of satisfied patients with a telemedicine consultation is inferior to that of a traditional visit by ≥ 15%
H_1: Share of satisfied patients with a telemedicine consultation is non-inferior to a traditional visit by a margin of < 15%
Thus, the definitions of type 1 and 2 errors are in fact reversed as compared to a superiority trial.

A type 1 error would be to claim that telemedicine is non-inferior by a prespecified margin to a traditional visit, when it is truly inferior (erroneously rejecting H_0). Intention-to-treat analysis may increase the risk of type 1 error in non-inferiority trials. In our trial, we saw that missing answers in the questionnaire "diluted" the share of satisfied patients (Paper II and III), and drew the conclusion towards rejecting H_0, or even claiming superiority in some satisfaction variables (Paper III). Conversely, intention-to-treat analysis preserves the value of randomization, and mirrors reality [125]. In our trial, the per-protocol and the intention-to-treat analysis coincided in that both concluded non-inferiority of telemedicine (Paper II – IV).

A type 2 error would be failure to reject the H_0 hypothesis when telemedicine consultations are truly non-inferior by a prespecified margin. This type of error can be caused by a too small sample size, a too short follow-up period or flawed design. To avoid type 2 errors, we made a prespecified power analysis for the primary satisfaction variable(s), and ensured

enough included patients. Additionally, patients were followed up by questionnaires at 3 and 12 months, and to ensure a dynamic long-term evaluation, we combined the satisfaction variables at 3 and 12 months (Paper III). We did not calculate statistical power of other variables, but in our analysis, we did not conclude that telemedicine consultations are inferior to traditional consultations. Thus the risk of making a type 2 error was removed in the primary analysis, but would still be possible in the subgroup analysis.

6.4 External validity

During the trial period, we mirrored daily life in our Department of Neurology by consecutively recruiting and consulting 72.2% of all the referred nonacute headache patients. The study participants did not significantly differ in age and gender to the 27.8% who did not participate. Moreover, patients in our trial are similar in characteristics to those with primary headaches referred to other secondary neurologic departments and headache clinics: a high proportion of women and migraineurs, in fertile age, and with a high headache burden [57, 126]. To the extent possible, we also followed and reported study findings according to the CHEERS and CONsolidated Standards Of Reporting Trials (CONSORT) statements [80, 117, 120]. For these reasons, generalizability is a strength of this trial. The fact that our trial was retrospectively registered in a World Health Organization (WHO) registry (before inclusion of the first patient) could make it more prone to reporting and publishing bias [122]. However, the trial was registered in time at the Norwegian Research and Management database. In order to improve the research transparency, and prevent distortion of the scientific evidence, we labelled prespecified and non-prespecified outcomes in the papers [122].

A limitation is that we did not include patients older than 65 and younger than 16 years of age, neither did we include patients with suspected secondary headaches (except MOH). The results in this trial can thus not be generalized to patients beyond this age range, and not to patients with suspected secondary headache other than MOH.
Since the headache patient and neurologist were in the same location (but different rooms), the trial provides a proof of concept (as for a feasibility study), but is not equivalent to a consultation where patients are going to a satellite clinic (presumably closer to their home) and being connected to a remote neurologist (presumably located at a major neurologic

center). Our design obviously increases the internal validity at the expense of the external validity of the study. On the other hand, the remote technology has gained momentum, and the technology needed for a remote consultation, with similar qualities as those we did in hospital 2-3 years ago, is available in most households in Europe [127]. Additionally, telemedicine does not depend on distance; the neurologist is not physically present in the consultation room.

The rural areas, which are expected to benefit the most from telemedicine, are sparsely populated. To enroll enough patients in a “real life” study, we would need multiple telemedicine satellite locations spread out over these rural areas (Figure 2). Such a study would be very challenging. It would be extremely expensive, and very problematic to both educate and maintain appropriate scientific personnel in all areas. Prior to this trial, the researchers actually made an attempt in a rural hospital in Mosjøen (see Preface) with an area of coverage of approximately 70 000, but failed to enroll enough patients and to maintain the scientific personnel necessary to continue this design. Based on these limitations, our study design, though a bit artificial, was the closest we could get to study telemedicine consultations for nonacute headaches in these areas.

7. GENERAL DISCUSSION

In this thesis, I present an alternative paradigm in the management of nonacute headache patients. In paper I, we assessed nonacute headache patients' acceptability of telemedicine, estimated time and cost savings and evaluated the feasibility of telemedicine by comparing it to the traditional in-person face-to-face consultation. In paper II and III, we assessed patients' satisfaction of telemedicine. Treatment efficacy of telemedicine was presented and compared to traditional consultations in paper I, II and IV. Finally, safety of telemedicine consultations was discussed in paper IV. Here, I further discuss acceptability, satisfaction, management, efficacy, cost, feasibility and safety of telemedicine consultations for nonacute headache disorders. It is complicated to perform a neurologic examination via telemedicine. Therefore, a part of this discussion is about the role of neuroimaging and examination of headache patients. In the last part of this discussion telemedicine dynamics, perspectives and implementation will be discussed.

7.1 Acceptability and satisfaction

An essential requirement in order to implement telemedicine successfully, is a patient centered view. Patients have to accept the consultation type, and be satisfied with the technology. We found a high share of telemedicine acceptance among nonacute headache patients. Although almost all who underwent the telemedicine visit in our study were satisfied with the video- and audio quality, a direct interview may cause bias due to patients being polite. However, high rate of acceptance is supported by findings in other telemedicine studies [128]. Conversely, previous surveys, including a survey from our own region, report low levels of satisfaction among headache patients [15, 107]. The huge and far-flung area of coverage with lack of headache specialists in most of the rural areas that we serve (Figure 2), brings challenges in providing proper specialist care for headache patients [15, 35], thus being an indirect cause of the previously reported high share of unsatisfied patients. Longer waiting time for patients in the rural areas (Table 4 in paper I), corresponds to the problematic travel logistics to get appropriate headache care.

According to Statistics Norway as of 1. October 2015, almost all of the Norwegian households have internet access, and 91% have a broadband internet connection at home

[129]. This corresponds with Eurostat data from 2016, which states that 85% of European households have access to the internet, and 83% have broadband connection [127]. Additionally, about half of the population in Europe, and 60% in the US, with internet connection use the internet for health related purposes [130]. According to these data, it is not about the access to high quality hardware and software, it is about the lack of access to specialist headache care [15]. Headache patients recognize the need for proper access and availability of headache specialists. This is reflected in the high proportion of telemedicine acceptance and satisfaction in our trial.

A weakness is that we failed to compare questions about satisfaction up against a standardized questionnaire or rating scale. On the other hand, similar satisfaction questions and aspects have been used by others [15, 107, 108, 131]. Although it is guaranteed that we did not cover all aspects of satisfaction in this trial, the other studies show that the questions we asked (Paper I, II and III) bring light to many of them (Table 6) [132]. High Cronbach's alpha shows that the satisfaction questionnaire at 12 months is reliable (Paper III). The high level of satisfied patients corresponds well to satisfaction reported on telehealth delivered to other pain conditions [133-135], as well as to other neurologic and medical conditions [108, 136].

7.2 Efficacy

The treatment efficacy outcomes were primarily evaluated by the use of the headache specific patient related outcome measure HIT-6 and by the visual analogue pain scale (VAS). The HIT-6 is both reliable and valid across different headache conditions, and considered as a main headache outcome measure [98, 137, 138]. It has been translated into 28 languages, and both the cultural and linguistic content were considered comparable in all the three Scandinavian languages [139]. Cronbach's alpha at baseline, 3 and 12 months correspond to high level of internal HIT-6 consistency. Specific patient related outcome measures, such as HIT-6, have the advantage that they are more target focused, thus get more relevance and become more responsive to the research question(s). The drawbacks are that they are not as extensive on health-aspects as the generic patient related outcome measures, and have limited potential to assess unexpected effects of treatments. In this trial, however, we had many variables that considered headache, general health and social aspects as well. VAS has

been found valid and reliable across different pain conditions as well as headache, and is further discussed in paper I [100, 101].

Although we found no differences in headache specific endpoints between the randomized groups (Paper II, III and IV), at 3 months more patients from rural areas visited their general practitioner in the traditional group (Table 5 in paper II). However, there was no difference in the 12-month material (unpublished data), and the 3-month significant findings could be caused by chance.

Nevertheless, it is conceivable that the decline in HIT-6 and probably VAS in our trial may be explained by a deviation to the mean, especially since a primary care cohort found similar changes in HIT-6 at 10 months follow-up [140]. Due to the long and tiresome travel conditions in our area of coverage, those who were referred in the first place were probably the most heavily afflicted and the most difficult to treat, and patients' symptoms may decline over time with or without treatment. It might be argued that non-inferiority of telemedicine compared to traditional consultations has been demonstrated. However, the efficacy of either treatment to usual care has not been demonstrated. Notably, however, about half of the consulted patients had a decrease in the HIT-6 and VAS scores beyond that of a minimal clinical improvement (Table 3 in Paper III) [99, 101].

7.3 Cost evaluation

After getting similar treatment and safety outcomes in the telemedicine and traditional groups, telemedicine moves towards quadrant 2 in the cost effectiveness plane (Figure 5). Based on quadrant 2, it is considered as unnecessary to calculate an ICER. Although we did not make a study on cost-effectiveness, the treatment and safety results at 12 months strengthen the cost analyses in paper I. In a cost minimization perspective, these results strongly indicate cost-effectiveness of telemedicine. In fact, we found that telemedicine visits were about 5 minutes shorter than traditional visits (Table 2 in paper I), which may add to its cost effectiveness. Moreover, since the regional health authority covers most of the patients travel costs, reducing patient travel may allocate more money to treatment (Paper I).

Few studies that explore structural changes or secondary causes of nonacute headaches give explicit information about the content of the neurologic examination that was performed [57]. PubMed searches on this topic 4.5.2017 did not reveal studies showing economic benefits of not performing a neurologic examination. However, a full neurologic examination is time consuming.

7.4 Feasibility and safety

Although we controlled for travel and location confounders, there was a high share of patient acceptance, a high proportion of both short and long-term satisfied patients and indifference to consultation type (Paper I, II and III). These findings add strength to the feasibility evaluation.

We only encountered minor technical problems, and most patients were satisfied with the quality of the telemedicine consultation (Table 2 in paper I). In consultation related outcomes, we found no differences favoring traditional visits, and the consultation time was actually in favor of telemedicine (Table 2 in paper I). The facts, that the follow-up questionnaires revealed no differences in headache related outcomes between the two randomized groups (Paper II, III and IV), that there was less follow-up in patients who underwent telemedicine (Paper II), and that no statistical difference in safety aspects after a thorough review of all participants electronic hospital records (Paper IV) was found, bring more credibility to telemedicine feasibility in the treatment of nonacute headaches. Although new issues come with new technology, these findings could lead towards a more beneficial and patient centered headache care in the future.

The major advantage of an in-person consultation is the direct physical interaction between the doctor and the patient, and the possibility to do a full physical and neurologic examination. A traditional view is that the examination brings reassurance, and strengthens the bond between the doctor and patient [141]. However, most patients would probably not like to be examined just for the sake of being reassured. Despite not being examined, 9 out of 10 patients were satisfied with the consultation in this trial. The physical presence tends to be provider centered, and thereby resulting in less power balance between the doctor and the patient [76]. A limitation of the traditional visits could be the lack of the

psychological and physical virtual space present in telemedicine [76]. However, this space could also be a barrier to proper care.

Why is it necessary to do a neurologic examination in a patient with nonacute headache? The main reason is to diagnose secondary causes to avoid unanticipated consequences of misdiagnosis and mistreatment. Therefore, examining a patient or not should primarily be based on medical reasoning. The amount of examination ought to be disease and situation specific. Physicians usually identify headache phenotypes and warning signs (Table 5) by a structured interview [57], and the neurologic examination has become less important due to the availability of neuroimaging [142]. In the trial, we only included patients with either a normal neurologic examination reported by the referring doctor, or no signs of pathology suggestive of a secondary headache cause on neuroimaging (Paper I) [25]. Thus, we acknowledge the uncertainty associated with quality of the clinical examinations reported in the referrals. Nevertheless, our data at one year revealed only one secondary headache in each of the randomized groups, suggesting that not performing a neurologic examination after these given criteria is safe. Support to this view is also found in neuroimaging studies [49-57].

7.5 Neuroimaging and examination

The US headache consortium made a meta-analysis of 1086 patients with migraine headache and normal neurologic examination in 2000 [92]. They found the frequency of intracranial pathology on neuroimaging to be 0.18%. Consequently, the consortium concluded that patients with a typical migraine and a normal neurologic examination are unlikely to have pathology on neuroimaging. However, a major weakness was that most of the studies they included did not inform about aspects of the neurologic examination. Furthermore, more than 2/3 of the patients were from studies made in the 70ties and 80ties, using low quality CT scans. Additionally, the meta-analysis comprised both CT and MRI studies, and did not differentiate between them. Neither did we differentiate between CT and MRI scan results.

In 2004, Sempere et al screened 1876 patients with nonacute headaches [57]. All underwent a "*tailored*" neurologic examination depending on patients' complaints [57]. Of these 1861

(99.2%) had a normal examination, 1432 underwent a CT, 580 an MRI and 136 both. Significant intracranial pathology was found in 1.17% (22/1876) [57]. Seventeen of the 1861 patients (0.91%) with normal examination had significant abnormalities on neuroimaging, and nine of these had either migraine or tension-type headache [57]. The five patients with findings on neurologic examination and neuroimaging had indeterminate headaches that would warrant a head scan anyway [57].

Sempere and colleagues found three patients with papilledema and normal neuroimaging; all were diagnosed with idiopathic intracranial hypertension [57]. Accordingly, findings of significant pathology on neurologic examination that lead to detection of a secondary headache cause was 0.16% (3/1876). Despite different methodology, this finding is comparable to our trial, in which a second opinion neuroradiologic investigation revealed signs of idiopathic intracranial hypertension in one patient.

Thomas and collaborators report brain CT scans of 215 nonacute headache patients from general practices in Scotland [53]. Three of the patients (1.4%) had significant structural findings related to their nonacute headaches; metastasis from lung cancer, a meningioma and an arteriovenous malformation [53]. These findings are also comparable to the finding in our trial. In contrast, a study from Africa reports significant pathology on almost half of the brain CT scans in patients with nonacute headaches [143].

By performing bibliographical searches on MEDLINE from 1966 until November 2005, Detsky and collaborators identified 11 neuroimaging studies of 3725 patients with headaches [58]. They concluded that abnormal findings on neurologic examination increase the likelihood ratio of intracranial pathology 5.3 times [58]. However, these patients had both acute and nonacute headaches. More than 85% underwent a CT scan, there was a long study span, and only one study informs about the content of the neurologic examination [58].

On one hand, in some studies significant pathology on neuroimaging in nonacute headaches does not exceed findings in a normal population [56, 92, 144, 145]. On the other hand, the share of significant pathological findings in the normal population is less than the share found in headache participants in a Norwegian population based study [49], as well as in our

trial. A meta-analysis of 19559 MRI scans from presumed healthy individuals found neoplastic lesions in 0.7% (72 meningiomas, 27 pituitary adenomas, 8 low grade gliomas, 5 acoustic neuromas, 6 lipomas, 3 epidermoid tumors and 14 unspecified tumors) [145]. The same meta-analysis found 375 non-neoplastic lesions in 15559 MRI scans of presumed healthy individuals [145]. These lesions included 67 aneurysms, 23 cavernomas, 7 arteriovenous malformations, 13 signs of demyelinations, 101 cysts, 71 Arnold-Chiari type I malformations, 15 signs of hydrocephalus, 4 extra-axial collections of cerebrospinal fluid, as well as 74 other abnormalities [145]. The prevalence of any of these incidental findings was 2.7%, but increased to 4.3% in MRI with higher resolution series [145]. Thus, the differences in these studies are not only caused by geographical disparity, but the use of different types of equipment and methodologies are also important confounding factors. Additionally, incidental findings and anatomical variants are commonly present in patients with primary headaches [146]. Due to the probability of incidental findings on neuroimaging, ordering head scans due to headache should be discussed with the patient in advance, and primarily be based on clinical indication (such as the criteria in Table 5).

One reason for performing neuroimaging in nonacute headache is screening for intracranial hypertension. In 2006, Bono et al found that 6.9% of 724 migraine patients without papilledema had bilateral transverse sinus stenosis, and 2/3 of these were diagnosed with idiopathic intracranial hypertension [147]. The same author found bilateral transverse sinus stenosis with idiopathic intracranial hypertension in 4.5% of 198 patients with chronic tension-type headache without papilledema [148]. De Simone published 44 patients with unresponsive chronic migraine, of whom 38 had increased intracranial pressure [149]. In a majority of these patients, the headache improved after lumbar puncture [147-149]. More studies are warranted to determine the proper clinical context in which lumbar puncture should be performed. Another important question is what diagnoses and treatment patients with a primary headache phenotype and increased intracranial pressure without papilledema should receive.

Even though significant brain MRI findings in migraine and tension-type headaches are rare, some literature recommend brain MRI to rule out secondary causes of tension-type headaches and chronic migraine [150, 151]. One reason is the last criterion in the ICHD-3

diagnosis of primary headaches, "*Not better accounted for by another ICHD- 3 diagnosis*". This criterion is made to rule out secondary causes, and the most sensitive method of ruling out a secondary cause is by brain MRI. Another reason for considering MRI in tension-type headache is that featureless headache is the typical brain tumor headache [23]. Then again, most brain tumor headaches have additional neurologic symptoms, and tension-type headache is the second most common disorder in humans [21, 23, 152].

Many review articles, as well as the European guidelines, recommend that neuroimaging should be performed with MRI technology in nonacute headaches with warning signs (Table 5) [51, 59, 153-155]. If warning signs are present and the MRI is normal, a neurologic examination and/or a control MRI with additional sequences should be considered. MRI is superior to CT in diagnosing secondary headache causes, and in addition gives no radiation [51, 59, 153, 154].

Conversely, there are many examples of secondary causes of migraine and tension-type headaches [23, 147-149, 156-161]. Both Semper, De Simone and Bonos' studies show that a normal neurologic examination cannot rule out intracranial pathology in patients with nonacute headaches, but neither can a normal CT or MRI brain scan [57, 147, 148]. In our trial, a radiologist overlooked signs of idiopathic intracranial hypertension in one patient (Paper IV). Studies confirm that CT brain scans are of low diagnostic value in nonacute headache diagnosis [51, 54], but still, the most common reason for requesting CT scans is headache [51]. Although a normal MRI brain scan may lead to patients and physicians' "false sense of security", it is usually more sensitive than a full neurologic examination. When a new imaging technique enters our diagnostic repertoire, or when an information and communication technology is implemented, it leads to realignment of our other diagnostic tools.

Referring patients to neuroimaging is often more driven by reassurance and patient expectations than by recommendations from guidelines [52, 142]. Some neurologists even refuse to admit nonacute headache patients unless the patient undergoes neuroimaging on beforehand [51]. A general problem is that existing guidelines often do not reflect the "actual needs" in clinical practices. Patients want reassurance, and doctors do not want legal

legislations. In the literature, ordering neuroimaging without clinical cues of a secondary headache (Table 5) is often referred to as overuse [162, 163]. An unanswered question is whether implementation of specialist telemedicine consultations for nonacute headaches would lead to an increase or a more selective use of neuroimaging.

7.6 Telemedicine dynamics

Despite many positive results of telemedicine applications in studies, few are implemented into clinical practice [91, 164]. From 2009 throughout 2013, neurologic telemedicine routine visits in Norway comprised only 0.01 – 0.02% of the total [165, 166]. Although planning stages for neurologic telemedicine projects are considered important for implementation on later stages, reports about such mainly exist for stroke [167].

Developing user-friendly medical information systems is a demanding task. It relies on well-organized teamwork, with close cooperation between healthcare personnel and designers, to become successful [91, 94]. Interdisciplinary communication between diverging branches that use specific languages is tough, and often leads to misunderstandings. Still, finding common grounds and understandings by teamwork is important to enhance proper development of a product [168]. However, the environment, in which information and technical systems work, is dynamic and in constant change. The dynamics makes it more difficult to design and implement information and communication technology successfully. It is impossible to foresee and adapt to all contingencies. This is why developing a system that automatically accommodates to these dynamic changes would be considered impossible.

Previous literature suggests to deal with these changes and technological inadequacies by different methods of avoidance, i.e. “fitting *augmenting* and *working around”* [169]. Due to constant dynamic changes in the social- and work environments, there is often a requirement for improvement, to make way for better compatibility between software systems and clinical practice. Sometimes, these methods can stimulate to a more participatory design, and thereby close gaps between interdisciplinary work between users and developers. On the other hand, avoiding problems usually do not make room for improvement. Similar approaches of avoidance are presented elsewhere. An example is a presentation of how it is possible to keep a process of coordination clean and standardized

[170]. Coordination is about how things are working together, and the coordination of avoidance is made by "*demarcating, procrastinating, delegating and accommodating"* [170].

7.7 Future perspectives

Today, the electronic patient record system in Northern Norway has already become an important part of a large, complex and heterogeneous informational infrastructure with many actors and actants in constant dynamic interactions (developers, users, hardware, software, maintenance personnel, etc.). The system has already reached a level of irreversibility and gained momentum. It is difficult to make changes in a big and complex informational infrastructure, and different aspects locally may lead to a sluggish negotiation process. The bigger this informational infrastructure grows, and the easier it is to use, the harder it is to see the processes that run inside the black-box. The hidden processes that are running behind will only be visible on system failures or system breakdowns [90]. The bigger the information and communication technology system with telemedicine and electronic patient records, the more actors and actants will be affected upon a system failure [90].

When all hospitals in Northern Norway became interconnected by the same electronic patient record, time consuming gathering of information from different electronic patient records ceased, and both patient and hospital staff were no longer dependent on site locations, but rather on one functioning electronic patient record in DIPS. Additionally, electronic patient referrals and electronic prescriptions have replaced the paper-based versions. Since Northern Norway has a defined telemedicine population, all the changes that were made in the information and communication network, and especially the shared electronic patient record, can promote the use of telemedicine technology. In the field of neurology, this could lead to reorganization of the specialized healthcare, giving rise to a system based more on patients' needs, possibly reducing access barriers and giving headache patients from different areas equal access to neurologic healthcare (Figure 13). However, technologies are not considered neutral entities, and all have more or less effect on the daily work. Implementing telemedicine might lead to a redistribution of tasks among health care personnel [171]. Such a shift can possibly strengthen the specialist headache care at the expense of local health care [171].

To be in alignment with an informational infrastructure, headache consultations via telemedicine should not replace the traditional neurologic visits. Instead, consultations through telemedicine should rather be viewed as an alternative for both headache patients and possibly patients with other neurologic disorders as well. In our study, some groups seemed to benefit more from telemedicine than others (paper I and III). Specialist telemedicine consultations could be used as a tool to tailor a more individual treatment approach and delineate geographical differences, i.e. geographical differences in access and availability. Consequences would be satisfied headache patients, less travel, and saving hospital budgets. In contrast, some neurologists are also travelling, often to make extra income. Adding new technology that competes with personal economic gains would likely meet some resistance, produce anti-programs and hinder alignment.

The possibility of implementing telemedicine consultations for headache patients in a rural far-flung geography, especially in areas such as Finnmark and Svalbard, may have several benefits: improved access to neurologic care, less geographic disparity, avoidance of travel and unnecessary time expense, and even easier recruitment for clinical trials are some possibilities [25, 77, 172]. But other barriers are reluctance to adopt new technology in clinical practice, expensive technology, liability concerns, and perhaps most importantly the difficulties in performing a proper neurologic examination [77, 172].

Another issue is that telemedicine tends to realign and relocate tasks from specialists to other healthcare workers, or from healthcare workers to non-healthcare workers (Figure 13) [171]. Even in our own project, we observed that the neurologic examinations were "transferred" to some of the referring general practitioners. Even if all doctors should be able to perform a neurologic examination, an examination by a specialist would possibly be more thorough and precise. New technologies, or use of technology in new fields, are not always tested thoroughly before implementation. A new medication has to undergo several stages of clinical testing in different studies before it is approved for patients, but this does not seem to be of much concern regarding implementation of some technologies used in diagnosing and treating patients.

What characterizes the telemedicine projects that have been successfully implemented? According to a qualitative literature review, implemented telemedicine applications have the following features in common: "*1) Local service delivery problems have been clearly stated, 2) telemedicine has been seen as a benefit, 3) telemedicine has been seen as a solution to political and medical issues, 4) there was collaboration between promoters and users, 5) issues regarding organizational and technological arrangements have been addressed, and 6) the future operation of the service has been considered*" [164]. In this thesis, and in paper I-IV, we described how telemedicine potentially can countervail the geographical disparities and provide equal specialist headache care regardless of the distance to our Department of Neurology. Although this thesis is mainly patient centered, some economic hospital perspectives (paper I and thesis) have been covered. The equipment infrastructure is incorporated in the Department of Neurology, but in use for other purposes. Finally, the local settings (Figure 13) and future perspectives have been considered, but more planning and funding remain to be elaborated on. The project, being built from a bottom-up approach, provides further optimism for successful implementation [63, 64]. Given the conditions in our area of coverage (Figure 2), this project has verified that telemedicine for headache patients could be successful in similar rural or remote areas, as well as in other areas where access to care is cumbersome. Because most households in our area have high speed internet connections, we plan to bypass the satellite locations in smaller rural hospitals. In the next headache project, we intend to investigate predictors for successful implementation of telemedicine by streaming audio- and video from a specialist center directly to patients' homes.

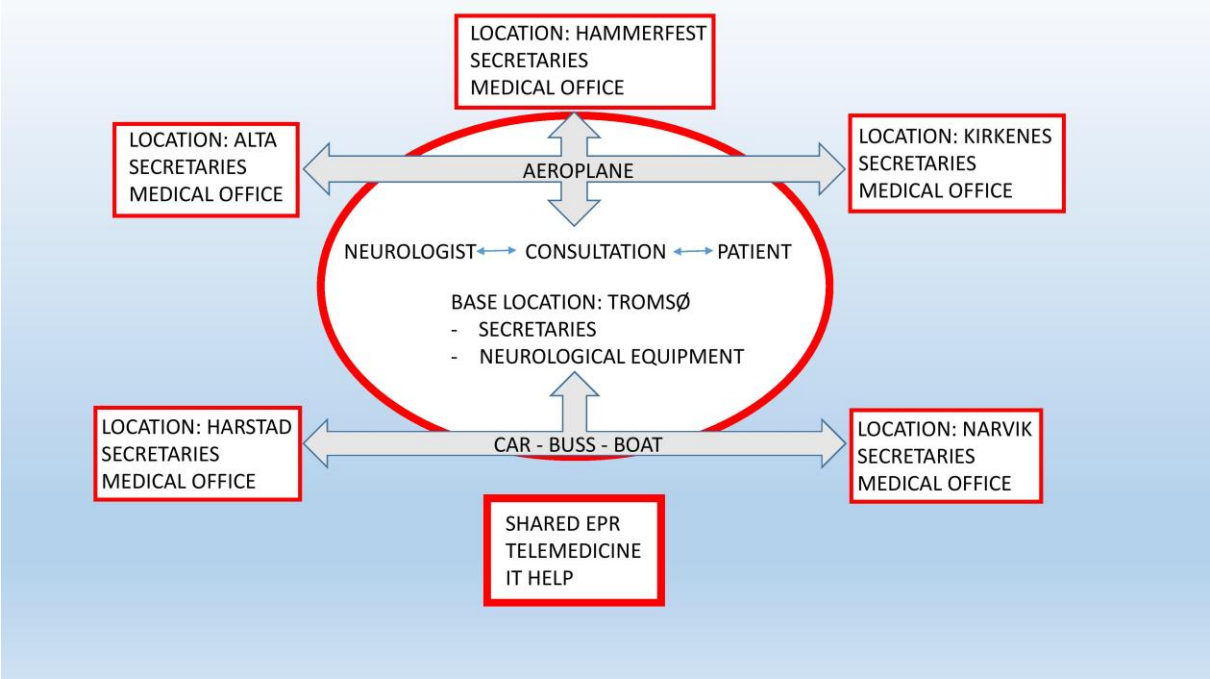


Figure 13 Key actors and actants in a future perspective of the neurologic situation in Northern Norway. A shared Electronic Patient Record (EPR) has already "replaced" all the local patient records. Implementation of telemedicine will probably lead to increased power and importance of the neurologic base in Tromsø, increased power and importance of the Information Technology (IT) help, and less travelling by headache patients, neurologists and other health care personnel. In general, such a change may additionally lead to realignment of neurologic patient follow-up, i.e. implementation of telemedicine may lead to less travel locations and to more follow-up by the general practitioner in the replacement of traditional neurologic follow-up.

8. CONCLUSIONS

This thesis shows that a telemedicine consultation is a good alternative to a traditional specialist headache consultation. It documents that most patients with nonacute headaches accept telemedicine, and that these patients are not less satisfied with telemedicine compared to a traditional in-person consultation. Although the trial is not a cost-effectivity study per se, it strongly suggests that telemedicine is cost-effective, and that the consultations are feasible. When selecting patients by given criteria, telemedicine is safe, and non-inferior to the traditional visit. Additionally, this study provides evidence that consulting patients with nonacute headaches without performing clinical neurologic examination is safe.

I suggest increased implementation of this consultation type in many neurologic departments, to increase access to specialist and offer better and more convenient follow-up [11, 12, 14, 35]. The trial, which this thesis is built on, is a good foundation for establishing telemedicine as a supplement for patients with nonacute headaches in the region of Tromsø University hospital, but probably also for many other health regions around the world. Therefore, our next step will be to implement telemedicine into clinical practice, with direct audio- and video communication from the Department of Neurology in Tromsø to headache patients' homes.

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10. Errata

Paper I

VAS, P = 0.49 not 0.82

HIT-6, P = 0.82, not 0.49

Paper IV

Paper IV is in a proof version. The final article will probably be published in July 2017.

Appendix I

Work instructions

Arbeidsbeskrivelse:

1. Søknader på pasienter med **hodepine** ”plukkes opp” fra søknadsbunken. Disse identifiseres via funksjonen ”eksterne søknader” som installeres via ”Help-desk”. Pasienter som ikke fyller kriteriene overføres til ekspedisjonen for vanlig timeoppsett (”nevrologiske henvisninger”), mens pasienter som oppfyller kriteriene overføres til KM, SIB eller CW for behandling.

2. Hvis kriteriene er oppfylt, sendes informasjonsbrev til pasienten. Deretter tas det kontakt med pasienten telefonisk for å sjekke om de aksepterer telemedisin og er interessert. Hvis pasienten samtykker (muntlig), oversendes **samtykkeskjema, spørreskjema og innkallingsbrev** til pasienten, og pasienten inkluderes i prosjektet.

- Hvis pasienten ikke gir samtykke sendes henvisningen tilbake til ansvarlig nevrolog som vurderer søknaden på vanlig måte.

3. Randomiseringskontoret kontaktes for å få randomisert nummer – telemedisin eller vanlig konsultasjon. **Randomiseringstelefon: 776 69117** (Ingrid Sandstad). Åpningstider: Mellom kl. **0800-1530**. Pasientene informeres om dette etter at de har kommet til sykehuset. Selve randomiseringen kan foretas i forkant (det avtales med randomiseringskontoret hvor lang tid man kan akseptere + prosedyre for å randomisere per lege, dvs. at det er tilfeldig hvilken lege som undersøker)

4. Pasienten **informerers om prosjektet etter at de har møtt opp** og det taes **blodtrykk, høyde og vekt (dette gjøres på dagenheten)**. Spørreskjemaet gjennomgåes for å kontrollere at det er utfylt riktig. Sykepleier følger pasienten til konsultasjonen.

5. **Nevrolog utfører enten telemedisinsk eller vanlig konsultasjon etter protokoll**. Konsultasjonen avsluttes på vanlig måte, og ansvarlig nevrolog gjør registreringsarbeidet i DIPS (avslutter eller setter opp til ny time)

6. Anna Kirsti oppdaterer **administrativ protokoll og følger opp med utsendelse og innhenting av spørreskjema etter 3 og 12 mnd**.

7. Administrator sender spørreskjema med frankert svarkonvolutt/Questback til pasientene etter 3 mnd og 12 mnd. og fyller ut administrativ protokoll. Det er viktig at tidsfristene overholdes. Purring hvis pasienten ikke svarer innen **2 uker**.

8. Dataregistrering i statistikkprogram utføres kontinuerlig av prosjektmedarbeiderne.

Appendix II

Data from referral letters

Telemedisinsk konsultasjon for hodepine

En randomisert studie blant hodepinepasienter henvist fra fastlege til nevrolog

Innhold

1. Registrere informasjon fra henvisningen (nevrolog)
2. Telefonintervju (prosjektkoordinator)
    a. Informasjon om prosjektet
    b. Avklare inklusjonskriterier og akseptans av telemedisin, (dvs. om pasienten egner seg for å være med)
    c. Registrere telefonnummer og e-post adresse
3. Spørreskjema (Fylles ut ved oppmøte før konsultasjon)
4. Konsultasjon hos nevrolog
5. Tre-måneders oppfølging (Student)
    a. Sende ut spørreskjema
    b. Evt. purre
6. Tolv-måneders oppfølging (Student)
    a. Sende ut spørreskjema
    b. Evt. purre

Pasient randomiseringsnummer: (0 til 400, første pasient starter på nr. 22)

Kjønn: 1. mann 2. kvinne

Alder:

1. Opplysninger hentet fra henvisningen

1a. Årsak til henvisning (sett ett kryss)

____ Avklare diagnosen

____ Behandling av hodepinen

____ Henvisningsårsaken fremgår ikke av søknaden

____ Annet, beskriv_____

1b. Diagnose fra henvisningen

____ Migrene

____ Tensjonshodepine

____ Migrene+tensjonshodepine

____ Cluster

____ Hodepine (uspesifisert)

____ Fremgår ikke

____ Annen diagnose

2. Hvem henviste? (sett ett kryss)

____ Fastlegen

____ Vikarlege

____ Turnuslege

____ Andre, beskriv_____

3. Avklaring av inklusjonskriterier så langt som mulig basert på henvisningen (kryss av)

____ Alder 16-65 år

____ Ikke vært hos nevrolog de siste 2 år pga. hodepine

____ Ingen kjent sykdom som kan forklare hodepinen

____ Ventetid under 4 måneder

____ Behersker norsk språk

4. Påvirker hodepinen utførelsen av daglige aktiviteter? (sett ett eller flere kryss kryss)

____ Nei

____ Ja, sykmeldt / arbeidsufør

____ Ja, hodepinen begrenser utførelsen av daglige aktiviteter

____ Ikke angitt i henvisningen

5. Foreligger det opplysninger om utredning og behandling i søknaden? (sett ett eller flere kryss)

____ Nei

____ Ja, smertestillende medikamenter, hvilke(n)_____

____ Ja, andre medikamenter mot hodepine, hvilke(n) _____

____ Ja, migrenemedisiner, hvilke(n) _____

____ Ja, blodtrykksmedisin mot hodepine

____ Ja, epilepsimedisin eller andre medisiner mot hodepine

____ Andre medikamenter

____ Medikamentbruk ikke angitt i henvisningen

____ Fysioterapi

____ Andre behandlingsformer

____ MR undersøkelse

____ CT undersøkelse

Appendix III

Participants' pre-filled questionnaire

Deltaker nr _____

Telemedisinsk konsultasjon for hodepine

En randomisert studie blant hodepinepasienter henvist fra fastlege til nevrolog

Spørreskjema 1

Spørreskjemaet fylles ut og tas med til undersøkelsen ved
Nevrologisk avdeling, UNN

3. Spørreskjema (blodtrykk måles av forskningsmedarbeider, resten gjør pasienten selv)

6. Personlige data

____ Mann

____ Kvinne

____ Gift/samboer

____ Enslig

Høyde: ……cm

Vekt:……kg

Blodtrykk: ...../……

7. Hva var hovedhensikten med å bli henvist til nevrolog. Sett ett eller flere kryss

____ Diagnostisk avklaring (usikker diagnose)

____ Manglende effekt av behandling for hodepine

____ Mistanke om annen sykdom som årsak til hodepinen

____ Kronisk hodepine

____ Forsikring for pasienten eller pårørende

8. Har du tidligere vært undersøkt av nevrolog p.g.a. hodepine?

____ Nei

____ Ja, når (år) _____

9. Har du noen gang vært innlagt på sykehus p.g.a. hodepine?

____ Nei

____ Ja, når (årstall) _____

10. Hvem foreslo å henvise deg til nevrolog for hodepine? (sett ett kryss)

- ↑ Fastlegen
- ↑ Andre leger (hvem)_____
- ↑ Andre helsepersoner (hvem)_____
- ↑ Pasienten selv
- ↑ Pårørende
- ↑ Andre (hvem)_____

11. Hva er din høyeste fullførte utdanning? (ett kryss)

____ Grunnskole eller folkehøyskole

____ Yrkesfaglig videregående, yrkesskole eller realskole

____ Allmennfaglig videregående skole eller gymnas

____ Høyskole eller universitet, mindre enn 4 år

____ Høyskole eller universitetet, 4 år eller mer

12. Hvor mange års skolegang har du? (ta med folke- og ungdomsskole)

____ år

13a. Hva er din hovedaktivitet? (sett ett kryss)

____ Yrkesaktiv heltid. Angi yrke: _____

____ Militærtjeneste

____ Yrkesaktiv deltid

____ Arbeidsledig

____ Hjemmeværende

____ Pensjonist/trygdet

____ Student

____ Fødselspermisjon

____ Annet, beskriv _____

13b. Har du skiftarbeid?

____ Ja

____ Nei

14. Mottar du noen av følgende ytelser?

____ Alderstrygd, førtidspensjon (AFP) eller etterlattepensjon

____ Sykepenger (er sykmeldt)

____ Rehabiliterings-/attføringspenger

____ Uføreytelse/pensjon, hel

____ Uføreytelse/pensjon, delvis

____ Dagpenger eller arbeidsledighet

____ Overgangsstønad

____ Sosialhjelp/-stønad

____ Annet, beskriv _____

15. Hvis du er sykmeldt; hva er årsaken til det?

____ Hodepine

____ Annet, beskriv _____

15b. Hvor lenge har du vært sykmeldt?

____ Uker

16. Familiær situasjon / hodepine i familien

____ Gift, samboer

____ Enslig

____ Annet, beskriv _____

____ Nærmeste slektninger (foreldre, barn) har lignende hodepine som meg

____ Andre slektninger (besteforeldre, tanter, onkler, søskenbarn etc) har lignende hodepine som meg (sett strek under)

17.Hvor ofte driver du mosjon? (med mosjon mener vi at du for eksempel går en tur, går på ski, svømmer eller driver trening/idrett)

____ Aldri

____ Sjeldnere enn en gang i uken

____ En gang i uken

____ 2-3 ganger per uke

____ Omtrent hver dag

18. Hvor hardt mosjonerer du da i gjennomsnitt?

____ Tar det rolig uten å bli andpusten eller svett

____ Tar det så hardt at jeg blir andpusten og svett

____ Tar meg neste helt ut

____ Mosjonerer ikke

19. Hvor lenge holder du på hver gang i gjennomsnitt?

____ Mindre enn 15 minutter

____ 15-29 minutter

____ 30 minutter – 1 time

____ Mer enn 1 time

20. Bruker du medikamenter eller andre preparater?

____ Smertestillende

____ P-piller

____ Annen medisin, hvilken _____

____ Ingen medisiner (reseptbelagte og/eller reseptfrie)

____ Kosttilskudd, hvilke(n) _____

____ Naturpreparater, hvilke(n) _____

____ Andre ”alternative preparater”, hvilke(n) _____

____ Annen alternativ behandling, hvilken(n) _____

21. Hvor ofte bruker du smertestillende medisiner? Sett ett kryss

____ Hver dag

____ Minst 3 dager per uke

____ 1-2 dager per uke

____ Mindre enn 1 dag per uke, men minst annenhver uke

____ Sjeldnere enn hver annen uke

____ Minst 14 dager per måned

22. Hvis du bruker smertestillende, oppgi navn på medisinen(e):

_____

23. Bruker du migrenemedikamenter?

____ Ingen

____ Imigran/Zomig/Naramig/Maxalt/Relpax/Almogran (sett strek under)

24. Hvor ofte bruker du migrenemedisiner?

____ Hver dag

____ Minst 3 dager per uke

____ 1-2 dager per uke

____ Mindre enn 1 dag per uke, men minst annenhver uke

____ Sjeldnere enn hver annen uke

____Minst 14 dager per måned

25. Hvis annen medisin, skriv navn på medikamentet

_____

25a. Hvor ofte drikker du alkohol?

____ Aldri

____ Månedlig eller sjeldnere

____ 2-4 ganger hver måned

____ 2-3 ganger pr. uke

____ 4 eller flere ganger pr. uke

25b. Hvor mange enheter alkohol (en øl, et glass vin, eller en drink) tar du vanligvis når du drikker?

____ 1-2

____ 3-4

____ 5-6

____ 7-9

____ 10 eller flere

25c. Har du røykt / røyker du daglig?

____ Ja, nå

____ Ja, tidligere

____ Aldri

26. VAS (smerteskala der du skal angi grad av smerte)

Vi ber deg angi graden (intensiteten) av hodepine fra svært lite til svært mye. Skalaen går fra 1-10 der 1 er lite intens hodepine, mens 10 er svært intens hodepine.

Min nåværende hodepine: _____ (angi et tall fra 0-10)

27. HIT-6

Spørre skjema om innvirkningen av hodepine på livet ditt. Dette spørreskjemaet er blitt utformet for å hjelpe deg med å beskrive og gi uttrykk for hvordan du har det, og hva du ikke kan gjøre pga. hodepine.

Vennligst kryss av i passende rute for hvert spørsmål:

1. Når du har hodepine, hvor ofte er smertene sterke? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
2. Hvor ofte begrenser hodepinen deg til å utføre vanlige daglige gjøremål slik som husarbeid, arbeid, skolearbeid eller å ha sosial omgang? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
3. Når du har hodepine, hvor ofte ønsker du at du kunne legge deg ned? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
4. I de siste 4 ukene, hvor ofte har du følt deg for trett til å utføre arbeid eller daglige gjøremål på grunn av hodepine? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
5. I de siste 4 ukene, hvor ofte har du følt deg lut lei eller irritert på grunn av hodepine? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
6. I de siste 4 ukene, hvor ofte har hodepinen begrenset din evne til å konsentrere deg om arbeid eller daglige gjøremål? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid

Appendix IV

Structured interview (The consultation)

4. Konsultasjon hos nevrolog

28. Undersøker: _____

29. US dato: _____

30. Ventetid (dager) _____

31. Tidspunkt for start av konsultasjon: Time _____ Min _____

32. Spørreskjemaet som pasienten har fylt er sjekket og funnet i orden

___ Ja

33. VAS på konsultasjonstidspunktet: _____

34. HIT-6 på konsultasjonstidspunktet: _____

35. Randomisert til:

____ Telemedisin

____ Ordinær konsultasjon

36. Spørsmål som stilles alle pasientene (som hjelp til å klassifisere hodepinen). Gjelder den mest fremtredende hodepinen (hvis pasienten har flere hodepiner) + nevrologens vurderinger

1. Er hodepinen ____ konstant eller ____ anfallsvis? _____ begge deler
2. Er hodepinen ____ ensidig eller ____ dobbeltsidig eller ____ begge deler
3. Er hodepine ____ pressende / klemmende _____ pulserende ____ stikkende
4. Hvor lenge varer hodepinen? ____ timer eller dager (stryk det som ikke passer)
5. Hvor hyppig kommer hodepinen? ____ antall ganger om dagen, uka, måneden (stryk)
6. Har pasienten tilleggssymptomer? Hvilke(n) _____
7. Er hodepinen ____ mild, ____ moderat eller ____ sterk? (kryss av)
8. Forekommer det ____ en eller ____ flere typer hodepine? (kryss av). Antall: _____
9. Utløsende faktorer? Hvilke(n) _____
10. Er det forvarselsymptomer før hodepinen ____ Nei ____ Ja, hvilke(n)_____
11. Fysisk aktivitet fører til 1. forverring, 2. bedring 3. ingen innvirkning
12. Hodepinen er relatert til menstruasjon 1. Ja 2. Nei

37. Spørsmål som stilles alle pasientene (for å kartlegge sekundær hodepine)

1. Ny eller annerledes hodepine
2. ”Thunderclap” hodepine (max intensitet innen sekunder til minutter)
3. Alvorligste hodepine noen gang
4. Ledsagende fokale nevrologiske symptomer
5. Endring av eksisterende hodepine
6. Nyoppstått hodepine etter 50 år
7. Hodepine assosiert med systemiske symptomer (feber, vekttap etc)

38. Antall hodepinedager siste måned:

____ over 15 dager

____ 7-15 dager

____ under 7 dager

39. Hvis varigheten av hodepinen er < 4 døgn (dvs. dersom migrene eller annen anfallsvis hodepine forekommer): Hvor mange ”anfall” per måned (gjennomsnitt siste 3 måneder):

____ anfall

40. Ved daglig hodepine: Hvor mange ”anfall” per dag (gjennomsnitt siste 3 måneder)?

____ anfall

41. Har symptomene endret seg i ventetiden? (sett ett eller flere kryss)

____ Ja, bedre

____ Antall hodepinedager har avtatt

____ Hodepinen har blitt mindre intens

____ Annet, beskriv _____

____ Nei, uforandret

____ Nei, verre

____ Antall hodepinedager har økt

____ Hodepinen har blitt mer intens

____ Annet, beskriv _____

42. Bortsett fra hodepine, hvilke andre sykdommer har du eller har du hatt (sett strek under)

____ Frisk

____ Høyt blodtrykk

____ Andre nevrologiske sykdommer, beskriv _____

____ Andre systemiske, ikke-nevrologiske sykdommer _____

43. Har du i løpet av det siste året hatt smerter eller stivhet i nakke- og/eller skulder muskulaturen som har vart minst 3 måneder sammenhengende?

____ JA

____ NEI

44. Har du i løpet av det siste året hatt smerter eller stivhet i muskulaturen (utenom nakke/skuldre) som har vart minst 3 måneder sammenhengende?

____ JA

____ NEI

45. Hvis ja, angi hvilken muskulatur _____

46. Alder da hodepinen begynte og varighet av hodepinen (år):

____ alder

____ varighet

47. Klassifikasjon av hodepine (IHS-kriteriene). Sett 1 foran den mest fremtredende hodepinen, deretter 2,3 osv for de øvrige hodepinene avhengig av hvor fremtredende de er

____Migrene uten aura

____ Migrene med aura

____ Familiær hemiplegisk migrene

____ Basilarismigrene

____ Kronisk migrene

____ Episodisk tensjonshodepine

____ Kronisk tensjonshodepine

____ Episodisk hortons hodepine (klasehodepine)

____ Kronisk hortons hodepine (klase)

____ Episodisk CPH

____ Kronisk CPH

____ Kronisk daglig hodepine

____ Medikament overforbrukshodepine (mistanke)

____ Annen primær hodepine (jfr. IHS-kriteriene), beskriv: _____

____ Annen trigeminoautonom hodepine, beskriv _____

____ Ikke-klassifiserbar hodepine (verken primær eller sekundær hodepine)

48.Informasjon om diagnosen er gitt til pasienten

____ Ja

____ Nei

50. Har du søvnproblemer?____

____ Nei

____ Ja

51a Når du har søvnproblemer, har du minst 3 ganger per uke, og i mer enn 1 måned hatt problemer med å sovne inn og/eller vansker med å holde søvnen ved like?

____ Nei

____ Ja

51b Hvis anfallsvis hodepine – har du mer anfall om natten?

____ Nei

____ Ja

51c Hvis anfallsvis hodepine – har du mer anfall om dagen?

____ Nei

____ Ja

51c Hvis anfallsvis hodepine – har du mer anfall i helgene?

____ Nei uendret

____ Nei mindre

____ Ja mer

51d Hvis anfallsvis hodepine (også kronisk hodepine med anfallsvise forverringer) – har du mer anfall i den lyse eller mørke årstiden (om sommeren)?

____ Nei

____ Ja, mer anfall i den lyse årstiden

____ Ja, mer anfall i den mørke årstiden

____ Ja, mer anfall i overgangen til den lyse årstiden

____ Ja, mer anfall i overgangen til den mørke årstiden

____ Nei, ingen månedsvariasjon

____ Ja, mer anfall følgende måned(er): _____

51e Hvis anfallsvis hodepine - er du lysoverfølsom mellom anfallene

____ Nei

____ Ja

51f Brukes ”hjelpemidler” for å redusere lyspåvirkningen (slå av lys, solbriller, persienner etc)?

____ Nei

____ Ja, beskriv hvilket tiltak: _____

51g Er sollys eller annet sterkt lys en utløsende mekanisme for hodepine?

____ Ja

____ Nei

52. Er det startet behandling mot hodepine ved konsultasjonen?

____ Nei

____ Nei, men riktig bruk av medikamenter ble anbefalt pga. feilbruk, beskriv_____

____ Ja, medikamenter (hvilke) _____

____ Ja, annen behandling (beskriv) _____

52b Er det gitt råd til pasienten om hvordan hodepinen kan takles bedre?

____ Ja, hvilke råd: _____

____ Nei

53. Har nevrolog rekvirert supplerende undersøkelser?

____ Nei

____ Ja, MR/CT (beskriv) _____

____ Ja, annen utredning (beskriv) _____

54a. Er det gjort avtale om oppfølging?

____ Nei

____ Ja, oppfølging hos fastlegen (hva skal følges opp) _____

____ Ja, oppfølging hos nevrolog (hva skal følges opp)_____

54b Er diagnosen fra nevrolog endret i forhold til henvisningsbrevet

____ Nei

____ Ja, diagnosen fra henvisningen var riktig, men nevrolog fant en eller flere tilleggshodepiner

____ Ja, diagnosen fra feil, dvs. at nevrolog har anført ny diagnose

55. Tidspunkt for avslutning av konsultasjon:

Time _____

Min _____

56. Konsultasjonstid: _____ minutter

57. Problemer med videoutstyret:

____ Ja, beskriv _____

____ Nei

____ Fornøyd med videooverføring

____ Fornøyd med Lydoverføring

Appendix V

Participants' 3-month questionnaire

Deltaker nr_____

Telemedisinsk konsultasjon for hodepine

En randomisert studie blant hodepinepasienter henvist fra fastlege til nevrolog

Spørreskjema 2

3-måneders oppfølging

Spørreskjemaet fylles ut og returneres
Nevrologisk avdeling, UNN, i vedlagte svarkonvolutt

59. Dato for utfylling: _____

60. Var du fornøyd med konsultasjonen hos nevrolog?

____ Ja

____ Nei, hvorfor _____

____ Jeg var misfornøyd med å treffe spesialist gjennom videooverføring

____ Jeg var fornøyd med å treffe spesialist gjennom videooverføring

61. Har hodepinen forandret seg siden konsultasjonen? Sett ett eller flere kryss

____ Ja, bedre

____ Antall hodepinedager har avtatt

____ Hodepinen har blitt mindre intens

____ Annet

____ Nei, uforandret

____ Nei, verre

____ Antall hodepinedager har økt

____ Hodepinen har blitt mer intens

____ Misfornøyd med å treffe spesialist gjennom videooverføring

____ Annet

62. Hvor mange hodepinedager har du hatt i gjennomsnitt de siste 3 måneder?

____ over 15 dager

____ 7-15 dager

____ under < 7 dager

63. Hvis varigheten av hodepinen er under 4 døgn: Hvor mange slike ”anfall” per måned har du hatt i gjennomsnitt de siste 3 måneder?

____ anfall per måned

64. Hvis du har daglig hodepine: Hvor mange ”anfall” per dag (gjennomsnitt siste 3 måneder)?

_____ hodepineanfall per dag

65. Bruker du medikamenter nå?

____ Smertestillende

____ P-piller

____ Annen medisin, hvilken _____

____ Ingen medisiner (reseptbelagte og/eller reseptfrie)

____ Kosttilskudd, hvilke(n) _____

____ Naturpreparater, hvilke(n) _____

____ Andre ”alternative preparater”, hvilke(n) _____

____ Annen alternativ behandling, hvilken(n) _____

66. Hvor ofte bruker du smertestillende medisiner?

____ Hver dag

____ Minst 3 dager per uke

____ 1-2 dager per uke

____ Mindre enn 1 dag per uke, men minst annenhver uke

____ Sjeldnere enn hver annen uke

____ Minst 15 dager per måned

67. Hvis du bruker smertestillende, oppgi navn på medisinen(e):

_____

68. Bruker du migrenemedikamenter?

____ Nei

____ Imigran/Zomig/Naramig/Maxalt/Relpax/Almogran (sett strek under)

69. Hvor ofte bruker du migrenemedisiner?

____ Hver dag

____ Minst 3 dager per uke

____ 1-2 dager per uke

____ Mindre enn 1 dag per uke, men minst annenhver uke

____ Sjeldnere enn hver annen uke

____ Minst 15 dager per måned

70. Hvis annen medisin, skriv navn på medikamentet

_____

71. Hvilken diagnose fikk du hos nevrolog?

_____

____ Husker ikke

72. Dersom du fikk anbefalt medikamentell behandling hos nevrolog; har du brukt disse som foreskrevet?___

____ Ja

____ Nei

Hvis ikke; hvorfor: _____

73. VAS (smerteskala fra 0-10)

Vi ber deg angi graden (intensiteten) av hodepine fra svært lite til svært mye. Skalaen går fra 0-10 der 0 er ingen hodepine, mens 10 er svært intens hodepine.

Min nåværende hodepine: _____ (angi et tall fra 0-10)

74. HIT-6

Spørre skjema om innvirkningen av hodepine på livet ditt. Dette spørreskjemaet er blitt utformet for å hjelpe deg med å beskrive og gi uttrykk for hvordan du har det, og hva du ikke kan gjøre pga. hodepine.

Vennligst kryss av i passende rute for hvert spørsmål:

1. Når du har hodepine, hvor ofte er smertene sterke? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
2. Hvor ofte begrenser hodepinen deg til å utføre vanlige daglige gjøremål slik som husarbeid, arbeid, skolearbeid eller å ha sosial omgang? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
3. Når du har hodepine, hvor ofte ønsker du at du kunne legge deg ned? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
4. I de siste 4 ukene, hvor ofte har du følt deg for trett til å utføre arbeid eller daglige gjøremål på grunn av hodepine? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
5. I de siste 4 ukene, hvor ofte har du følt deg lut lei eller irritert på grunn av hodepine? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
6. I de siste 4 ukene, hvor ofte har hodepinen begrenset din evne til å konsentrere deg om arbeid eller daglige gjøremål? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid

75. Hva er din hovedaktivitet? (sett ett kryss)

____ Yrkesaktiv heltid

____ Militærtjeneste

____ Yrkesaktiv deltid

____ Arbeidsledig

____ Hjemmeværende

____ Pensjonist/trygdet

____ Student

____ Annet, beskriv _____

76. Mottar du noen av følgende ytelser?

____ Alderstrygd, førtidspensjon (AFP) eller etterlattepensjon

____ Sykepenger (er sykmeldt)

____ Rehabiliterings-/attføringspenger

____ Uføreytelse/pensjon, hel

____ Uføreytelse/pensjon, delvis

____ Dagpenger eller arbeidsledighet

____ Overgangsstønad

____ Sosialhjelp/-stønad

____ Annet, beskriv _____

77. Hvis du er arbeidsufør pga. hodepine; hvor lenge har arbeidsuførheten vart:

____ uker

78. Har det vært endring i din trygdestatus i oppfølgingstiden?

____ Nei

____ Ja, friskmeldt pga. hodepine

____ Ja, friskmeldt pga. sykdom

____ Ja, sykmeldt pga. hodepine (tidligere vært arbeidsfør)

____ Annet, beskriv

79. Antall konsultasjoner pga. hodepine hos fastlegen i oppfølgingstiden:

____ konsultasjoner

80. Årsak(er) til konsultasjon hos fastlegen i oppfølgingstiden

1. konsultasjon
   ____ Hodepine

   ____ Annet, beskriv: _____
2. konsultasjon
   ____ Hodepine

   ____ Annet, beskriv: _____
3. konsultasjon
   ____ Hodepine

   ____ Annet, beskriv: _____

Appendix VI

Participants' 12-month questionnaire

Deltaker nr_____

Telemedisinsk konsultasjon for hodepine

En randomisert studie blant hodepinepasienter henvist fra fastlege til nevrolog

Spørreskjema 3

12-måneders oppfølging

Spørreskjemaet fylles ut og returneres
Nevrologisk avdeling, UNN, i vedlagte svarkonvulutt

6. Tolv-måneders oppfølging (spørreskjema)

Dato for utfylling: _____

81. Var du fornøyd med konsultasjonen hos nevrolog pga. hodepine for ett år siden?

____ Ja

____ Nei

Angi på en skala fra 0 til 10 der 0 er minst fornøyd og 10 er mest fornøyd:

____ Jeg var misfornøyd med å treffe spesialist gjennom videooverføring

____ Jeg var misfornøyd med å treffe spesialisten direkte gjennom konsultasjon

Var du fornøyd med informasjonen om din hodepine hos nevrolog?

____ Ja

____ Nei

Var du fornøyd med diagnosen du fikk hos nevrolog?

____ Ja

____ Nei

Var du fornøyd med de rådene du fikk av nevrolog for å bedre hodepinen?

____ Ja

____ Nei

Var du fornøyd med medisinen du fikk av nevrolog for hodepine?

____ Ja

____ Nei

Var du fornøyd med kommunikasjonen med nevrolog?

____ Ja

____ Nei

82. Er du fornøyd med behandlingen og oppfølging for din hodepine av fastlegen?

____ Ja

____ Nei

Var du fornøyd med informasjonen om din hodepine hos fastlegen?

____ Ja

____ Nei

Var du fornøyd med diagnosen du fikk hos fastlegen?

____ Ja

____ Nei

Var du fornøyd med de rådene du fikk av fastlegen for å bedre hodepinen?

____ Ja

____ Nei

Var du fornøyd med medisinen du fikk av fastlegen for hodepine?

____ Ja

____ Nei

Var du fornøyd med kommunikasjonen med fastlegen?

____ Ja

____ Nei

83. Har hodepinen forandret seg siden konsultasjonen? Sett ett eller flere kryss

____ Ja, bedre

____ Antall hodepinedager har avtatt

____ Hodepinen har blitt mindre intens

____ Annet_____

____ Nei, uforandret

____ Nei, verre

____ Antall hodepinedager har økt

____ Hodepinen har blitt mer intens

____ Annet_____

84. Hvor mange hodepinedager har du hatt i gjennomsnitt de siste 3 måneder:

____ over 15 dager

____ 7-15 dager

____ under < 7 dager

85. Hvis varigheten av hodepinen er under 4 døgn: Hvor mange slike ”anfall” per måned har du hatt i gjennomsnitt de siste 3 måneder?

____ anfall per måned

86. Hvis du har daglig hodepine: Hvor mange ”anfall” per dag (gjennomsnitt siste 3 måneder): _____ hodepineanfall per dag

87. Bruker du medikamenter eller andre preparater?

____ Smertestillende_____

____ P-piller

____ Annen medisin, hvilken _____

____ Ingen medisiner (verken reseptbelagte eller reseptfrie)

____ Kosttilskudd, hvilke(n) _____

____ Naturpreparater, hvilke(n) _____

____ Andre ”alternative preparater”, hvilke(n) _____

____ Annen alternativ behandling, hvilken(n) _____

88. Hvor ofte bruker du smertestillende medisiner?

____ Hver dag

____ Minst 3 dager per uke

____ 1-2 dager per uke

____ Mindre enn 1 dag per uke, men minst annenhver uke

____ Sjeldnere enn hver annen uke

____ Minst 14 dager per måned

89. Hvis du bruker smertestillende, oppgi navn på medisinen(e):

_____

90. Bruker du migrenemedikamenter?

____ Nei

____ Imigran/Zomig/Naramig/Maxalt/Relpax/Almogran (sett strek under)

91. Hvor ofte bruker du migrenemedisiner?

____ Hver dag

____ Minst 3 dager per uke

____ 1-2 dager per uke

____ Mindre enn 1 dag per uke, men minst annenhver uke

____ Sjeldnere enn hver annen uke

____ Minst 14 dager per måned

92. Hvis annen medisin, skriv navn på medikamentet

_____

93. Hvilken diagnose fikk du hos nevrolog? _____

____ Husker ikke

94. Dersom du fikk anbefalt medikamentell behandling hos nevrolog, hvilken?_____; ar du brukt den/disse som foreskrevet?

____ Ja

____ Nei

Hvis ikke; hvorfor: _____

95. VAS (smerteskala fra 0-10)

Vi ber deg angi graden (intensiteten) av hodepine fra svært lite til svært mye. Skalaen går fra 1-10 der 1 er lite intens hodepine, mens 10 er svært intens hodepine.

Min nåværende hodepine: _____ (angi et tall fra 0-10)

96. Har du tatt bildediagnostikk av hodet?

____ Ja MR

____ Ja CT

____ Ja Begge deler

____ Nei

97. HIT-6

Vennligst kryss av i passende rute for hvert spørsmål:

1. Når du har hodepine, hvor ofte er smertene sterke? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
2. Hvor ofte begrenser hodepinen deg til å utføre vanlige daglige gjøremål slik som husarbeid, arbeid, skolearbeid eller å ha sosial omgang? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
3. Når du har hodepine, hvor ofte ønsker du at du kunne legge deg ned? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
4. I de siste 4 ukene, hvor ofte har du følt deg for trett til å utføre arbeid eller daglige gjøremål på grunn av hodepine? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
5. I de siste 4 ukene, hvor ofte har du følt deg lut lei eller irritert på grunn av hodepine? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid
6. I de siste 4 ukene, hvor ofte har hodepinen begrenset din evne til å konsentrere deg om arbeid eller daglige gjøremål? ↑Aldri ↑Sjelden↑Noen ganger ↑Svært ofte ↑Alltid

98. Hva er din hovedaktivitet nå? (sett ett kryss)

____ Yrkesaktiv heltid

____ Militærtjeneste

____ Yrkesaktiv deltid

____ Arbeidsledig

____ Hjemmeværende

____ Pensjonist/trygdet

____ Student

____ Annet, beskriv _____

99. Mottar du noen av følgende ytelser?

____ Alderstrygd, førtidspensjon (AFP) eller etterlattepensjon

____ Sykepenger (er sykmeldt)

____ Rehabiliterings-/attføringspenger

____ Uføreytelse/pensjon, hel

____ Uføreytelse/pensjon, delvis

____ Dagpenger eller arbeidsledighet

____ Overgangsstønad

____ Sosialhjelp/-stønad

____ Fødselspermisjon

____ Annet, beskriv _____

100. Hvis du er arbeidsufør pga. hodepine; hvor lenge har arbeidsuførheten vart:

____ uker

101. Har det vært endring i din trygdestatus i oppfølgingstiden?

____ Nei

____ Ja, friskmeldt pga. hodepine

____ Ja, friskmeldt pga. sykdom

____ Ja, sykmeldt pga. hodepine (tidligere vært arbeidsfør)

____ Annet, beskriv

102.Hvor ofte driver du mosjon? (med mosjon mener vi at du for eksempel går en tur, går på ski, svømmer eller driver trening/idrett)

____ Aldri

____ Sjeldnere enn en gang i uken

____ En gang i uken

____ 2-3 ganger per uke

____ Omtrent hver dag

103. Hvor hardt mosjonerer du da i gjennomsnitt?

____ Tar det rolig uten å bli andpusten eller svett

____ Tar det så hardt at jeg blir andpusten og svett

____ Tar meg neste helt ut

____ Mosjonerer ikke

104. Hvor lenge holder du på hver gang i gjennomsnitt?

____ Mindre enn 15 minutter

____ 15-29 minutter

____ 30 minutter – 1 time

____ Mer enn 1 time

105. Antall konsultasjoner pga. hodepine hos fastlegen etter konsultasjonen hos nevrolog for ett år siden:

____ konsultasjoner

106. Antall konsultasjoner pga. hodepine hos nevrolog etter konsultasjonen hos nevrolog for ett år siden:

____ konsultasjoner

107. Antall innleggelser på sykehus pga. hodepine etter konsultasjon hos nevrolog for ett år siden:

____ konsultasjoner

108. Sett i lys av min tidligere erfaring, vil jeg ved hodepine-konsultasjon hos spesialist foretrekke:

___Ordinær konsultasjon

___Videooverført konsultasjon

___Likegyldig

Appendix VII
Data from the Norwegian patient travel agency (Pasientreiser)

The cheapest means of public transport per headache patient from different municipalities to and from Tromsø University Hospital. Calculated with the Norwegian Patient Travel Agency probabilistic method.

Municipality/Location	€	NKR
Hammerfest	443	4000
Alta	443	4000
Kirkenes	443	4000
Varangerbotn	443	4000
Vardø	443	4000
Vadsø	443	4000
Bodø	443	4000
Vestre Jakobselv	443	4000
Sandnessjøen	443	4000
Gamvik	443	4000
Lakselv	443	4000
Hesseng	443	4000
Tana	443	4000
Kvalsund	443	4000
Øksfjord	443	4000
Hasvik	443	4000
Børselv	443	4000
Kjøllefjord	443	4000
Skarsvåg	443	4000
Bjørnevatn	443	4000
Nordvågen	443	4000
Båtsfjord	443	4000
Longyearbyen	443	4000
Dyfjord	443	4000
Karasjok	443	4000
Bjerka	443	4000
Honningsvåg	443	4000
Svanvik	443	4000
Rypefjord	443	4000
Melbu	443	4000
Kautokeino	443	4000
Havøysund	443	4000
Langfjordbotn	443	4000
Stokmarknes	443	4000
Sørvær	443	4000
Bogen i Lofoten	249	2250
Tovik	249	2250
Gratangen	249	2250
Ballangen	249	2250
Hamnvik	249	2250
Senjahopen	249	2250
Beisfjord	249	2250
Tennevold	249	2250

Grillefjord	249	2250
Hamnvik	249	2250
Bardu	249	2250
Gibostad	249	2250
Liland	249	2250
Fjordgård	249	2250
Flakstadvåg	249	2250
Kjøpsvik	249	2250
Grovfjord	249	2250
Stongelandeidet	249	2250
Kongsvik	249	2250
Harstad	83	750
Narvik	83	750
Finnsnes	83	750
Silsand	83	750
Sørstraumen	83	750
Sørkjosen	83	750
Sørreisa	83	750
Sørvik	83	750
Storslett	83	750
Rotsund	83	750
Vangsvik	83	750
Ankenesstrand	83	750
Evenskjær	83	750
Vannvåg	83	750
Burfjord	83	750
Bardu	83	750
Stakkvik	83	750
Bjerkvik	83	750
Rossfjordstraumen	83	750
Moen	83	750
Ankenes	83	750
Bardufoss	83	750
Bardufoss	33	300
Furuflaten	33	300
Hamneide	33	300
Hansnes	33	300
Karlstad	33	300
Kvaløya	33	300
Kvaløysletta	33	300
Laksvatn	33	300
Lyngseidet	33	300
Meistervik	33	300
Moen	33	300
Oteren	33	300
Ramfordbotn	33	300
Sjøvegan	33	300
Skjervøy	33	300
Sommarøya	33	300
Storsteinnes	33	300
Straumsbukta	33	300
Tromsø	6	50

Tromsdalen	6	50
Kvaløysletta	6	50
Tomasjord	6	50
Krokelvdalen	6	50
Kvaløya	6	50
Eidkjosen	6	50

Colour code:

Blue: Patients travelling by airplane (NKR 4000)

Red: Patients travelling by taxi and buss or boat (NKR 2250)

Orange: Patients living along the E6 road or can take the boat (NKR 750)

Yellow: Patients living outside Tromsø travelling by the district buss (NKR 300)

Green: Patients living in Tromsø City (NKR 50)

Study patients (N) location and travel cost in Euros (€) and Norwegian Kroner (NKR). Calculations of travel costs are based on the previous table.

Patient location	**N**	**€**	**NKR**
Alta	33	14619	132000
Ankenes	1	83	750
Ankenesstrand	5	415	3750
Ballangen	3	747	6750
Bardu	6	664	6000
Bardufoss	4	182	1650
Beisfjord	2	498	4500
Bjerka	1	443	4000
Bjerkvik	3	249	2250
Bjørnevatn	1	443	4000
Bodø	1	443	4000
Bogen i Lofoten	1	249	2250
Burfjord	1	83	750
Børselv	1	443	4000
Båtsfjord	2	886	8000
Dyfjord	1	443	4000
Eidkjosen	1	6	50
Evenskjær	4	332	3000
Finnsnes	9	747	6750
Fjordgård	1	249	2250
Flakstadvåg	1	249	2250
Furuflaten	1	33	300
Gamvik	1	443	4000
Gibostad	1	249	2250
Gratangen	1	249	2250
Grovfjord	1	249	2250

Gryllefjord	1	249	2250
Hammerfest	18	7974	72000
Hamneide	1	33	300
Hamnvik	3	747	6750
Hansnes	4	132	1200
Harstad	10	830	7500
Hasvik	4	1772	16000
Havøysund	1	443	4000
Hesseng	2	886	8000
Honningsvåg	2	886	8000
Karasjok	3	1329	12000
Karlstad	3	99	900
Kautokeino	3	1329	12000
Kiberg	1	443	4000
Kirkenes	3	1329	12000
Kjøllefjord	1	443	4000
Kjøpsvik	1	249	2250
Kongsvik	1	249	2250
Krokelvdalen	6	33	300
Kvalsund	3	1329	12000
Kvaløya	6	63	550
Kvaløysletta	19	249	2200
Lakselv	4	1772	16000
Laksvatn	1	33	300
Langfjordbotn	1	443	4000
Liland	2	498	4500
Longyearbyen	2	886	8000
Lyngseidet	2	66	600
Meistervik	4	132	1200
Melbu	1	443	4000
Moen	5	215	1950
Narvik	16	1329	12000
Nordvågen	1	443	4000
Oteren	1	33	300
Ramfjordbotn	2	66	600
Rossfjordstraumen	2	166	1500
Rotsund	1	83	750
Russenes	1	443	4000
Rypefjord	1	443	4000
Sandnessjøen	1	443	4000
Senjahopen	3	747	6750
Silsand	4	332	3000
Sjøvegan	3	99	900
Skarsvåg	1	443	4000
Skjervøy	6	198	1800
Sommarøya	1	33	300
Stakkvik	2	166	1500
Stokmarknes	1	443	4000
Stongelandeidet	1	249	2250
Storslett	7	581	5250
Storsteinnes	4	132	1200
Straumsbukta	1	33	300

Svanvik	1	443	4000
Sørkjosen	3	249	2250
Sørreisa	14	1162	10500
Sørstraumen	1	83	750
Sørvik	1	83	750
Sørvær	2	886	8000
Talvik	1	443	4000
Tana	6	2658	24000
Tennevold	2	498	4500
Tomasjord	8	48	400
Tovik	2	498	4500
Tromsdalen	14	84	700
Tromsø	62	372	3100
Vadsø	6	2658	24000
Vangsvik	1	83	750
Vannvåg	1	83	750
Varangerbotn	4	1772	16000
Vardø	3	1329	12000
Veste Jakobselv	1	443	4000
Øksfjord	4	1772	16000
Grand Total	**402**	**71832**	**648350**