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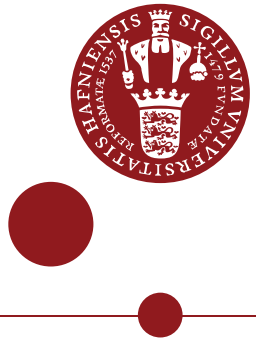

PhD thesis | Christian Pilely Olsen | 2021

Physiotherapy for minor musculoskeletal injuries in hospital emergency departments

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Preface

This PhD thesis is based on scientific work conducted from 2017 to 2020 at the emergency department at Slagelse Hospital, the Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals and the Parker Institute, Bispebjerg-Frederiksberg Hospital under the supervision of Professor Marius Henriksen, Professor Søren T. Skou and senior researcher Finn E. Nielsen. Næstved, Slagelse and Ringsted Hospitals' Research Fund and Slagelse hospitals internal research fund supported the work.

The PhD thesis includes three original studies listed below. The studies are presented as three separate manuscripts found as appendix II, III, and IV. The background, methods and the main results from each study are presented and discussed throughout the different sections of the thesis.

Study I *A prognostic evaluation by physiotherapists as a predictor of short-term outcome after treatment of minor musculoskeletal injuries in the Emergency Department: A prospective cohort study.* Olsen CP, Henriksen M, Nielsen FE, Skou ST. (In review)

Study II *Dual-panel translation and cross-cultural adaptation of the Danish Version of the Cumberland Ankle Instability Tool, Foot and Ankle Ability Measure & Lower Extremity Functional Scale.* Olsen CP, Skou ST, Nielsen FE, Henriksen M.

Study III *A randomised trial of pain guided early rehabilitation of acute lateral ankle sprains delivered by physiotherapists in the emergency department.* Olsen CP, Skou ST, Nielsen FE, Henriksen M.

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Summary

There is an increasing pressure and shortage of physicians and nurses in the emergency departments (EDs) throughout Denmark. One solution, to target these shortcomings, has been the introduction of physiotherapists to some Danish EDs. The rationale is to utilize the specific competencies physiotherapists display in the acute management of musculoskeletal injuries to provide fast and consistent high-quality treatment for patients. Despite this growing trend, little is known about the usefulness of physiotherapists in the Danish EDs. Therefore, the aim of this PhD study was to evaluate the caseload and effectiveness of physiotherapists in the treatment of minor musculoskeletal injuries in a hospital ED.

In this thesis, I showed that the most common diagnoses treated by the physiotherapists in the ED were ankle sprains, hand contusions and wrist fractures. Furthermore, I showed that the physiotherapists' evaluations of the prognosis for patients, attending with minor musculoskeletal injuries, were associated with the patients' symptomatic state four weeks after consulting the ED.

Prior to initiation of a randomised trial, I translated and cross-cultural adapted questionnaires commonly used in the evaluation of ankle sprains into Danish without any major inconsistencies. The randomised trial, comparing the effect of a pain-guided early rehabilitation approach and usual care (RICE) on ankle function for the treatment of acute lateral ankle sprains in the ED, showed no significant differences in short-term (four weeks) effects. However, the pain-guided early rehabilitation group experienced fever recurrent sprains compared to the usual care group within the first four weeks after injury. Patients were followed over a period of 12 month after inclusion, to evaluate long-term treatment effects. Unfortunately high attrition rates in both treatment groups made long-term assessments inconclusive.

Hence, this PhD thesis provides new knowledge into the caseload and effectiveness of implementing physiotherapists in the EDs in Denmark, which is relevant and useful when other EDs is considering introducing physiotherapists.

Dansk resume

Der er et stigende pres og mangel på læger og sygeplejersker på skadestuerne i Danmark. En løsning på dette har været ansættelsen af skadestuefysioterapeuter på nogle af de danske skadestuer. Rationalet er at udnytte de specifikke kompetencer fysioterapeuter har i den akutte håndtering af bevægeapparatsskader og derved sikre hurtig og ensartet høj kvalitet i behandlingen af patienterne. På trods af denne voksende tendens er skadestuefysioterapeuternes arbejde og effektivitet i de danske skadestuer ikke tidligere beskrevet. Formålet med denne ph.d.-afhandling var derfor at beskrive, hvilke patienter der ses af fysioterapeuterne på en dansk skadestue og måle effekten af skadestuefysioterapeuter i behandlingen af mindre bevægeapparatsskader.

Resultaterne fra denne afhandling har vist, at de hyppigst behandlede diagnoser blandt skadestuefysioterapeuter er ankelforstuvning, kontusion af hånd og håndledsfraktur. Derudover fandt jeg en sammenhæng mellem skadestuefysioterapeuternes prognose for patienterne og symptomer fire uger efter behandling for en mindre bevægeapparatsskade i skadestuen.

Før igangsættelsen af et randomiseret forsøg, oversatte og tilpassede jeg spørgeskemaer, som normalt anvendes ved forskning i ankelforstuvninger, til dansk uden større uoverensstemmelser. Det randomiserede forsøg, der sammenlignede behandling af akut ankelforstuvning med en smertevejledt tidlig rehabiliteringsstrategi og sædvanlig behandling (RICE), viste ingen signifikant forskel i effekten fire uger efter patientens behandling på skadestuen. Dog oplevede patienterne, som anvendte den smertevejledte tidlige rehabiliteringsstrategi, færre re-skader end gruppen som modtog sædvanlig behandling. For at kunne følge sygdomsudviklingen hos patienterne blev de fulgt over en 12 måneders periode. Desværre var der et højt frafald i begge behandlingsgrupper, hvilket medførte at langtidseffekten af behandlingstiltagende ikke kunne sammenlignes.

Således bidrager denne ph.d.-afhandling med ny viden om hvilke diagnoser der behandles af skadestuefysioterapeuter og effekten af implementeringen af skadestuefysioterapeuter i behandlingen af mindre bevægeappartsskader. Dette er relevant og brugbart for andre skadestuer, der overvejer at anvende fysioterapeuter for at imødekomme det stigende pres og manglen på læger og sygeplejersker.

Abbreviations

CAI	Chronic ankle instability
CAIT	Cumberland Ankle Instability Tool
COSMIN	The Consensus-based Standards for the selection of health status Measurement Instruments
DASH	Disability of the Arm, Shoulder and Hand score
ED	Emergency department
FAAM	Foot and Ankle Ability Measure
FAOS	Foot and Ankle Outcome Score
LAS	Lateral ankle sprain
LEFS	Lower Extremity Functional Scale
NSAID	Non-steroidal anti-inflammatory drugs
OAR	Ottawa ankle rule
PEACE AND LOVE	Protect, Elevation, Avoid anti-inflammatories, Compression, Education, Load, Optimism, Vascularization, Exercise
POLICE	Protect, Optimal Loading, Ice, Compression, Elevation
PRICE	Protect, Rest, Ice, Compression, Elevation
PROM	Patient reported outcome measure
RCT	Randomized controlled trial
RICE	Rest, Ice, Compression, Elevation
SF-36	The 36-item short form survey
SOP	Standard operating procedure

Background

Burden, epidemiology and overcrowding in the emergency department

The Danish healthcare system offers universal and free, equal access for all citizens. Patients presenting to an emergency department (ED) are either referred by the general practitioners or, if urgent or life-threatening, arrive on their own or by ambulance[1]. Very few patients present as ED walk-ins[2].

In Denmark, the rate of visits to the ED is between 108-201 per 1000 citizens per year[3]. The demand on EDs throughout Denmark has been, and is still, increasing[4]. Overall attendance to Danish EDs has increased from 875,767 patients contacts in 2013 to 1,204,648 in 2018[5], corresponding to an increase of 37.5%. This is in line with international studies showing similar trends of increasing pressure on the EDs[6–9]. Lindner et al.[6] reported an increase in emergency room outpatient consultations throughout Switzerland of 32% in the period from 2007-2011. In the study by Lindner et al. three main factors is highlighted as being the main reasons for overcrowding in the ED[6].

1. Input factors: The number of patients presenting at the ED increases.
2. Flow factors: The organization of the ED cause an increase in length of stay for patients.
3. Outflow factors: Lack of free beds for patients needed to be hospitalized.

Input factors

The increase of patients could be explained by several factors leading to in-appropriate use of EDs for nonemergency conditions and treatment of chronic diseases resulting in less effective disease management and increased health care costs[10].

In an American population, Rust et al. found several reasons why patients preferred the EDs rather than their general practitioner[10]. The reasons were: "couldn't get through on phone" (OR, 1.27; 95% confidence interval [CI], 1.02-1.59); "couldn't get appointment soon enough" (OR, 1.45; 95% CI, 1.21-1.75); "waiting too long in doctor's office" (OR, 1.20; 95% CI, 1.02-1.41); "not open when you could go" (OR, 1.24; 95% CI, 0.99-1.55); and "no transportation" (OR, 1.88; 95% CI, 1.50-2.35)[10]. This indicates shortcomings when patients have to schedule a visit to their general practitioners and shows that barriers limiting effective and timely access to care may contribute to an increased pressure on the EDs[10]. Other reasons for an increase in patient flow in the EDs are that patients choose the ED rather than their own general practitioner for the management and treatment of e.g.

minor musculoskeletal injuries because they think that their complaint is urgent[11,12]. Moreover the increased shortage of general practitioners may have an effect on the increased flow of patients presenting at the EDs in DK[13]. However, the exact factors contributing to the increasing patient flow on Danish EDs remain to be investigated.

The most common diagnostic group treated in EDs is injuries[14]. Injuries cause a great economic burden on society due to the combination of treatment costs and reduced level of function, thus loss of productivity[15]. This diagnostic group derives from the ICD-10 code system and is comprised of injuries such as fractures, dislocations, sprains, or strains i.e., minor musculoskeletal injuries. Minor musculoskeletal injuries are estimated to represent about 13% of all visits to the ED[16,17]. This number may be higher or lower, as EDs across countries and regions vary in scope of practice. Nevertheless, with an increasing ageing population the numbers will continue to rise throughout[18]. When divided into body regions, extremity injuries represents the greatest proportion of injuries in the ED, with the lower extremity being the primary body region injured[19]. It has previously been found that from all visits in EDs in the U.S. over a year, 14.6% of the visits were lower extremity injuries[20]. Sprains and strains have been found to account for more than one third of the lower extremity injuries in patients seeking health care in EDs in U.S, and fractures account for 18%[20]. The incidence of musculoskeletal injuries in the lower extremities is, however estimated to be much higher, as the numbers from the EDs only show their rate of patients. Many patients with musculoskeletal injuries is expected to seek treatment elsewhere, e.g. at their general practitioner or therapist[21].

Flow factors

In 2007, the Danish EDs were reorganized as 40 EDs were merged into 21 big EDs[2]. This shift was made to provide fast and consistent high-quality treatment to the acutely ill or injured patient in fewer hospitals with specialized clinical competences and specialized equipment at their disposal, allowing patients to be treated by specialists at an early stage of their disease[22]. In addition, this was also expected to save resources[23]. This ultimately resulted in different organization models, as the reorganization and restructure of the new EDs was done by the Danish Regions, in ways best fitting the individual hospitals. A study conducted by Møllekær et al.[2] identified three generic organizational models at the Danish EDs:

1. The virtual model: Staffed by junior physicians with tasks coordinated by other departments.
2. The hybrid model: Staffed by junior and senior physicians according to other departments and the ED. The ED coordinates all tasks.

3. The independent model: Staffed by junior and senior physicians and activities are coordinated by the ED.

Most Danish hospitals use a combination of the models: The hybrid model from 8 am to 4 pm and the virtual model outside this timeframe[2]. The challenges with the hybrid and the virtual models are that the ED relies on other departments to determine competency level and number of physicians sent to the ED. In most cases, this organization method will result in junior physicians and nurse practitioners as the primary contact for patients with minor musculoskeletal injuries[10,24]. Senior orthopedic physicians work as backup on call in the virtual model or are present in the hybrid model, if the orthopedic departments choose to do so. The result of this organization-plan is that patients with minor musculoskeletal injuries are treated primarily by junior physicians with limited experience in ED guidelines or standard operating procedures (SOPs)[2].

Triage is a priority tool to ensure that patients who have time-critical illness or injury are treated quickly[25]. Upon arrival at the ED, patients are divided into categories according to a combination of vital signs and presenting complaints. The triage category indicates a maximum time limit before medical assessment[3]. In Danish EDs most hospitals 16/21 (76%) use the DEPT triage model[25]. DEPT is a five-level triage system that categorizes the condition of the patient into five degrees: red (life threatening), orange (critical), yellow (stable, but potentially unstable), green (stable), and blue (unaffected)[25]. The color determines the urgency of attention required: red requires immediate attention, whereas blue demands reevaluation every fourth hour[26]. The Danish Regions have all made independent time targets, used as quality indicators for the treatment of patients with minor injuries (categorized as triage blue in the Danish EDs)[25]. The time target used is the patient waiting time and criteria varies between Regions: See Table 1 adapted from the 2016 progress report on the Danish EDs[25]. The regional differences in quality indicator targets display the variability in the Danish EDs across regions and reflects how this model may contribute to health inequity.

Table 1 - Target measures for waiting time* in patients with minor injuries (categorized as triage blue) in Danish EDs.

Danish Regions	Quality indicator target
The Capital Region	50 % within 1 hour and 95 % within 4 hours
Region Zealand	85 % within 1 hour
Region of Southern Denmark	75 % within 1 hour and 95 % within 3 hours
Region of Central Jutland	90 % within ½ hour
Region of Northern Jutland	85 % within 1 hour

*Waiting time is defined in hours as the time from presentation to commencement of service.

In the future, the organization of EDs in Denmark will change to be primarily the independent model[2]. In this model, other specialty competencies are combined into one specialty termed emergency medicine[3]. The emergency medicine specialty has broad competences in managing patients with acute injury, but lacks senior level competences in the treatment of minor musculoskeletal injuries, which may cause delays in injury treatment[24]. Junior physicians will likely continue to play an important role in the management and treatment of minor musculoskeletal injuries. A possible solution to secure high patient flow for patients with musculoskeletal injuries presenting at the Danish EDs is to introduce e.g. physiotherapists as primary contact practitioners for musculoskeletal injuries[25]. Physiotherapists working as primary contact practitioners were in a prospective observational study conducted at 19 EDs associated with a significant reduction in ED length of stay by 108 min and wait time to treatment by 10 min compared to those seen through usual care processes[27].

Outflow factors

The increasing pressure on EDs may lead to overcrowding, resulting in increased pressure on hospital resources, inefficient allocation of resources and reduced capacity to provide critical care in a timely manner[28–30]. In Denmark, overcrowding in EDs is a common and widely discussed topic in the lay press and with an increasing ageing population and shortage of doctors and nurses, the problem is suspected to carry on[13,31]. Overcrowding with long patient waiting times pose a risk to the quality of care provided for all patients[6,28]. This could result in neglect of minor musculoskeletal injuries as more urgent or life-threatening injuries need the specific competencies of medical doctors or nurses, ultimately leading to lack of available beds for patients. A possible solution to the problem could be the implementation of a physiotherapist as part of the interdisciplinary team working with the patients at the ED. The physiotherapists have specific competencies in the delivery of gate aids, orthoses and mobilization of patients and thus would be able to contribute to the discharge of patients without the need for hospitalization preventing bottlenecks in the ED flow.

Physiotherapy in the ED, scope of practice

In the thesis and the manuscripts pertaining the thesis I have chosen to use the term ED as this has become the term used in Denmark since 2007. Thus, people still use other terms as: accident & emergency department (A&E), emergency room (ER), emergency ward (EW); casualty department and emergency clinic.

Within the ED, patients presenting with minor injuries are treated on site by the available nurse practitioners, junior doctors, senior physicians and in some EDs also physiotherapists. Typically,

the treatments of these patients are located in an independent area with waiting area and beds allocated to the specific function. The patients allocated to this area are patients who are expected to be treated within 4 hours of presentation. The type of injuries treated consists of e.g., fractures, contusions, sprains/ruptures, dislocations and lacerations (non-urgent injuries). The patients treated in this category are primarily patients triaged as blue (low priority). Other patients with injuries needing urgent treatment, such as acute neurological disease, musculoskeletal multi-traumas or acute exacerbation in COPD, are triaged as red, orange, yellow or green and are typically handled in the EDs but in different areas. In Denmark, physiotherapists also work with these patients, triaged as red, orange, yellow or green, but do not have the same primary contact role as described in this thesis.

Outside the ED, physiotherapists traditionally play an important role in the management of minor musculoskeletal injuries. Some years ago, physiotherapists were introduced in the interdisciplinary team at the EDs to improve the overall flow of patients and insure quality in the treatment of patients with minor musculoskeletal injuries[32]. At first, physiotherapists were introduced as secondary contact practitioners in the ED[33,34], where they, after referral from physicians or emergency nurse practitioners, assessed and managed injuries[35,36]. Their main tasks were assessment and treatment of minor musculoskeletal injuries; mobility and vestibular assessment; and assisting in discharge of patients[33,34].

The role of the physiotherapists has now evolved into a primary contact role, where the physiotherapists have the same authorities as the physicians for the treatment of minor musculoskeletal injuries[37]. This role includes independent assessment and treatment of minor musculoskeletal injuries; imaging prescriptions; prescription of relevant non-steroidal anti-inflammatory drugs (NSAID's); education of patients; provision of walking aids and gait training; referring of patients; and provision of bandages and orthoses[33,37,38]. However, the scope of practice of physiotherapists in the ED varies depending on the country and even varies between individual EDs within countries[36]: In some EDs the physiotherapists are implemented as usual physical therapy care and in others the physiotherapists work in what is called "advanced practice" or "extended scope practice"[36,39–42].

As the nature of an ED is a high flow and often a stressful environment, interprofessional joint effort in managing all patients across diagnoses is important. Therefore, physiotherapists working in the EDs will also have to aid other allied health professionals with tasks relevant within their competence level. This ultimately includes helping physicians and nurses with patients who fall outside the primary focus of the physiotherapists' scope of practice, which is patients not presenting with minor musculoskeletal injuries[33]. Patients treated by physiotherapists within this "joint effort"

role, their diagnosis, triage categories and the physiotherapists' specific tasks remain to be evaluated and described in detail. Patients managed within the joint effort role could be patients with more complex injuries e.g., musculoskeletal multi-traumas, dislocations, or open fractures. In these cases, the roles and responsibilities are tailored to the specific setting and context in which they are feasible, resulting in heterogeneity across EDs.

In Denmark the skillset of a physiotherapist working in the ED are recommended to follow the national competence profile developed by the national physiotherapy association[43]. The physiotherapists have been suggested to complete relevant courses amounting to 30 ECTS (European Credit Transfer System). Furthermore, it is advised that the EDs implement an internal certification procedure to ensure quality and patient safety, emulating the program used for the training of junior physicians.

Research in physiotherapists in the ED

Research into the caseload treated by primary contact physiotherapists in the EDs is scarce. One study conducted by de Gruchy et al.[17] presented in detail the patient diagnostics although contributed to a single ED in Melbourne, Australia. It is however unknown how the caseload on physiotherapists in ED in Denmark is, including the patient demographics and which diagnoses the PTs manage in the EDs. Part one of the aim of Study I, presented in this PhD, was therefore to describe the caseload of patients treated by primary contact physiotherapists in a Danish ED.

Multiple studies have investigated the effect and different efficiency measures when implementing physiotherapists in the ED. Eight prospective observational studies[17,27,44–49] and two retrospective studies[50,51] provide information on efficiency measures such as patient waiting time, treatment time and overall length of stay. Five studies[27,44–46,50] demonstrated a significant reduced waiting time for patients treated by ED physiotherapists, three studies[17,44,46] showed significant reduced treatment times and five studies[27,44,45,49,50] showed reduced length of stay, with two studies showing an increased percentage of patients discharged within emergency access benchmarks (4 hours)[44,46]. Four studies[27,44,46,51] evaluated the efficiency measures when patients were stratified by emergency triage categories and found that physiotherapists were associated with more efficient care across triage categories. This highlights the positive contribution of physiotherapist in the EDs, when the physiotherapists are implemented successfully, and was shown across multiple sites despite varying policies and practices. These studies, investigating ED efficiency measures e.g., treatment time, have all shown positive results for the implementation of a physiotherapist in the EDs. However, a major limitation of all the studies is the lack of a comparison of the ED as a whole. It would seem

unlikely to get a negative result, as the physiotherapists provided an additional clinical staff member to the workforce. Similar results might be achievable by the addition of a physician or nurse practitioner, with the same primary scope of managing patients with minor musculoskeletal injuries.

Two studies on the secondary contact role of physiotherapists concluded that patients who received care by a physician first, followed by a physiotherapist had a prolonged length of stay, waiting time and treatment time compared to other care pathways including physiotherapists as the primary contact or usual care by physician[27,46], why it may not be beneficial to introduce physiotherapists in the role of a secondary contact for the treatment of minor musculoskeletal injuries.

Studies, investigating the patients satisfaction with care found an increased satisfaction for physiotherapy compared to usual care in the EDs[27,45–48,52]. The method used when investigating patients satisfaction usually consists of a specific patient satisfaction questionnaire [48,53]. One study across 19 EDs in New South Wales, Australia found that more than 95% of patients who received care by a physiotherapist were satisfied with the management of their condition, understood the advice given, understood discharge information provided and had enough time to ask questions[27]. A prospective observational study by Guengerich et al.[45] found greater satisfaction with physiotherapy compared to physician care regarding education, or first aid advice and receiving written information about injury.

Effectiveness of care measured as e.g. patient-reported outcomes (PROs) or activity-reported outcomes was investigated in six studies[45,48,54–57] of which two were randomised trials[54,55].

In a prospective observational study, McClellan et al. investigated the patient satisfaction of patients with peripheral soft tissue injury and fractures (not related to the ankle) seen by physiotherapists and compared the satisfaction to patients seen by nurse practitioners or ED doctors[48]. They found that 55% of patients seen by physiotherapists strongly agreed that they were satisfied with the treatment they received, compared with 39% for nurse practitioners and 36% for doctors ($p=0.048$)[48]. However, in a later RCT by McClellan et al., investigating the clinical outcomes of soft tissue injury in patients treated by physiotherapists, nurse practitioners, or ED doctors, no differences in PROMs between treatment groups were observed at two- or eight-week follow-up[55]. Another RCT by Richardson et al.[54] investigated the effectiveness of physiotherapy treatment in patients presenting to the ED with soft tissue injury (without fracture) and compared to routine practice by a doctor and/or nurse practitioners. No statistical differences in the primary activity-reported outcome, time to return to usual activities, were found between groups: 41 days in the physiotherapist group compared with 28.5 days in the usual care group ($p= 0.071$). A significant difference in patient satisfaction were found between groups: physiotherapy group 89% compared

to 74% in the usual care group ($p<0.0001$)[54]. As suggested by the authors, this difference may be explained by the physiotherapists being more likely to provide aids and appliances and giving advice and reassurance[54]. At the three-month follow-up the physiotherapy group reported a slightly better function measured by EQ-5D index score, HAQ score and self-reported pain scale compared to the usual care group, but the difference was not found at six-month follow up[54]. Data on effectiveness is best derived from RCTs. Nonetheless, no significant differences were found between groups for functional or pain-related outcomes in two prospective observational studies investigating the effectiveness of physiotherapist treating patients with musculoskeletal conditions in the ED [45,57].

No trials have evaluated the cost-effectiveness of ED physiotherapists[36,37]. In two RCT trials the treatment costs of ED physiotherapists were compared to routine care[54,58]. In the study by Richardson et al.[54] costs did not differ significantly between the groups (difference in mean costs shows a reduction of £1.33 [95% CI -£1.96 to +£4.49]). In the study by McClellan et al.[58] the average cost per hour of patient contact was calculated to £80.91 [CI 66.5 to 101.6] for doctors and £89.71 [73.0 to 118.7] for ED physiotherapists. In future studies, the cost-effectiveness of implementing physiotherapists in the ED should be evaluated.

The existing literature on implementation of physiotherapist to the EDs have been reviewed in several studies[36,37,39,59]. A systematic review by Matifat et al.[36], reviewing the effect of musculoskeletal physiotherapy in EDs, found that the evidence is heterogenous and that the roles of the physiotherapists vary between settings and studies and only a limited number of high-quality studies is found[36]. This was also supported by a scoping review by Ferreira et al.[37] suggesting that the available evidence shows that physiotherapists may be as effective as other health providers in managing low urgency musculoskeletal conditions in the ED. However, there is uncertainty about appropriate training and a lack of robust studies investigating the efficiency, safety and cost-effectiveness[37]. A literature review by Mcclellan et al.[59] concluded that ESPs could provide high standard of care at an affordable cost, whilst positively influencing patient satisfaction in the EDs. The literature review also concluded that the use of ESPs working in the ED, carrying out duties traditionally undertaken by doctors, could provide one of the solutions to staffing shortages in emergency care[59]. Another systematic review by Kilner, E. showed that the evidence to support physiotherapists at EDs is insufficient from a system and provider level, however, at patient level, there might be benefits in terms of improved pain control and reduced disability in the short term[39]. In conclusion, these reviews of the current literature show that there is substantial lack of evidence from randomised trials, to conclude and support the use of physiotherapists in EDs, why further research is needed.

In daily clinical practice at the ED, physiotherapists and other ED staff will only manage patients in a short timeframe, typically unaware of the outcome after discharge. During treatment of patients, the ED staff will have a "hunch" of how the prognosis will be for the patient. Studies using the physiotherapists "hunch" as a predictor for prognosis are scarce with the few available studies demonstrating that the physiotherapist can predict the outcome in patients with neck or low back pain[60–62]. However, it remains unknown if this "hunch" is a reliable predictor of the outcome after treatment in the ED. If the physiotherapist can predict the outcome after treatment in the ED, this knowledge can be used to reliably identify candidates who may need referral to further treatment, thereby potentially reducing the considerable subgroup experiencing recurrent or persistent symptoms[63]. An important aspect of a clinical service is the ability to provide a prognosis of individual patients. However, the prognosis as judged by physiotherapists in an ED setting has not been evaluated before. To support the value of physiotherapists in an ED department it is thus important to assess if the PTs prognoses associate with the actual outcome.

Therefore, as a part of Study I, presented in this PhD, we assessed if physiotherapists, attending patients with minor musculoskeletal injuries presenting to the ED, could predict the short-term recovery.

Acute lateral ankle sprain

Lateral ankle sprain (LAS) is a common musculoskeletal injury in the general population[21] and in sports and recreational activities[64]. Acute LAS is defined by Delahunt et al.[65] and endorsed by the International Ankle Consortium (IAC)[66] as: *"An acute traumatic injury to the lateral ligament complex of the ankle joint as a result of excessive inversion of the rear foot or a combined plantar flexion and adduction of the foot."* Acute LAS is common in the ED, representing between 3-5% of the overall attendances[67], with incidence rates expected to be considerably higher in the general population[68]. Acute LAS is the most commonly treated musculoskeletal injury in the ED[69,70]. In the Danish EDs, more than 36,000 ankle sprains, accounting for 4% of all injuries managed each year, has been reported[71]. Ankle sprain injuries are a significant source of economic and societal burden. The overall costs (combining direct and indirect costs) of ankle sprain treatment are estimated to range between $1809 to $5271 per person (2016 USD)[72]. Ankle sprains significantly affect quality of life both acutely, due to reduced mobility and pain, and longer term due to high rates of recurrent sprains and ongoing instability[73,74,64].

Clinical assessment of acute LAS in the ED

The clinical assessment of acute LAS in the ED is typically composed of the patient history and the initial physical examination, followed by a possible X-ray scan in three views if the patients Ottawa ankle rule (OAR) is positive[75]. The OAR is used to determine the patients' need for radiography and ultimately to rule out fractures[76,77].

The OAR is an assessment of the patients' ability to bear weight and a palpation of the bony structures around the ankle joint area[76]. If the patient presents with pain to the malleolar or midfoot zone and has either an inability to bear weight for four steps with, or without pronounced limping or tenderness in any of the specific bony areas to the malleolar zone or mid-foot zone results in a referral for radiography[77]. The OAR is highly accurate in excluding fractures for patients presenting to an ED. Evidence shows that less than 2 % of the patients will be wrongly classified as not having a fracture, when they actually have one[76].

The patients history should include a detailed description of the mechanisms that resulted in their presentation to the ED[75]. For acute LASs, a history of a sudden rapid inversion and internal rotation of the foot and ankle complex would be expected[78] and patients may report a history of hearing a cracking sound, but this is not related to fracture or ligament lesion[79]. A history of previous ankle sprain indicates if a patient has persistent mechanical and sensorimotor impairments following prior major injury and is indicative of Chronic Ankle Instability (CAI)[65]. The patient history should also include self-reported pain severity e.g., using the verbal rating scale (VRS). Ultimately, as the nature of the ED is high flow and many patients with varying co-morbidities present, it is important to exclude serious red flags for alternative or compromising diagnoses, e.g., diabetes or deep vein thrombosis[75]. A local advice, implemented in the ED at Slagelse Hospital, Denmark, is to ask the patient for consumption of analgesics prior to the clinical assessment because this may interfere with the reliability of the tests used, as e.g., OAR relies only on pain and therefore could lead to a higher false negative rate in this test. Further research is needed to determine if this caution is relevant for clinical practice in the future.

The physical examination consists of an observation of the ankle joint in regards to the degree of swelling, deformity, redness, hematoma or other associated signs[75]. A neurovascular examination; strength testing; and active and passive range of motion testing are commonly used, but provide limited information in the acute clinical assessment of acute LAS[75]. In the acute phase at the EDs the anterior drawer test has shown a sensitivity of 71% and specificity of 33% in identifying patients with a ruptured ligament[79].

Acute treatment of acute LAS in the ED

Numerous ways of treating acute soft tissue injuries, such as acute LAS, have been proposed in the past, starting with the introduction of the RICE principles. The definitions of RICE and the following terms describing treatment of soft tissue injuries are found in Table 2. The principle of RICE was updated in 2007 by Bleakley et al.[80] to PRICE and has progressed throughout time to POLICE[81] and now recently PEACE AND LOVE[82]. The most apparent difference between PRICE and POLICE is the substitution of R (Rest) with OL (Optimal Loading). Optimal loading can be achieved by manipulating the magnitude, nature, intensity, or frequency of exercises[83]. The acronym PEACE AND LOVE has proposed several new introductions to the treatment approach[82]. In the acute management, Ice (I) in RICE/PRICE/POLICE is substituted with Education (E) and Avoid anti-inflammatories (A) in PEACE. In addition, PEACE AND LOVE introduces recommendations regarding Optimism, Vascularization and Exercise to Optimal loading (LOVE) after the first days have passed.

Table 2 - Acronyms for RICE/ PRICE, POLICE and PEACE AND LOVE

RICE / PRICE	POLICE	PEACE AND LOVE
Protect	**P**rotect	**P**rotect
Rest	**O**ptimal loading	**E**levation
Ice	**I**ce	**A**void anti-inflammatories
Compression	**C**ompression	**C**ompression
Elevation	**E**levation	**E**ducation
		After the first days have passed
		Loading
		Optimism
		Vascularization
		Exercise

Most EDs still use RICE as the primary acute treatment for acute LAS[84]. However, this may need updating or refinement. In an updated evidence-based clinical guideline on the diagnosis, treatment and prevention of ankle sprains by Vuurberg et al.[85] the use of RICE as conservative treatment was evaluated. The authors concluded that there is no evidence for the use of RICE alone and that RICE has no positive influence on pain, swelling or patient function. Despite this, the authors also conclude that RICE is a conservative treatment method that has not been rigorously investigated in the literature. Based on two systematic reviews the authors concluded that the efficacy of RICE for

reducing acute LAS injury-associated symptoms is unclear (33 randomised controlled trials (RCTs), n=2337) (level 1)[85]. In a 2017 rapid review series, investigating the best practice management of common ankle and foot injuries in the EDs, a treatment approach consisting of pharmacological management and non-pharmacological management was recommended[75]. The pharmacological management consisted of prescription of paracetamol and anti-inflammatories (if appropriate), and restricting the use of opioids to selected patients with moderate to severe pain[75]. The non-pharmacological management consisted of RICE, with progressive rehabilitation as tolerated; immobilization using an external support for all grades of the injury to promote recovery; advice and education in home exercises and gradual return to rehabilitation and functional activities; and a clinical reassessment four to five days after the treatment in the ED to more accurately diagnose the severity of the sprain, if pain and swelling precludes[75]. The clinical based guideline by Vuurberg et al. did not incorporated treatment strategies related to the specific treatment of patients in the ED. This work was presented in the rapid review series by Strudwick et al. Similarities in treatment regimens in the acute phase of injury exist in regard to immobilization and the use of a brace to prevent recurrent sprains.

Different management strategies for acute LAS outside the ED have been assessed in randomised controlled trials (RCTs) with mixed results. Bleakley et al.[86] showed favorable results towards an accelerated functional treatment approach. An overall treatment effect within the first 4 weeks was in favor of the exercise group (P=0.0077); this was significant at both week 1 (baseline adjusted difference in treatment 5.28, 98.75% confidence interval 0.31 to 10.26; P=0.008) and week 2 (4.92, 0.27 to 9.57; P=0.0083). The effect was not significant at the 3- and 4-week follow-up. Furthermore the results failed to reach an effect larger than the 9 point MCID for the primary outcome Lower Extremity Functional Scale (LEFS)[87]. Brison et al.[88] did not demonstrate a greater improvement in outcome with the addition of supervised physiotherapy to usual care after standard treatment in the ED. In the study by Brison et al. 503 participants were followed over a six-month period. The absolute proportion of patients achieving excellent recovery, defined as a score ≥450/500, at the three-month follow-up was not significantly different between the physiotherapy (98/229, 43%) and usual care (79/214, 37%) groups (absolute difference 6%, 95% confidence interval −3% to 15%)[88]. In the study by Brison et al. 152/253 (60%) in the physiotherapy group and 147/250(59%) in the usual care group reported previous injury to the reference ankle which might have introduced confounding effects on the results. Furthermore the investigators stated they used an intention to treat analysis for all their primary assessments, however only 443/504(88%) was analyzed at the 3 month follow-up[88]. Generally Intention-to-treat analysis is favored in pragmatic RCT studies because it avoids bias associated with non-random loss of participants[89–91]. Hultman et al.[92] showed

significant treatment effects six weeks after injury compared to a control group (RICE) in all of the FAOS subscales after instructions in an homebased exercise program commenced as soon as possible after the injury(range 1-14 days, median 4 days) (pain p=0.001, symptoms p=0.018, ADL p=0.002, sport/rec p=0.008, QOL p=0.017*)*. At the 3 months follow-up the results were the same (pain p=0.025, symptoms p=0.046, ADL p=0.003, sport/rec p=0.029) except for the subscale QOL (p=0.135). Together these results show that an accelerated approach with early weight bearing and exercise may improve self-reported function after an acute LAS.

The majority of treatment regimens are typically composed of a treatment approach consisting of Rest, Ice, Compression and Elevation (RICE), with advice about complete rest the first 48-72 hours after injury[81]. The more recent POLICE guidelines follow the same core treatments with the addition of protection (P) and optimal loading (L), although optimal loading is not well defined[81].

One of the main concerns related to LAS is the development of chronic ankle instability (CAI). Doherty et al 2016 showed that poor functional status within the initial 2 weeks after injury is predictive of CAI[93]. The study showed that motor control deficits within 2 weeks of a first-time LAS and poorer dynamic postural control and lower self-reported function 6 months after a first-time LAS were predictive of eventual CAI outcome[93] This suggests that early and targeted interventions for providing optimal loading in the acute phase by physiotherapists in the EDs may be beneficial to increase the functional status early after injury and thereby, mitigate the risk of developing CAI. From this, we hypothesized that a low activity level in the early stages after a LAS results in impairments in ankle function and increase the risk of CAI. This was investigated in Study III as a part of this PhD thesis. The aim of this study was to compare the functional outcomes following acute LAS managed by usual care (RICE) or by a treatment approach consisting of pain-guided early rehabilitation in a randomised controlled trial.

As part of Study III, patient allocated to the treatment group received advice and instructions in accelerated and early rehabilitation, commencing at discharge. They were advised to load and exercise the ankle joint and accepting pain (during loading/exercising) up to, but not exceeding 5 on a 0-10 NRS rating scale (NRS). If patients experienced pain exceeding NRS 5 they should RICE until pain levels was below the NRS pain threshold again. When pain levels had decreased to <6 they should restart the pain-guided early rehabilitation approach. This approach was initiated to guide optimal loading in the acute phase following the acute LAS. The term optimal loading is discussed below.

In 2012, Bleakley et al.[81] introduced the term optimal loading, as researchers were concerned with patients being overly conservative when handling their acute injury[81]. Specifically the researchers

were concerned that patients who were using Protection and Rest from the PRICE principles would fail to harness the proven benefits of progressive tissue loading through an optimized exercise program[83].

The definition of optimal loading has been proposed by Glasgow et al.[83] as:

The load applied to structures that maximizes physiological adaptation.

The way of achieving optimal loading by the individual is done by manipulation of a wide range of variables known to have profound effect on the structure and function of the wider neuromusculoskeletal system[83]. The loading variables are nature; frequency; duration; intensity; direction and magnitude. All of these variables are related to the exercise performed by the injured person and should help in finding the balance between too much or too little, but few examples are presented in the article[83], making it difficult to translate into clinical practice and society. In the model, described by Glasgow et al.[83], the outcome of optimal loading is optimal form and function. However, when has the balance point tipped and how do we measure if a patient is doing too much or too little in the acute phase of injury?

The initial focus in treatment programs used in acute LAS research has been: decrease/avoid excessive swelling and decrease pain[75]. This first focus of treatment consists of the RICE principle. Rest/unload the injured foot for the first 48-72 hours and then gradually progress rehabilitation throughout to ensure optimal loading[84]. A problem with this approach is that swelling, measured with the figure of eight method, does not correlate with the patient's pain and functional limitation in the acute phase of injury[94]. If the degree of swelling were to be used as guidance for optimal loading, this would possibly result in a prolonged resting phase.

Commonly, pain is used as guidance for the clinician and the patient on when to progress through to exercises, e.g. the PEACE and LOVE guideline[82] states:

…Rely on pain signals to guide removal of protection and gradual reloading.

Few studies has tried to use pain as guidance for progression in exercises[92,95,96], but to our knowledge, no study has used it as guidance for "24h"-optimal loading in the acute phase after injury. A previously used model developed by Silbernagel et al. has been used for patients with Achilles tendinopathy and showed no negative effects from continuing Achilles tendon-loading activity, such as running and jumping, with the use of a pain-monitoring model, during treatment[95]. However, it is unknown if a physiotherapist administered pain-induced management of acute LAS starting already in the ED will result in improved short-term outcomes and thereby long-term outcomes as well.

Long term consequences of acute LAS

An abundance of literature has described the detrimental long-term consequences of sustaining an acute LAS. Acute LAS is not only highly present within the sporting community but also displays high incidence rates in the general population of two to seven ankle sprains per 1000 person-years treated in the ED with overall incidence rates suspected to be 5.5 times higher[68]. LASs have the highest recurrence rate of any lower limb musculoskeletal injury, leading to persistent and residual symptoms resulting in the development of CAI[73]. The prevalence of CAI one year after initially ankle sprain is 40%[97]. CAI is associated with reduced functional activity and quality of life and is the main cause of ankle joint post-traumatic osteoarthritis[98]. The documentation provided, of what most people falsely refrain to as a ”simple” acute LAS, highlights the urgent need for good quality research investigating optimized treatment approaches in the acute, sub-acute and late phase of this injury. Because of this, the patients in Study III were followed for one year after inclusion to the study.

Monitoring changes in patient response in acute LAS

In evidence-based medicine, treatment and rehabilitation, clinical tests and scales, measuring pain, joint motion and functional level, have previously been the primary tools for monitoring changes in patient responses and evaluating treatment[99]. For the assessment of function in the lower extremity, numerous rating scales have been developed. Around 140 different assessment tools have been described in research in relation to function in just the lower leg[100]. Combined with rating scales, the importance of monitoring the patient’s perspective has become more recognized. It is used increasingly, as it is a significant criterion for evaluating effectiveness of interventions and treatment[99,101]. Patient reported outcome measures (PROMs) consider the patients perspective on participation, restrictions and decreased quality of life, thus they are recommended as primary outcome measures over clinician-rated measures[102]. PROMs exist as both generic, or more region- and disease specific assessment tools. In the assessment of ankle injuries or ankle disorders, Cumberland Ankle Instability Tool (CAIT), Foot and Ankle Ability Measure (FAAM) and Lower Extremity Functional Scale (LEFS) are well known measurement tools that are widely used for measuring lower limb functional status in clinical research. In the ROAST consensus statement from the International Ankle Consortium the FAAM and the Foot and Ankle Disability Index (FADI) are recommended[78]. The FAAM and CAIT is recommended to be used by the International Ankle Consortium for enrolling patients with CAI in research[103]. LEFS[86,104,105], FAAM[106–115], and CAIT [106,114,116–120] have been used in numerous studies related to acute LAS or CAI (see Table 3 for overview)**.**

Table 3 - The use of LEFS, FAAM and CAIT in RCT studies related to acute LAS or CAI across the published literature.

Participants	Objective	Design	Setting	PROM	Conclusion	Reference
101 patients with an acute grade 1 or 2 ankle sprain	Compare early therapeutic exercise after acute LAS with RICE	RCT	Accident and emergency department and university-based sports injury clinic	LEFS	An accelerated exercise protocol during the first week after ankle sprain improved ankle function; the group receiving this intervention was more active during that week than the group receiving standard care.	Bleakley et al. [86]
74 patients with acute LAS	Compare the effectiveness of manual therapy and exercise (MTEX) to a home exercise program (HEP) in the management of individuals with acute LAS	RCT	Four physical therapy clinics	LEFS, FAAM-ADL FAAM-Sports NRS	A MTEX approach is superior to an HEP in the treatment of inversion ankle sprains.	Cleland et al. [105].
37 patients with severe ancle sprain	Compare patient function in patients receiving standard therapy IV Platelet-rich plasma and patients who receive standard therapy plus sham injection (placebo)	Prospective randomized double-blinded placebo-controlled trial	Emergency department	LEFS, VAS	No statistically significant difference in VAS and LEFS scores between groups	Rowden et al. [104]
43 patients with CAI	Compare the effectiveness of three rehabilitation programs on clinical measures of balance and self-reported function in individuals with CAI	RCT	Laboratory setting	FAAM-ADL CAIT	All 3 rehabilitation groups demonstrated improvement compared with the control group. Evidence was too limited to support a superior intervention	Cain et al. [106]
40 patients with CAI	Investigate the effect of corrective exercises on functional movement patterns, sensorimotor function, self-reported function, and fatigue sensitivity in athletes with CAI	RCT	Laboratory setting	FAAM-ADL	Eight weeks of corrective exercises enhanced movement efficiency, sensorimotor function, and self-reported function in collegiate athletes with CAI	Bagherian et al. [107]
10 patients with CAI	Investigate the effects of joint mobilization timing	Randomized two-group	Laboratory setting	FAAM-ADL DPA	Timing of joint mobilization in conjunction with calf	Feldbrugge et al. [108]

	during a four-week calf stretching intervention in individuals with CAI	pretest posttest design		FABQ	stretching does not effect treatment efficacy. The combination of joint mobilization and calf stretching can improve dorsiflexion ROM and self-reported function in individuals with CAI	
18 patients with CAI	Investigate the effects of progressive hop-to-stabilization balance (PHSB) program compared with a single-limb balance (SLB) program in individuals with CAI.	RCT	Laboratory setting	FAAM-ADL FAAM-Sports	A four-week PHSB or SLB can be used in athletes with CAI to improve self-reported function, dynamic postural control, and joint position sense	Anguish et al. [109]
39 patients with CAI	Determine the improvement of patient-reported outcomes after balance- and strength-training and control protocols among individuals with CAI	RCT	Laboratory setting	FAAM-ADL DPA FABQ VAS	Participants in both the balance- and strength-training–protocol and control groups improved in global and regional health-related quality of life	Hall et al. [110]
50 patients with CAI	Investigate the effectiveness of specific collagen peptide supplementation (SCP) to improve ankle stability in athletes with CAI	Randomized double-blinded and placebo-controlled study	Laboratory setting	CAIT FAAM-ADL	Specific collagen peptide supplementation in athletes with CAI results in significant improvements in subjective perceived ankle stability	Dressler et al. [111]
26 patients with CAI	Determine the effects of hip strengthening on clinical and self-reported outcomes in patients with CAI	RCT	Laboratory setting	FAAM-ADL FAAM-Sports	The training group displayed significantly improved clinical and patient-reported outcomes	Smith et al. [121]
80 patients with CAI	Determine the effects of two weeks of sensory-targeted rehabilitation strategies (STARS) on patient- and clinician-oriented outcomes in individuals CAI	RCT	Laboratory setting	FAAM-ADL FAAM_Sports	All STARS groups improved patient-oriented outcomes with joint mobilization having the most meaningful effect immediately after the intervention and plantar	McKoen et al. [122]

					massage at the one-month follow up	
84 patients with CAI	Determine the comparative efficacy of two ankle rehabilitation techniques: wobble-board balance training and ankle strengthening using resistance tubing in individuals with CAI.	RCT	Laboratory setting	FAAM-ADL FAAM_Sports ADL SF-36 GFR	A single-exercise four-week intervention can improve patient- and clinician-oriented outcomes.	Wright et al. [114]
26 patients with CAI	Compare the effect of a four-week rehabilitation program that includes destabilization devices to rehabilitation without devices in patients with CAI	RCT	Laboratory setting	FAAM-ADL	Both groups had large improvements in self-reported function and ankle strength. No differences between the no-device and device groups for any measure.	Donovan et al. [115]
70 patients with CAI	Determine and compare the influence of adding self-mobilization of the ankle joint to CrossFit training versus CrossFit alone or no intervention in patients with CAI	RCT	Laboratory setting	CAIT	Ankle-joint self-mobilization and CrossFit training were effective in improving ankle Ankle-dorsiflexion range of motion, dynamic postural control and self-reported instability in patients with CAI.	Cruz-Diaz et al. [116]
22 patients with CAI	Examine the effect of therapeutic exercise performed on sea sand on pain, fatigue, and balance ability in patients with CAI.	RCT	Laboratory setting	CAIT VAS	Therapeutic exercise on sea sand effectively improved balance and decreased pain and fatigue.	Shin et al.[123]
30 patients with CAI	Assess improvement of quantitative neurosensory indicators after short-foot exercise and to determine the effect of proprioceptive sensory exercise in patients with CAI.	RCT	Laboratory setting	CAIT	SFE is more effective than PSE for treating ankle sprain patients.	Lee et al. [124]
70 patients	Determine the	RCT	Laboratory	CAIT	Exercise therapy training	Cruz-Diaz et

with CAI	effectiveness of a six-week balance training program on patients with CAI		setting		based on multi-station balance tasks led to significant improvements in dynamic balance and self-reported sensation of instability in patients with CAI	al. [119]
90 patients with CAI	Evaluate the effects of joint mobilization, in which movement is applied to the ankle's dorsiflexion, on patients with CAI	A double-blind, placebo-controlled, randomized trial	Laboratory setting	CAIT	Joint mobilization techniques applied to subjects suffering from CAI were able to improve ankle Dorsiflexion Range of Motion, postural control, and self-reported instability	Cruz-Diaz et al. [125]

LEFS

LEFS is a self-reported questionnaire that measures the patient's subjective lower extremity function through 20 items on functional level. Every item is rated on a 5-point scale, indicating whether the patient is unable to perform the activity (0 points) or able to perform the activity without difficulties (4 points). Highest achievable score 80 correlates to a high functional level[126]. LEFS was originally developed in English, and has been found to have an excellent test-retest reliability (R= .94), in many different clinical patient groups with musculoskeletal disorders in their foot or lower leg[87,127]. A systematic review published by Mehta et al.[128] concluded that the MCID is 9 points in patients with lower extremity musculoskeletal conditions.

CAIT

The CAIT questionnaire is a simple reliable and validated PROM that identifies and measures the severity of functional ankle instability. CAIT can also be useful in monitoring progress and effect of treatment[129]. CAIT consists of 9 items designed to assess several aspects of functional ankle instability. All questions are answered separately for the right and left ankle, although no comparison should be made between the two. The total score of the 9 items ranges from 0, indicating severe ankle instability, to 30, indicating normal ankle stability[129,66]. The English version of CAIT were found to have acceptable construct validity and internal reliability with a Cronbach α = .83, together with an excellent test-retest reliability with an intraclass correlation coefficient type 2,1 (ICC) = 0.96[129]. The MCID of the CAIT questionnaire ≥3 points[130].

FAAM

The FAAM questionnaire is a region-specific PROM designed to measure limitations and restrictions in participation in patients with foot and ankle disorders[131]. The questionnaire consists of 29 items divided into two subscales regarding activities of daily living (ADL) in 21 items, and Sports in 8 items. Each item is scored on a 5-point Likert scale ranging from 0 (unable to do) to 4 (no difficulties at all) with a lower score representing a lower level of physical function[131]. FAAM has been found to be a reliable measurement tool with an intraclass correlation coefficient 2.1 at .89 for the ADL subscale and 0.87 for the Sports Subscale[132]. A systematic review published by Eechaute et al.[132] concluded that for the ADL and Sport subscales of the FAAM, MCID of respectively 8 and 9 points.

The CAIT, FAAM and LEFT questionnaires are used in Study III, but prior to the studies presented as a part of this PhD thesis, these questionnaires have not been translated into Danish. A translation of the questionnaires is important for use in daily clinical practice as well as in the implementation of international research studies. Therefore, the aim of Study II was to translate the CAIT, FAAM, and LEFS questionnaires from English too Danish and too cross-culturally adapt the Danish versions of the questionnaires.

Aims and hypothesis

The overarching aim of the PhD study was to evaluate the caseload and effectiveness of physiotherapists in the treatment of minor musculoskeletal injuries in a hospital ED.

The project resulted in three studies with the following specific aims and hypothesis.

Specific aims

Study I: The aim of this study was to assess if physiotherapists, attending patients with minor musculoskeletal injuries in the ED, can predict the short-term recovery. Furthermore, we investigated the caseload treated by the physiotherapists in the ED.

Study II: The aim of this study was to translate (from English to Danish) and cross-cultural adapt the Danish versions of the questionnaires: Cumberland Ankle Instability Tool, Foot and Ankle Ability Measure, and Lower Extremity Functional Scale.

Study III: The aim of this study was to compare the functional outcomes following acute LAS managed by usual care (RICE) delivered by physicians or by a treatment approach consisting of pain-guided early rehabilitation delivered by physiotherapists in a randomised controlled trial.

Hypotheses

Study I: Physiotherapists can predict the short-term outcome for patients with minor musculoskeletal injuries treated in the ED.

Study II: No hypotheses was specified for conducting the translation and cross-cultural translation study.

Study III: The functional outcome following presentation to an ED with acute LAS is superior when managed with a pain-guided early rehabilitation approach compared to usual care (RICE).

Methods

Method descriptions and the rationale behind the choice of methods for the three studies: Study I, II and III, are found in the following sections.

Study I

To investigate the caseload treated by physiotherapists in a Danish ED and to assess if physiotherapists, attending patients with minor musculoskeletal injuries in the ED, can predict the short-term recovery, we performed Study I.

Study I was designed as a prospective, pragmatic cohort study with four weeks follow-up recruiting patients over a three-month period from July 15th, 2019 to October 15th, 2019. The study was conducted in accordance with the Helsinki Declaration and ICH Good Clinical Practice, and conformed to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for reporting cross-sectional studies[133]. The protocol was submitted to and approved by the local Health Research Ethics Committee (J.nr. 19-000067) and was registered at www.clinicaltrials.gov (NCT04011917) before commencement of the study.

Setting

We recruited participants in the ED at Slagelse Hospital, Denmark - one of four hospitals in Region Zealand with an ED. The ED at Slagelse Hospital has a 24h service and treats approximately 49.000 patients annually. The Danish healthcare system offers equal access for all citizens. The patients are either referred by general practitioners or, if urgent, arrive on their own or by ambulance[1]. Private hospitals do not provide acute treatment of patients in Denmark. The physiotherapists working in the ED are an integrated part of the staff. Five physiotherapists worked in a rotating shift work schedule, with one physiotherapist present each day from 12:30 – 21.00 in the ED. The physiotherapists independently diagnosed and treated patients presenting with minor musculoskeletal injuries. The physiotherapists work as primary contact practitioners with the same role and responsibilities as the physicians in the ED for the management and treatment of minor musculoskeletal injuries. The skillset of a physiotherapist working in the ED in Denmark are recommended to follow the national competence profile developed by the national physiotherapy association[43].

Participants

All patients treated during the three-month period in the ED by a physiotherapist as primary contact or in a joined effort role were included in the caseload study.

From the population of patients included in the caseload study, patients diagnosed and treated by a physiotherapist (primary contact) for a minor musculoskeletal injury in the ED, aged >18 years and with an e-mail address were invited to participate in the prediction cohort study. Patients under the influence of drugs or alcohol, or a condition that, in the opinion of the investigator, would preclude participation in the study (e.g., not having access to the internet, cognitive impairments etc.) were excluded. Patients received oral and written information about the study procedures before giving oral and written informed consent.

Baseline characteristics

In the prediction cohort study, gender, age, height, weight, educational level, and the International Statistical Classification of Diseases and Related Health Problems 10 (ICD-10) codes for the injury on which the patient sought treatment were registered by the physiotherapist based on the examination, while only gender, age and ICD-10 codes and the reason for not being included in the prediction cohort study were collected in the caseload study.

The follow-up assessment in the prediction cohort was conducted using an internet-based platform (Research Electronic Data Capture; REDCap), with personal links sent via email to the participants. REDCap is a secure, web-based software platform designed to support data capture for research studies[134,135]. Via REDCap, individual internet-hyperlinks were emailed to the participants four weeks after the ED visit. The hyperlinks led to a secured webpage on which the patients answered questionnaires. Up to three reminders were sent every other day, if the participant did not respond.

Physiotherapists' prognosis score

The physiotherapists were asked to estimate each participant's outcome four weeks after the visit to the ED, based on the complete session including triage, history, examination, treatment and discharge in the ED. The physiotherapists were instructed to score each participant on a 15-points numerical rating scale ranging from -7 (suggesting a very poor projected outcome) to 7 (suggesting an excellent projected outcome). The patients were kept blinded to the prognostic scores.

Pain

At baseline (in the ED) and after four weeks, current pain intensity was assessed using a 100 mm visual analogue scale (VAS), which has been widely used in many adult populations[136,137]. The

scale is a unidimensional continuous scale comprised of a horizontal line, anchored by two verbal descriptors, one for each symptom extreme (0 = "no pain", 100 = "worst imaginable pain"). Self-reported VAS pain in rest and during activity was recorded at baseline and follow-up.

Health status and quality of life survey (EQ-5D-3L)

At the 4-week follow-up the EQ-5D-3L was measured. The EQ-5D[138,139] is a measure of current health status developed by the EuroQol Group for clinical and economic appraisals. The questionnaire consists of a descriptive system and an EQ Visual Analogue Scale (EQ VAS). The descriptive system comprises of five questions assessing five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension was rated by the participants on three levels: no problems, some problems and extreme problems. From the answers an EQ-5D index score is calculated based on Danish normative values[140]. The index ranges from -0.624 (worst) to 1.000 (best). The EQ VAS was used to record the participants self-rated health at 4 weeks follow-up on a horizontal 100 mm VAS with endpoints labelled *'best imaginable health state'* and *'worst imaginable health state'*. The EQ-5D-3L was only collected at follow-up.

Patient Acceptable Symptom State (PASS)

At the 4-week follow-up Patient Acceptable Symptom State was evaluated at follow-up using a single item with response categories ''Yes'' or ''No'': *''Taking into account all the activities you have during your daily life, your level of pain, and also your functional impairment, do you consider your current [injury site]-state following your 4-weeks-old injury to be satisfactory?''*. Injury site was automatically replaced with the site of injury reported at baseline.

Protocol deviations

We pre-specified the global perceived effect questionnaire as the primary outcome. Unfortunately, the participants were not able to answer the question satisfactorily. The question aimed at assessing the participants' change following treatment compared to their pre-injury health status on a 15-points numerical rating scale ranging from -7 (much worse) to 7 (much better) relating to pre-injury state. As the patients were in the ED with acute musculoskeletal injuries, most patients were expected to score ≤0, as 0 would represent their habitual health status for most people. However, this was not the case as most patients reported above 0, suggesting that they had a better overall health compared to before their injury. Because of this unexpected deviation, we choose to disregard the prespecified primary outcome and analyze only the other outcome measures as a representation of the 4-week follow-up status.

Statistics

For the caseload study we present patient demographics and diagnoses seen by the physiotherapists. To assess the association between the physiotherapists' prognostic scores and the 4-week outcomes we first performed Spearman's bivariate correlations. For the analyses of the dichotomous PASS question, we analysed differences in the baseline prognosis between participants answering 'yes' and 'no' to PASS using un-paired t-tests.

We used logistic regression analyses to calculate odds ratios (OR) with 95% confidence intervals (CI) for reporting a positive answer ('yes') on the PASS at the 4-week follow-up with higher prognostic scores. P-values of <0.05 were considered statistically significant. None of the underlying statistical assumptions of the logistic regression analysis were violated.

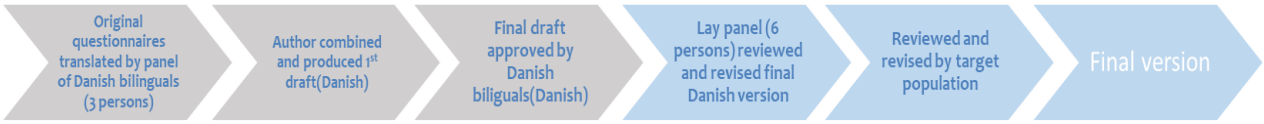
Study II

The CAIT, FAAM and LEFT questionnaires have not previously been translated into Danish. A translation of the questionnaires is important for use in daily clinical practice as well as in the implementation of international research studies. Therefore, the aim of Study II was to translate the CAIT, FAAM, and LEFS questionnaires from English too Danish and too cross-cultural adapt the Danish versions of the questionnaires.

Method

The questionnaires were translated in parallel using a dual-panel approach as described by Hagell et al.[141]. A schematic representation of the ttranslation process is found below (Figure 1).

Figure 1 - Dual-Panel translation process:



Two panels, a bilingual panel (panel 1) and a panel consisting of laymen (panel 2), conducted the translation process. Panel 1 consisted of three Danish bilingual persons with extensive English language competences. Each bilingual person independently provided translations of all the questionnaires. The questionnaires were then condensed into one single draft by one of the group members (CPO). The bilingual panel approved the draft, if there was any disagreement regarding the translations: this was discussed until consensus was reached via online feedback.

The Danish translations of the questionnaires were reviewed and revised by a second panel consisting of Danish laymen who were blinded to the original version of the questionnaire. This panel was instructed to ensure that the average Danish person would understand the wording of the translated questionnaires. The panel consisted of six persons (three women and three men) with an average level of education and no previous history of ankle injuries. After reviewing the questionnaires independently, a focus group-interview was held with all panel 2 members present. At the focus group interview all suggestions for alternate wording was discussed in plenum, until the panelists agreed on the specific wording.

Methodological considerations

Patient-reported outcome measures often refer to questionnaires that are used in clinical setting and in clinical trial. Due to the international nature of many clinical studies and trials it is often necessary to produce several language versions of specific measures[142]. The translated version of the questionnaire needs to be conceptually equivalent which emphases the importance of a cross-cultural adaptation.

Traditionally, forward-backward translation of questionnaires has been the recommended methodology[143–145]. Forward-backward translation consist of obtaining one or several forward translations by independent translator. The translated questionnaires are then back-translated to the source language. The two versions of the questionnaire in the source language are then compared and discrepancies are highlighted. However, this method has several drawbacks and is very time consuming, and even if a translation is good, the back-translation may look nothing like the source questionnaire[142].

An alternative to the forward-backward method is the dual-panel method. This method has been widely and successfully used in several studies in the adaptation of questionnaires[146–152]. Using this method, you avoid the drawback of back-translation, but the method is highly dependent on the panels used to produce the translations[141]. Translating is never a straightforward process. In practice the process is very dependent on the wording and cannot be viewed as a task of "just" finding equivalents of words and stringing them together[142]. Different languages have different and specific ways of putting life into words depending on the context. Using the dual-panel approach, the process of producing a version of a specific questionnaire in another language is considered a process of adaptation rather than translation, which is why the dual-panel approach was chosen in Study II[142].

This study is a first step towards a full validation of the three questionnaires in Danish. A major limitation of the methodology chosen for this study is the lack of establishment of the psychometric

properties following the translation and cross-cultural adaptation[145]. The findings from this translation study most go through rigorous testing before generalizability is established. Testing the generated questionnaires validity, reliability and responsiveness following the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist will be performed, but is not included in this PhD[153].

Study III

To compare the functional outcomes following acute LAS managed by usual care (RICE) or by a treatment approach consisting of pain-guided early rehabilitation we performed Study III.

The study was designed as a multicenter open-label, two-arm, parallel-group, superiority, RCT, with the primary endpoint at four weeks. A methodological protocol was completed before the trial began and can be found as Appendix I. The protocol was submitted to and approved by the local Data Protection Agency (REG-141-2017), the Health Research Ethics Committee in Region Zealand (SJ-628) and was registered at www.clinicaltrials.gov (NCT03527121) before commencement of the trial. The trial was conducted in accordance with the Helsinki Declaration and ICH Good Clinical Practice (GCP). This study follows the CONSORT reporting guidelines for RCTs[89,90].

Setting and eligibility criteria

We recruited participants between May 2018 and January 2020 from the ED at Slagelse Hospital and Horsens Hospital in Denmark. Patients aged ≥18 years were included if they had a grade 1 or 2 ankle sprain sustained within 24 hours of randomization. Patients were excluded if they were unable to bear weight un the affected foot for four steps with/without pronounced limping; were diagnosed with CAI on the affected limb[65,66]; had a fracture diagnosed by X-ray; had previous enrollment in the same study; had major lower limb surgery or other severe lower extremity injury in the past three months on the affected limb; were under the influence of drugs or alcohol; or had a condition that, in the opinion of the investigator, would preclude participation in the study (e.g. not having access to the internet, immobilization etc.).

Procedures

Potentially eligible participants were identified in the ED and received oral and written information about the study and study procedures and underwent a screening examination to assess eligibility. All included participants gave oral and written informed consent.

Descriptive data (age, height, body weight, previous lateral ankle sprain, limb dominance, injured limb left/right, time since injury, education, employment, contact details) were recorded in the ED. All follow-up assessments were collected using an internet-based survey platform (Easytrial), with personal links sent via email to the participants. The online follow-up assessments were performed prior to randomization and at 1, 2, 3 and 4 weeks and 3, 6 and 12 months after enrollment and the windows for completion were ± two days (week one-four) and ± two weeks (month three-twelve).

Randomization and treatment allocation

After inclusion in the ED, the participants were randomised to either pain-guided early rehabilitation or usual care. The online data management program Easytrial produced the blinded randomisation sequence, only revealing treatment allocation of the individual participant to the physiotherapist working in the ED after informed consent and baseline assessment had been completed. Patients were enrolled allocating participants in permuted blocks of 2 to 6 to either the pain-guided early rehabilitation or usual care group (1:1).

Treatments

Participants allocated to usual care followed standard guidelines consisting of advice about Rest, Ice, Compression and Elevation (RICE) provided by the physician at work. The advice also included avoidance of activities with risk of re-injury for a few months, and gradually putting more weight on the ankle, with slow progression to running and twisting.

Participants allocated to pain-guided early rehabilitation received instructions from a physiotherapist on how to manage their acute LAS together with a written homebased exercise program. The participants received advice and instructions in accelerated and early weight bearing, commencing at discharge. It was advised to load and exercise the ankle joint and accepting pain (during loading/exercising) up to, but not exceeding 5 on a 0-10 numerical rating scale (NRS). The written homebased exercise program was initiated at discharge from the hospital. If patients experienced pain exceeding NRS 5, they should follow the same guidelines as the usual care group consisting of Rest, Ice, Compression and Elevation until pain levels was below the NRS pain threshold again. When pain levels had decreased to <6 they should restart the pain-guided early rehabilitation approach. This approach was initiated to guide optimal loading following the acute LAS. Compression, with an elastic bandage, was administered in the ED and instructions on how to apply and manage the bandage correctly were given. The bandage should be worn all day, including during nighttime for three weeks. The elastic bandage should also be used as protection when performing exercises and activities that increased the risk of recurrent sprain for at least three months after the initial injury. Participants were instructed to follow the homebased exercise

program three times each day from discharge to 4-weeks follow-up. It consisted of ankle rehabilitation exercises focusing on walking with full weight bearing, neuromuscular training, balance training, muscle strengthening and jumping (details in Appendix I). The physiotherapists in the ED, which had received specific training in the treatment protocol, instructed the participants in the home exercise program.

A treatment approach of educating patients in full rehabilitation at discharge, commencement of exercises and daily routines already at discharge from the hospital, with NRS pain as modulator for when the tipping point had gone too much to the excessive side (NRS pain ≥ 6) meaning that when patients experienced pain excessive of NRS pain ≥ 6 they should R.I.C.E their foot until pain levels decreased again.

This model has previously been used for patients with Achilles tendinopathy with success[95]. Because of this, we expected patients to experience an increased amount of swelling, but as no study has linked increased swelling in the acute phase with a negative long-term functional outcome, we weighted the potential benefits of increased optimal loading higher. We speculated that implementing a tool for patients to self-administer progression via a pain NRS, when finding the optimal loading after leaving the ED, would secure the most aggressive approach to treatment.

Outcome measurements

As we expected maximal clinical effects on ankle function of the physiotherapists management after four weeks, the primary outcome was chosen as the self-reported ankle function, assessed using the LEFS after four weeks[126]. The LEFS is a patient reported outcome measure providing a total score based on the patient's subjective ankle function. The scale consists of 20 functional leg activities, each scored on a five-point Likert scale (0 impossible, 4 no difficulty), giving a total score of 0 (worst) to 80 (best).

Secondary outcomes included pain at rest and with activity, assessed using 0-10 NRS[136,154]; the foot and ankle ability measure (FAAM) that is divided in two subscales: the FAAM activities of daily living and the FAAM Sports subscales[131]; the Cumberland ankle instability tool[129]; recurrent sprain experienced within last follow up (dichotomized as yes/no); and the EuroQol Health-related quality of life (EQ-5D-3L) questionnaire[155]. Furthermore, global perceived effect (GPE) of treatment was assessed using a transition questionnaire on which the participants would answer if their current LAS-related health status was "unchanged", "worse" or "better" compared to their pre-LAS status[156]. Also, the patient acceptable symptom state (PASS) was assessed by the answer (yes/no) to the question: ''*Taking into account all the activities you have during your daily life, your level of pain, and also your functional impairment, do you consider your current state is satisfactory?*''[157].

Sample size

The study was powered to assess superiority in a comparison between the participants allocated to pain-guided early rehabilitation and those allocated to receive RICE. Assuming that pain-guided early rehabilitation would produce a LEFS score at week 4 that was 9 points larger than the usual care, with a standard deviation of 17 points, we calculated that we would need 112 patients in the intention-to-treat (ITT) population (56:56) to test a two tailed hypothesis with more than 80% power (91%) at a 5% statistical significance level. The 9 point change in LEFS score were based on the systematic review published by Mehta et al.[128], which concluded that the MCID was 9 points in patients with lower extremity musculoskeletal conditions. The SD of 17 points were obtained from the article presented by Bleakley et al.[86]. Although we also investigated effects on other secondary outcomes, we did not power the trial for this because we had no a priori assumptions about effect sizes, and a larger trial may be needed to reliably detect these.

Statistical analysis

Statistical analyses were done on the ITT population, including all randomized participants in the analysis, all retained in the group to which they were allocated. A blinded investigator (CPO) did the initial data handling and all hypothesis testing.

We analyzed continuous outcomes using repeated measures mixed linear models including participants as a random effect, with group (2 levels) and week (4 levels: week 1, 2, 3, and 4) as fixed factors with the corresponding interactions. To assess the adequacy of the linear model(s) describing the observed data - as well as checking the assumptions for both the systematic and the random parts of the models - we investigated the model features via the predicted values and the studentized residuals: i.e. the residuals had to be normally distributed (around zero), and be independent of the predicted values. Results are expressed as estimates of the between group differences in the outcomes at week 1, 2, 3, and 4 visits with 95% confidence intervals to represent the precision of the estimates. Missing data were not imputed but were handled implicitly by the mixed models (maximum likelihood) approach.

Dichotomous outcomes were analyzed using Chi-square statistics or Fisher's Exact test. Results are expressed as number and proportions in each group at week 1, 2, 3 and 4.

We set the statistical significance for hypothesis tests at the conventional level of 0.05. All analyses were done using SAS statistical software (version 9.4).

Results

Highlights of the results presented in the three studies (Study I, II, and III) are listed below.

Study I -	**A prognostic evaluation by physiotherapists as a predictor of short-term outcome after treatment of minor musculoskeletal injuries in the Emergency Department: A prospective cohort study**

- The most common injuries treated by the physiotherapists in the ED are ankle sprains, hand contusions, and wrist fractures
- Physiotherapists' prognoses associate with the patients' symptomatic state four weeks after consulting the ED due to a minor musculoskeletal injury

Study II -	**Dual-panel translation and cross-cultural adaptation of the Danish Version of the Cumberland Ankle Instability Tool (CAIT), Foot and Ankle Ability Measure (FAAM), and Lower Extremity Functional Scale (LEFS)**

- The translation of the CAIT, FAAM and LEFS into Danish and its cross-cultural adaptation to a Danish speaking population were done carefully and without any major inconsistencies

Study III -	**A randomised trial of pain-guided early rehabilitation of acute lateral ankle sprains delivered by physiotherapists in the emergency department**

- Treatment of acute LAS in the ED by pain-guided early rehabilitation did not result in a significant increased effect in the patients' self-reported function after four weeks compared to usual care (RICE)
- The group treated by pain-guided early rehabilitation showed a decrease in recurrent sprains compared to usual care (RICE)
- Unfortunately there were high attrition rates at the 3-, 6- and 12-month follow-ups, which precluded statistical comparisons.

The findings of the PhD-thesis are presented as three separate manuscripts found as Appendix II, III, and IV. The results are also presented in the following sections.

Study I

Caseload study

In total, the physiotherapists in the ED managed and treated 432 patients during the 3-month inclusion period. Most of the patients, 339 (78.47%) were treated with the physiotherapists working as the primary contact health professional. The most common diagnoses treated by the physiotherapists in the ED were ankle sprains (11.3%), hand contusions (8.6%) and wrist fractures (8.6%).

Prediction cohort study

One-hundred-nine patients (55% females) were included in the prediction cohort study. The mean age was 40.3 years (SD 16.3), and mean BMI was 26.4 (SD 5.1). In the ED, the patients reported pain with activity of 72.5 mm (SD 20.2) and pain at rest of 36.5 mm (SD 22.2). At the 4-week follow-up, 61 participants (56%) answered the follow-up questionnaires. Except for the proportion of females, the responders and non-responders were similar at baseline (Table 2, Appendix II).

The physiotherapists' prognostic scores ranged from -7 to 2 (mean -1.92).

At the 4-week follow-up, the average VAS pain with activity had decreased to 40.9 mm (SD 28.8) and the average VAS pain with rest had decreased to 23.5 mm (SD 22.6).

The physiotherapists' prognostic scores were significantly and negatively correlated with VAS pain at rest (r_s= -0.31; *P*=0.017) and at activity (r_s= -0.32; *P*=0.013). The prognostic scores were positively correlated with EQ-5D index (r_s=0.36; *P*=0.004) and EQ VAS (r_s=0.32; *P*=0.012) at the 4-week follow-up. Altogether the results suggest that a higher prognostic score at baseline is associated with a better outcome after 4 weeks.

At the 4-week follow-up 23 (38.3%) participants answered 'yes' to the PASS and had an average prognostic score at baseline of -1.2 (SD 1.6). Thirty-seven participants (62.7%) answered 'no' and had an average baseline prognostic score of -2.4 (SD 1.7). There was a statistically significant difference in the baseline prognostic scores between participants who answered 'yes' and 'no' to the PASS questions at the 4-week follow-up (mean difference: 1.2 points (95%CI 0.3 to 2.1).

The prognostic scores were statistically significantly associated with the PASS question as the logistic regression analyses resulted in an odds ratio of a positive answer ('yes') of 1.61 (95%CI 1.11 to 2.35; P=0.013) with each one-unit increase in prognostic scores.

Study II

During the translation process, the two panels (panel 1 and 2) provided feedback that resulted in adjustments in the final version of the translated questionnaires (Table 1, 2, 3, Appendix III). The participants in both panels found no difficulty in understanding most of the items. In general, they found the LEFS short and easy to understand; the QAIT questionnaire to be long and difficult to fill out; and the FAAM to be long but very relevant for patients with acute ankle injuries.

Study III

Between May 2018 and January 2020, 77 patients were included in this study to receive either usual care (n=38) or pain-guided early rehabilitation (n=39). 33 (43%) participants (20 usual care; 13 pain-guided early rehabilitation) completed the 4-week assessment. Figure IV.A summarizes the recruitment, randomization, and follow-up rates. Table IV.A summaries the baseline demographic and clinical characteristics of the participants and Table IV.B and Table IV.C the primary and secondary outcomes. See Appendix IV for Figure IV.A and Table IV.A-C.

Except for the GPE (Mean difference -1.96; 95% CI [-3.51 to -0.41]) and FAAM Sport (Mean difference 13.84; 95% CI [0.58 to 27.1]), all in favor of the usual care group, there were no statistically significant group differences at the 4-week follow-up (Table IV.B and IV.C). The statistically significant group differences in GPE and FAAM-Sport at the 4-week follow-up favoring usual care correspond to effect sizes of 0.57 and 0.47, respectively, indicating moderate effects.

In the 4-week follow-up period, 8/39 (21%) participants in the pain-guided early rehabilitation group and 14/38 (37%) in the usual care group reported a recurrent sprain of the same ankle, with no significant difference between the two trial arms (P=0.14).

Unfortunately, there were high attrition rates at the 3-, 6- and 12-months follow-ups, which precluded statistical comparisons. For completeness of reporting, we therefore present raw data across all follow-ups as Appendix IV.B.

Discussion

This chapter includes a short discussion of each study. This is accompanied by a collective discussion, including the clinical relevance of the results obtained during the PhD study, and considerations regarding overall strengths and limitations.

Study I

Physiotherapists in the ED have been implemented across several countries. However, the caseload treated in a Danish context had not previously been described. In this study, we showed that the most common injuries treated by the physiotherapists in the ED are ankle sprains, hand contusions and wrist fractures. Moreover, we wanted to investigate the physiotherapists' ability to predict the short-term outcome after treatment in the ED. The results showed that the physiotherapist's prediction was associated with the patient's short-term outcome.

The ED is often the first point on which patients seek contact to the healthcare system. This gives the physiotherapists a potential for providing the best possible quality of care at the earliest phase of the injury. Early phase optimized treatment holds the potential to counteract a negative spiral of increased pain and reduced function, which ultimately leads to the development of chronic conditions[97].

Normally, all patients leaving the ED with a minor musculoskeletal injury are told to contact their general practitioner if ongoing symptoms pertains for more than 7-10 days. This information is however not based on the individual patient and so may not be sufficient instruction for some patients[75,158,159]. The physiotherapists "hunch" is however, as shown in Study I, a valid tool to identify these patients. Some patients may benefit from being treated by a physiotherapist because of the added competencies in musculoskeletal injuries, but also because physiotherapists are able to provide guidance extending beyond the normal scope. Having a physiotherapist available in the ED gives the opportunity to provide treatments ranging further into the expected future. Further studies are needed to evaluate the impact of early phase optimized treatment regimens and their role in preventing chronicity in musculoskeletal injuries.

Few studies have evaluated the effectiveness of physiotherapists in the ED and only two randomized controlled trials (RCTs) have reported on PROMs[55,56]. A study by McClellan et al.[55] published in 2012 compared the overall effectiveness of physicians, nurses, and physiotherapists working in a single ED in UK. The study results showed no significant difference between the three groups (patients treated by physicians, nurses, or physiotherapists) during the 8-week follow-up

period in change of the DASH (Disability of the Arm, Shoulder and Hand score) for upper-extremity injuries or the LEFS for lower-extremity injuries. This indicates that nurses and physiotherapists provide equivalent clinical outcomes to physicians. However, there is a strong need for elaboration into these findings and future randomised studies comparing physiotherapists with standard care across multiple EDs. This could greatly enhance the external validity of the findings.

There are several limitations to study I. First, the study was limited to a single centre. Although presentations to the ED may be comparable to other EDs, variations in the scope of practice will exist due to different healthcare authorization legislations and local hospital policies. Furthermore, patients presenting outside normal working hours for the physiotherapists were not included in this cohort study (12.30-21.00). The flow of patients in the ED peak at around 11.00 o'clock and continues to be high throughout the day to around 20.00/21.00 o'clock[160]. Further studies are needed to clarify the distribution of patients arriving at the ED categorized as triage blue, which constitutes patients relevant for primary contact physiotherapists in the ED. This may compromise the generalizability of the results gathered in our study. Secondly, the physiotherapists in this study follow the national competence profile developed by the national physiotherapy association[43], which is a requirement for independent roles in an ED, but at the same time limits the generalizability to other settings without highly trained physiotherapists. Thirdly, the distinct nature of some injuries may influence the physiotherapists' prediction as 4 weeks follow-up will not sufficiently represent end of recovery for some injuries. We did not assess the prognostic results within specific diagnoses due to a limited study sample but speculate that for some injuries longer follow-up is needed to evaluate prediction of full recovery. However, the 4-week time frame may have been incorporated in the physiotherapists' prognoses of these patients, thus resulting in lower prognostic scores for these patients. Further, other types of information could have been useful in identification of potentially modifiable factors that associate with the prognoses. Such information could have helped identifying the underlying factors that the physiotherapists based their prognoses on and used to propose interventions to mitigate negative outcomes. Finally, the low response rate (56%) to the 4-week follow-up survey is a limitation, although only the distribution of females was significantly different between responders and non-responders.

With the results gathered in Study, I it would be possible to identify specific injuries of interest and target validated PROMs to that injury. Further studies are needed to validate the physiotherapists' "hunch" as a predictor for musculoskeletal injuries after treatment in the ED.

Study II

In the assessment of ankle injuries or ankle disorders, the questionnaires CAIT, FAAM and LEFS are well-known measurement tools that are widely used for measuring lower limb functional status. A Danish version of the questionnaires did not exist prior to this study. We therefore translated and cross-cultural validated the questionnaires into pre-final versions before commencement of the randomised trial.

A major limitation of the of this study is the lack of establishment of the psychometric properties following the translation and cross-cultural adaptation[145]. The process of psychometric evaluation of CAIT, FAAM and LEFS, including validity and reliability, is discussed below.

To investigate the psychometric properties, the pre-final versions of the CAIT, FAAM and LEFS questionnaires, presented in Study II, should follow the measurement properties provided in the checklist from The Consensus-based Standards for the selection of health status Measurement Instruments (COSMIN)[153,161,162].

The ability of the questionnaires to discriminate between participants with/without foot and ankle disorders and/or CAI should be assessed by comparing the score of the individual items to the total score across the groups.

Concurrent validity should be determined by assessing whether the score of the Danish versions of questionnaires CAIT, FAAM and LEFS correlate with the score of a gold standard PROM. To validate the questionnaires, CAIT, FAAM and LEFS they could be compared to an already validated generic health surveys regarding the overall quality of life such as the 36-item short form survey (SF-36)[163,164] or the Foot and Ankle Outcome Score (FAOS)[165,166].

Factor analysis should be used to examine the construct validity of the Danish version of CAIT, FAAM and LEFS. Floor and ceiling effect should be deemed present if 15% or more of the participants reach the lowest or highest achievable score[167]. This psychometric property would only be assessed among participants with a lower extremity disorder, as a ceiling effect is expected among participants with no lower extremity disorders.

The reliability should be determined by assessing internal consistency and the test-retest reliability. Internal consistency should be assessed by calculating the interrelatedness between the items within the questionnaire. This should be calculated using Chronbachs alpha in the answers from the initial questionnaire. Internal consistency is considered to be satisfactory when Cronbachs alpha is between 0.70 and 0.95[167]. Test-retest reliability is the degree to which test scores remain unchanged when measuring a stable individual characteristic on different occasions[162]. Test-retest reliability

should be measured by the use of intraclass correlation coefficient between the scores of the initial and second test.

Study III

Acute LAS was found to be the most common injury treated in the ED in Study I and a high proportion of patients with acute LAS is known to develop long-term impairments[97]. With this study, we aimed to compare if pain-guided early rehabilitation was superior to RICE in treatment of acute LAS in the ED. The study showed that pain-guided early rehabilitation did not result in a significant increased effect in the patients' self-reported function after four weeks. Unfortunately, there were high attrition rates at the 3-, 6- and 12-month follow-ups, which precluded statistical comparisons. For completeness of reporting, we therefore present raw data across all follow-ups in Appendix IV.B.

Prevention of recurrent sprains is important in the first months after the initial sprain. In a review[168], including 20 studies investigating treatment strategies for acute ankle injuries, with eight studies scoring ≥7 on the AMSTAR tool. The study concludes that there is strong evidence for exercise therapy and bracing in preventing ankle sprain recurrence across injury types[168]. These findings are backed up in a more recent review by Vuurberg et al[85], promoting that bracing or taping is effective at preventing recurrent ankle sprains. In the EDs in Denmark, the current treatment approach is not to use bracing or taping when treating grade 1 or 2 ankle sprains. In this study, we speculated that the introduction of a treatment approach consisting of bracing with orthoses would not be feasibly after completion of the study. Because of this, we choose to educate people in applying a figure of eight bandage. This was used both as protection against new injury but also served as compression in the first three weeks after the initial injury. The elastic bandage used is commonly available in the EDs and we favored it compared to the widely used Tubigrip®. This is in line with current literature stating that Tubigrip® has no positive effect on functional recovery and may increase the requirement for analgesia[169]. The approach of teaching patients in applying the figure of eight elastic bandage may have contributed to the result that fever patients experienced a recurrent sprain in the intervention group (21% in the pain guided group and 37% in the usual care group) in our study. A study providing an overview of the existing literature on the epidemiology of acute ankle sprains stated that the proportion of recurrent ankle sprains are reported between 12%-47%[70]. Thus, highlighting the need for research into the time-dependent measure as a predictor of recurrent ankle sprain. In this study, we followed patients for 12 months after inclusion, unfortunately due to high attrition rates in both groups no clear conclusion can be made on the long-term effects of the two allocated treatment regimes. For future epidemiological studies we however not that within the 12-

month follow-up period 32/77(42%) participants reported a minimum of one re-injury of the same ankle please see Appendix IV.B for details.

Pediatrics and adolescents (patients under the age of 18) were excluded from the study. This was the most common reason for being excluded (42.8%). Experiencing a first time acute LAS is common among patients under 18 and is linked to prolonged instability and functional impairments, ultimately leading to CAI later in life[170]. Unfortunately the literature has limited evidence in the treatment of this subgroup[170]. Further research in the treatment of acute LAS in pediatric and adolescents is needed as they represent a considerable subgroup of the patients treated in the EDs.

Patients presenting with CAI were also excluded from the study. The definition of CAI used in this study, was as proposed by Delahunt et al.[65]:

…To be classified as having chronic ankle instability, residual symptoms (''giving way'' and feelings of ankle joint instability) should be present for a minimum of 1 yr post-initial sprain[171].

We chose to use the proposed selection criteria for patients with CAI by Gribble et al.[66] to ultimately exclude patients with CAI in the ED. The selection criteria elucidates on the criteria "residual symptoms" in the definition presented by Delahunt et al[65]. Residual symptoms are characterized as being present if the patient has occurred a minimum of two episodes of either "recurrent sprain" or "giving way" within the past six months prior to enrollment. During the process of setting up and training of investigators, some unclarity with the proposed exclusion criteria arose. The investigators were unsure of the numbering of episodes described by the patients.

As patients were to be included in the study if they had a grade one or two acute LAS. This ultimately resulted in these guidelines, regarding giving way and recurrent sprain:

- Exclude patients if they had had a minimum of two episodes of giving way six months prior to their ED visit
- Exclude patients if they had had a minimum of two episodes of recurrent sprain six months prior to their ED visit

This approach was chosen due to uniformity and making it easy for the investigators to implement. We are however aware that the definitions do not completely follow the ones proposed by Gribble et al. as the patients with "recurrent sprain" would have sustained two recurrent episodes AND one new episode (the one they are presenting with). This means that the patient should have sustained a minimum of three "recurrent sprains" to be excluded. We were unsure if the guidelines could be combined, e.g. patients reporting one episode of giving way and one episode of recurrent sprain

should be diagnosed with CAI in the ED. Ultimately we chose to follow the precise wording, indicating that a combination was not accepted. This approach resulted in a broader inclusion criterion as patients were allowed to have two episodes and not only one before their enrollment. Future studies on the selection criteria for acute LAS are needed to specify precise and uniform inclusion and exclusion criteria, providing comparable data across research.

There are several limitations to this study. Importantly, we experienced a relatively high attrition rate across all follow-ups. The questionnaires were sent to the participants in the study at 1, 2, 3 and 4 weeks and 3, 6, and 12 months. The data was collected using an internet-based platform (Easytrial). Even though, the participants were reminded to answer the questionnaires by text messages and e-mail, the attrition rate was high. This might be because the questionnaires were too comprehensive and time consuming to answer, or the non-responders recovered fully and lost interest. There can be many other explanations and any attempts to explain it will be very speculative. A higher response rate might have been achieved if the participants were scheduled for appointments to answer the questionnaires. We used a pragmatic approach and did not choose to incorporate clinical follow-up visits with a physiotherapist, as this is not current practice. Other studies investigating patients treated in the ED have shown similar difficulties with high attrition rates[172]. The high attrition rate may cause bias, positive or negative, and poses a serious risk for the studies external validity. We expected the group who completed the HEP to perform better, including in the FAAM-Sport. However as indicated by our results a pain-guided approach as compared to RICE may not be superior. Further studies are needed to evaluate effects on long-term follow-ups. Also, an important limitation is that we did not survey the participants' adherence to the allocated treatment strategies. The lack of between-group differences could be speculated to reflect a low adherence to the early pain guided loading strategy, although adherence was not evaluated. Finally, as we did not receive our pre-defined sample size, further confirmatory trials are needed.

Collective discussion

Advances in the literature aiming at enhancing the outcome of commonly treated musculoskeletal injuries following presentation to an ED exist[75,158,159,173–176]. Despite this fact, there seems to be a lack of EDs keeping up with the evidence produced on the topic, failing to implement the results in their clinical practice guidelines[84,177]. This could be due to musculoskeletal injuries being regarded as small innocuous injuries that will heal spontaneously by the majority of the current staff at the ED. To ensure that quality in treatment is up to date, focus on the substantial group of patients being treated with musculoskeletal injuries should be increased. This could be solved by expanding the group of health care providers in the ED with physiotherapists. Both patients and the allied health

professionals view physiotherapists as having expert clinical skills and an educational role in the treatment of acute musculoskeletal injuries in the ED[178]. An updated status report on the ongoing progress of implementing physiotherapists in the EDs in Denmark is needed to provide knowledge translation across healthcare professions, organizations and politicians.

Physiotherapists working in the EDs, who are managing and treating patients with musculoskeletal injuries, are a valuable asset[179]. Not only are they managing a broad caseload of patients independently, but are also contributing to the interprofessional collaboration with key expertise knowledge. This expertise knowledge is based on the foundation from basic physiotherapy training and are supplemented with a specialist education in musculoskeletal injuries. Current practice for the management and treatment of musculoskeletal injuries in the EDs is not to schedule follow visits. In some cases, this may contribute to the progression of recurrent or persistent symptoms. However, as we showed in Study I, the physiotherapists are capable of identifying the patients who may benefit from referral to further treatment, why scheduling of follow-up visits could be considered when assessing future clinical practice.

The application of using the translated and cross-cultural validated LEFS, FAAM and CAIT in clinical practice, would give clinicians, treating patients after ankle injuries, a tool to follow progression over time. This would be informative during follow-up visits or in identifying the patients who may benefit from referral to further treatment.

In the RCT, we did not observe a significant effect of the pain-guided early rehabilitation approach within the four-week follow up in ankle function. The group however showed a decrease in recurrent sprains which could contribute to the prevention of CAI. The approach can be implemented directly to an ED setting, but additional training of the health care providers may be needed.

Study design

In all clinical studies, we used a pragmatic trial design. The definition of a pragmatic clinical trial has been proposed by Califf and Sugarman[180]:

Designed for the primary purpose of informing decision-makers regarding the comparative balance of benefits, burdens and risks of a biomedical or behavioral health intervention at the individual or population level.

This design was chosen, as we wanted results that could be directly attributed to clinical practice in the EDs. To achieve generalizable results that could be implemented as usual care without the need for huge changes to the EDs; all studies were carried out to ensure a low impact on the daily

routines of the physiotherapists, physicians and nurse practitioners. The ED is already a stressful environment and we wanted to avoid an increase to this by making significant changes to the staff burden. Furthermore, it was not possible to blind study participants or clinicians for treatment allocation in Study III. This may have resulted in bias, e.g., patients allocated to usual care might have been disappointed with not receiving "physiotherapy" and therefore sought treatment elsewhere. Unfortunately, we were not able to implement an activity tracker to accurately investigate differences between groups, reflecting adherence to the study protocol. Retrospective data accessed from the patients smartphone or smartwatch may provide an indication of the patients' compliance. In Study III Patients in the pain-guided early rehabilitation group were instructed to exercise three times each day for 4 weeks following the acute ankle sprain. We therefore used the 4-week follow-up as the primary endpoint in this RCT. However, up to 40% of patients develop residual physical disability, such as CAI, extending beyond the 4-week period, why long-term follow-up are advised for future studies.

Study population

All patients included in Study I and III presented to an ED and were managed and treated by a primary contact physiotherapist in the acute setting. This was done due to the nature of the ED with a management approach of see and treat. The patients included in the prediction cohort Study I and Study III were all aged ≥18 years. Inclusion of patients aged <18 would have brought new insights to a commonly treated group of patients in the EDs, both in regard to the prediction cohort and the acute LAS treatment study, why this should be considered in future studies.

Physiotherapists in the ED

The role of physiotherapists in EDs varies within the context and the scope of practice of the ED. The foundation and rationale for implementing the physiotherapists were set of by the increasing demand on the EDs and reflect the direct value for the organization's needs. As shown previously, the regions across Denmark operate with a variety of quality indicators, e.g. patient waiting time or patient satisfaction. These quality indicators ensure value for the health-care system but may provide limited value for the individual patient treated in the ED. This illustrates the needed shift in the research of physiotherapy in the ED to provide the best available evidence mixed with the clinical expertise treatments for the patient.

With Study I, we wanted to investigate the caseload treated by the physiotherapists, providing quantifiable results on the value of implementing physiotherapists in the ED to health-care providers. Moreover, the study provided information on the physiotherapists' ability to predict the

associated outcome four weeks after their visit, which provide value in finding the best possible care for patients with acute minor musculoskeletal injuries. Future studies should aim at determining the other potential aspects of the value added to the ED by implementing physiotherapists, such as the socioeconomic value and the value for the individual patient e.g., cost-effectiveness analysis and PROMs.

PROMs in acute LAS research in EDs

LEFS was the most feasible instrument to measure patient reported lower limb function at baseline in the ED. The instruments instruction in scoring is:

...Today, do you or would you have any difficulty at all with:

The wording "…would you have…" is important because of the acute nature of the patient's injury, as patients are not expected to have commenced in the functional tasks within each item before presentation to the ED. With the expression "would you have" the patients are able to answer all items despite the fact that they haven't tried it yet e.g. getting into or out of the bath.

We translated and cross-cultural validated three commonly used questionnaires in LAS research before initiation of the randomised trial. This approach was chosen to strengthen the results and enhance the validity of the outcomes.

In and exclusion criteria in acute LAS research

There is a great variation in the in- and exclusion criteria when performing acute LAS research, thus potentially leading to heterogeneous results. In a systematic review and meta-analysis it was described that studies had a significant overlap regarding the injury type of interest, acute LAS or acute recurrent sprain[168].

A pragmatic approach would have been to enroll all patients with acute LAS. However, the distinction was important as the treatment of recurrent sprains in CAI and acute LAS incorporate different rehabilitation exercises and other modalities aiming at, and ultimately leading to, different endpoint outcomes. Identifying people with CAI presenting to the ED with a recurrent ankle sprain could positively contribute in the enhancement of the following rehabilitation. We were unable to retrieve guidelines for the acute treatment after a recurrent ankle sprain in patients with CAI[84]. Future studies should investigate the optimal acute, sub-acute and long-term treatment approach after a recurrent ankle sprain in patients with CAI, highlighting similarities and difference between acute LAS injuries.

"Giving way" is a common term found in the literature when investigating CAI and acute LAS. A laboratory, capturing giving way episode, highlighted the mechanism associated with the term in a

patient diagnosed with CAI, describing it as: plantar flexion of the ankle joint, as well as internal rotation and adduction of the ankle-foot complex[181]. Recently Hertel et al.[74] proposed an updated model of CAI that holds eight primary components for the development of a patient's clinical outcome: (1) primary tissue injury; (2) pathomechanical impairments; (3) sensory-perceptual impairments; (4) motor-behavioral impairments; (5) personal factors; (6) environmental factors; (7) component interactions; and (8) the spectrum of clinical outcomes. The model proposes a continuum of possible outcomes following initial LAS, ultimately divided in five groups: LAS Coper; CAI Asymptomatic; CAI Occasional giving way; CAI Frequent giving way; and CAI Recurrent sprains (Figure 2). In the study no reference are provided for the distinction between occasional and frequent giving way[74], which would lead to an unclear application of the instrument in future clinical research.

Furthermore, the study describes the link between increasing giving way episodes and further secondary tissue damage, thus leading to a negative pathomechanical vicious cycle ending with poorer outcome[74]. This means that a person gradually moves from being a LAS Coper to developing CAI, thus moving down the ladder (Figure 2). This negative spiral is widely accepted in the literature as the path to CAI[73].

Figure 2 - The proposed outcomes by Hertel et al.[74]

The best conservative treatment of CAI consists of high dose (>900 min) exercise therapy and use of an external support[168]. For a person with CAI, commencing in these treatment strategies, the goal is, among others, to prevent recurrent sprains. But, as shown with the ladder presentation in Figure

2, this “jump” may be too high for the patient to make in one go, thus ending in a group still diagnosed with CAI but experiencing giving way. In this case, the person is actually moving up the ladder, as the person is preventing recurrent sprains but still experiencing giving way. With this, giving way episodes become a positive outcome.

General limitations

The limitations pertaining to the individual studies have been outlined in the sections describing the individual studies (see Study I, Study II and Study III). A major limitation to Study II is that no assessment of the psychometric properties of the Danish version of the three questionnaires was done. Psychometric properties refer to the validity and reliability of the questionnaire. To state that a questionnaire is reliable and valid, the psychometric properties must be evaluated extensively. Due to limited time and resources, this was not done with the questionnaires in Study II, but should be done in a future study, before the questionnaires can be used in the clinic. In Study III, we used the Danish versions of the questionnaires CAIT, FAAM and LEFS. The translation to Danish and the cross-cultural adaption is a strength to the study interpretation. However, the lack of assessment of the psychometric properties of the Danish versions of the questionnaires is a limitation.

In Study III, a relatively high attrition rate across all follow-ups were found, which is a major limitation to the study. Other studies investigating patients treated in the ED have shown similar difficulties with high attrition rates[172]. Incorporation of clinical follow-up visits with a physiotherapist might have reduced the attrition in both groups. During the study, we used a pragmatic approach and did not choose to incorporate clinical follow-up visits with a physiotherapist, as this is not current practice, but could be considered in future studies. The high attrition rate may cause bias, positive or negative, and poses a serious risk for the studies external validity. The interpretation of Study III must be made with extreme caution.

Future perspectives

The current thesis aimed to evaluate the caseload and effectiveness of physiotherapists in the treatment of minor musculoskeletal injuries in a hospital ED, however, several important questions remain to be answered.

In the prediction cohort, we showed that physiotherapist's prognosis is associated with the patient's acceptable symptom state four weeks after consulting the ED due to a minor musculoskeletal injury. Future studies investigating the physiotherapists' ability to predict long-term function and diagnose-specific function should be considered.

The questionnaires CAIT, FAAM and LEFS were translated into Danish and cross-cultural adapted, but future studies should aim at examining the questionnaires validity, reliability and responsiveness following the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist. A well designed clinimetric study assessing the Danish translated questionnaires psychometric properties will give clinicians and researchers new ways of measuring ankle foot function in a Danish context.

Findings from Study III showed no additional short-term effect in ankle function after the pain-guided early rehabilitation approach when compared to usual care. The attrition rate was relatively high across all follow-ups and we only included 69% of the estimated number of patients needed, resulting in low statistical power. Because of the study being underpowered, the results cannot be generalised to the greater patient population. In retrospect, we would advise other researchers conducting randomised trials in EDs on ankle sprains to conduct a feasibility study before commencement. Future studies could aim at investigating the effect of optimal loading, in the acute phase, on the functional status early after injury and the risk of developing CAI, but the studies should consider scheduling follow-up visits at the ED to improve the treatment approach and lower the attrition rate.

Conclusion

The demand on EDs throughout Denmark is increasing. Physiotherapists were introduced in the ED to improve the flow of patients and ensure quality in treatment of patients with minor musculoskeletal injuries. The role of the physiotherapist has now evolved into a primary contact role, where the physiotherapists have the same authorities as physicians for treatment of minor musculoskeletal injuries.

In the prediction cohort study (Study I), we showed that the physiotherapist's prognosis associates with the patient's acceptable symptom state four weeks after consulting the ED due to a minor musculoskeletal injury. Within the study, we also investigated the caseload managed and treated by the physiotherapists working in the ED and found that ankle sprains, hand contusions and wrist fractures are the most common diagnoses treated. In Study II, the questionnaires CAIT, FAAM and LEFS were translated into Danish. The cross-cultural adaptation of each questionnaire to a Danish speaking population was done carefully and without any major inconsistencies and the questionnaires can now be further tested for implementation in Danish settings. The functional outcomes following acute LAS managed by usual care (RICE) delivered by physicians was compared to a treatment approach consisting of pain-guided early rehabilitation delivered by physiotherapists in a RCT (Study III). Findings from Study III showed no additional short-term (four weeks) effect in ankle function after the pain-guided early rehabilitation approach when compared to usual care. The pain-guided early rehabilitation group experienced fever recurrent sprains compared to the standard care group within the first four weeks after injury, but the pain-guided early rehabilitation group used more analgesia than the standard care group four weeks after injury.

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Appendix I – RCT protocol

CLINICAL STUDY PROTOCOL

Management of acute lateral ankle sprains: A randomized, controlled trial

Principal Investigator:	Christian Olsen, PT, MSc., PhD Candidate
Investigators:	Marius Henriksen, PT, PhD, Professor Søren Thorgaard Skou, PT, PhD Finn Erland Nielsen, MD, DMSc
Sponsor:	Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals.
NCT ID:	Not yet assigned
Unique Protocol ID:	SJ-628
Date:	10/4 2019

Study committees

Protocol Development Committee:

Name	Title & Position	Affiliation
Christian Olsen	PT, MSc, PhD Candidate	Næstved-Slagelse-Ringsted Hospitals
Marius Henriksen	PT, PhD, Professor	Bispebjerg-Frederiksberg Hospital
Søren Thorgaard Skou	PT, PhD, Head of Research	Næstved-Slagelse-Ringsted Hospitals
Finn Erland Nielsen	MD, DMSc	Næstved-Slagelse-Ringsted Hospitals
Mikael Elsborg	PT	The Regional Hospital in Horsens

Flow Charts

Enrollment process

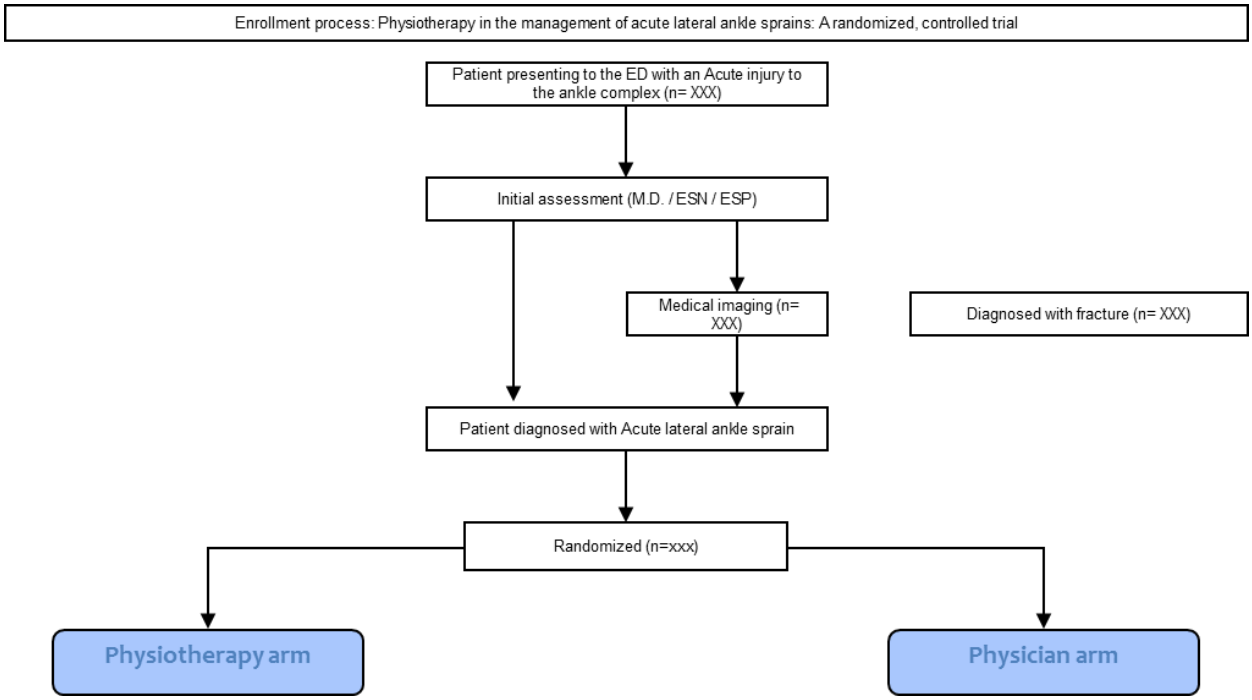

Figure 1 Enrollment process

Study flow chart

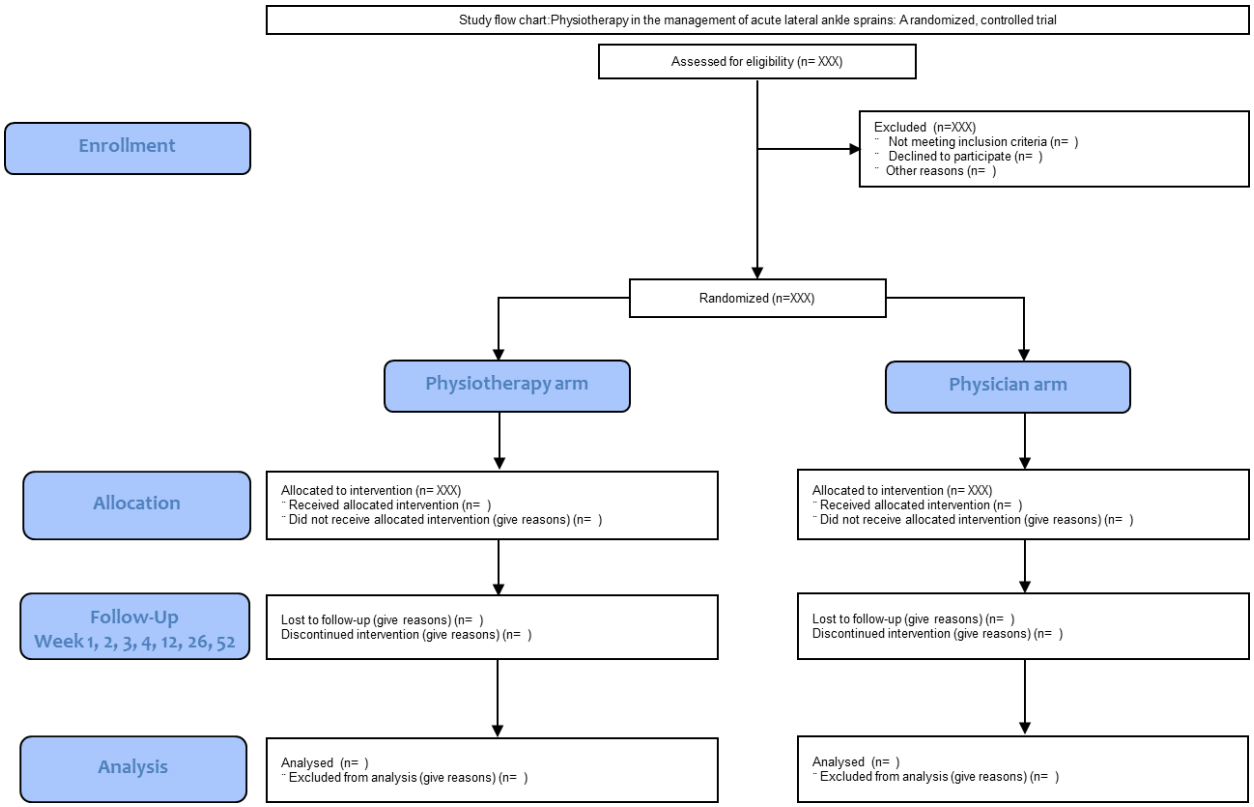

Figure 2 Study flow chart

Visit schedule

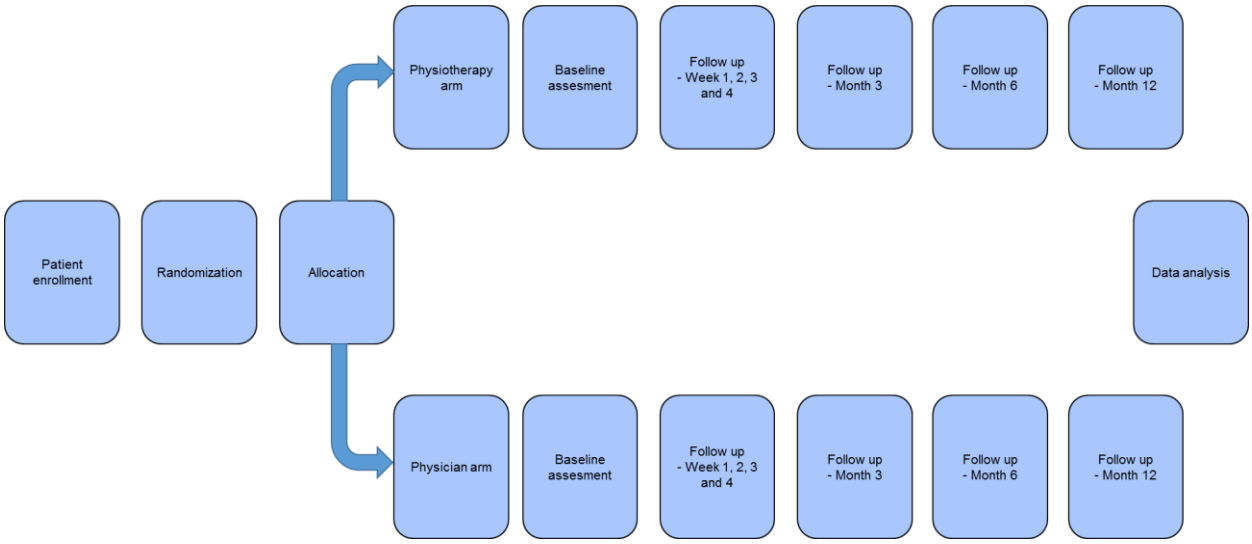

Figure 3 Visit schedule

Trial Identifier

Full title of trial

Management of acute lateral ankle sprains: A randomized, controlled trial

Short title

Management of acute lateral ankle sprains

Acronym

Pending

Health Research Ethics Committee Number

SJ-628

Trial registration identifier and date

Pending

Version number and date

Version 1.0 (first draft for committee review; pre-authorisation version)

Version 1.1 (Updated with changes, as specified by the secretary, before presentation to the health research ethics commitee)

Version 1.2 (Updated with changes, as specified by the regional health research ethics committee)

Version 1.3 (Updated with changes, as specified by reviewers from www.clinicaltrials.com)

Version 1.4 (Updated with changes, re-calculation of sample size)

Revision history

Version #	Issue date	List of major changes
1.0	May 29, 2017	This is the first draft
1.1	June 8, 2017	All questionnaires will be translated to Danish before trial start. The Study will be carried out following "The Act on Processing of Personal Data" All positive, negative or inconclusive results will be published at www.clinicaltrials.gov.
1.2	July 25, 2017	Mikael Elsborg is included in the study committee. The economic properties for this study is included in the written information.
1.3	May 3, 2018	Translated all information to English before publication on www.clinicaltrials.com. Updated the first page to include the unique Human Subjects Review board number: SJ-628 and date.
1.4	April 10, 2019	Re-calculation of sample size added. Sample size target: 112 patients.

Sponsor

The Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals.

Background Information

Lateral ankle sprains (LAS) is the most common injury in the active population [1–4]. Not only is the injury prevalent within organized sports, but also display high prevalence in the general population

presenting at the emergency departments (ED) [2,5]. LAS accounts for about 3-5% of all visits to the ED, but total LAS incidence rates are increasing in the general population[6 10].

Acute LAS is defined by Delahunt et al.[8] and endorsed by the International ankle consortium[9] as: *"An acute traumatic injury to the lateral ligament complex of the ankle joint as a result of excessive inversion of the rear foot or a combined plantar flexion and adduction of the foot."* The treatment of LAS in the emergency department consists of initial assessment and acute management of the injured foot, traditionally done by a physician. The typical assessment consists of ruling out severe injury, i.e. fracture, using the Ottawa ankle foot rules [10,11]. The acute management of the injured ankle is typically composed of a treatment approach consisting of Rest, Ice, Compression and Elevation (RICE).

Extended Scope of Practice (ESP) physiotherapists in EDs have shown to generate high levels of patient satisfaction[12,13], reduce patient waiting times[14] and have high clinical effectiveness[13], yet high quality randomized trials investigating the clinically effectiveness of ESP physiotherapy are lacking. Acute LAS is one of the most common injuries managed in EDs and poor functional status within the initial 2 weeks after injury is predictive of development of chronic ankle instability (CAI)[15], which can be a serious barrier for future physical activity and occupational performance. Early and targeted interventions provided in the emergency department by ESP physiotherapists may therefore prove to be beneficial for the patients and the society.

We therefore propose this trial that aims to assess the effectiveness of ESP physiotherapy as a mean to enhance the outcome of acute LAS following presentation to an emergency department.

Study Hypothesis

Hypothesis

The functional outcome following presentation to an ED with an acute LAS is superior when managed by an ESP physiotherapist compared to usual procedures.

Study Design

Description of the protocol

This is a randomized, pragmatic, superiority study with 1, 2, 3 and 4 weeks, and 3, 6 and 12 months of follow-up (figure 2). The study will be carried out in the emergency department at 2 large public hospitals in Slagelse and Horsens, Denmark. One-hundred-twelve adults with an acute lateral ankle sprain will be included in this study.

The participants will be randomly allocated to one of two treatment strategies:

> **Strategy A**: A single session with advice and instructions from an ESP physiotherapist in rest, ice, compression and elevation AND pain guided early weight bearing plus a written home-based exercise program (ESP physiotherapy group).

or

> **Strategy B**: A single session with advice and instructions from a physician in rest, ice, compression and elevation (usual care).

The randomized allocation will be equal (1:1).

Justification of a pragmatic trial design

The pragmatic trial design has the benefit of making employees and decision-makers in the emergency department aware of the protentional benefits in early weight bearing and exercise in the large group of people presenting with an acute LAS. Participants receiving information and advice from a physiotherapist in the emergency department, will be giving instructions in early weight bearing and exercise and the participants receiving usual care will not, because it is the effects of these two strategies, when administered in the emergency department, we want to compare. The pragmatic design means that the trial will provide valuable information that will help clinicians and decision-makers decide if advice from a physiotherapist in the emergency department improves the clinical outcomes of acute LAS.

Duration of study participation

The study's duration is 12 months after randomization.

Selection and Allocation of participants

Number of participants planned

It is anticipated that 112 participants will be enrolled in this study. A participant may be enrolled in this study provided he/she has met all the inclusion criteria and has not met any of the exclusion criteria.

Inclusion Criteria

An individual will be eligible for study participation if he/she meets the following criteria:

1. A grade 1 or 2 LAS sustained within 24 hours of randomization
2. To be a minimum age of 18

3. Signed informed consent

Exclusion Criteria

A participant will be excluded from the study if he/she meets any of the following criteria:

1. A grade 3 LAS injury sustained
2. Diagnosed with chronic ankle instability (CAI) on the affected limb
3. Fracture diagnosed by X-ray
4. Previous enrollment in the same study
5. Major lower limb surgery or other severe lower extremity injury in the past 3 months on the affected limb
6. Under the influence of drugs or alcohol
7. A condition that, in the opinion of the investigator, would preclude participation in the study (e.g., not having access to the internet, immobilization etc.)

Grading of LAS

The grading of each patient is following Standard Operating Procedures (S.O.P.) (Appendix 1).

1.° LAS (At present the patient can bear weight)

2.° LAS (Pronounced limping, major pain)

3.° LAS (The patient cannot bear weight on the foot)

Chronic ankle instability

The participant should report a minimum of one major LAS injury sustained a minimum of 12 months prior to assessment for eligibility of enrolment in the study. After this injury, the participant should have experienced the classical signs of decreased function and swelling.

Participants should report at least two episodes of 'giving way' or have sustained two or more ankle sprains to the same ankle in the 6 months prior to the study enrolment to be diagnosed with CAI [9].

We endorse the definition of giving way as: *"The regular occurrence of uncontrolled and unpredictable episodes of excessive inversion of the rear foot (usually experienced during initial contact during walking or running), which do not result in an acute lateral ankle sprain"* [8].

Allocation of participants and sequence generation

We will stratify the randomization by

- Site (2 levels; Slagelse Hospital and The Regional Hospital in Horsens)

The allocation ratio will be 1:1.

Randomization lists will be computer-generated based upon permuted random blocks of variable size (2 to 6 in each block).

Blinding

Data analysts will be blinded to treatment allocation.

Treatments

Usual care

Participants allocated to usual care (Strategy B) will receive instructions in managing their acute LAS accordingly to the S.O.P. at the site (Appendix A). These guidelines consist of advice provided by the physician at work in; Rest, Ice, Compression and Elevation. Avoiding new stretches/ sprains for a few months after the injury is advised and gradually putting more weight on the ankle, progressing to running and twisting.

Physiotherapy

Participants allocated to ESP physiotherapy (Strategy A) will receive instructions on how to manage their acute LAS and a written homebased exercise program by an ESP physiotherapist. The instructions on how to manage their acute LAS will consist of written and oral advice. The protocol consists of advice in accelerated weight bearing, already at discharge. It is advised to bear weight and exercise with pain up to, but not exceeding, VAS 5. The written homebased exercise program should be initiated at discharge from the hospital. When patients are experiencing pain exceeding VAS 5 they will follow the same guidelines as the usual care group consisting of Rest, Ice, Compression and Elevation.

Compression, with an elastic bandage, is administered in the ED and instructions on how to apply and manage the bandage correctly, will be given. The bandage should be worn all day, including at night for 3 weeks. The elastic bandage should also be worn as protection when performing exercises and activities that increases the risk of reinjury for a minimum of 3 month after injury.

ESP physiotherapy

An ESP Physiotherapist is a clinical physiotherapy specialist with an extended scope of practice. This implies working beyond the recognized scope of physiotherapy practice, for example requesting investigations e.g. X-rays; using the results of investigations to assist clinical diagnosis and appropriate management of patients; and referring to other professionals. The ESP physiotherapist will have a minimum of 2 years of relevant clinical experience in assessment, diagnosing and treating of patients with minor musculoskeletal injuries. The ESP physiotherapist

has taken or are currently enrolled in supplementing their basic professional training with additional courses in musculoskeletal physiotherapy.

Exercise program for the physiotherapy group

The exercise program from baseline to 4 weeks follow-up will consist of ankle rehabilitation exercises focusing on walking with full weight bearing, neuromuscular training, balance training, muscle strengthening and jumping. The participants will be asked to perform the exercises on a daily basis. The exercises should be performed with pain up to but not exceeding 5 on an 0-10 VAS pain scale. If the patient experience VAS pain ≥6 he/she should follow the standard guidelines of rest, ice, compression and elevation. The patient will receive information on how to perform the exercises by the ESP physiotherapist and an exercise program will be handed out in the ED (Appendix 2). A link will be sent to the participants with the same exercise program including online videos describing the exercise in detail.

Concomitant Therapy

Participants will be asked to register the type and frequency of any concomitant therapy. There will be no restrictions in concomitant therapy.

Outcome Assessments/Variables

Primary Outcome

Lower extremity functional scale

The primary outcome measure is the change from baseline in the Lower extremity functional scale (LEFS)[16] assessed at 4 weeks after randomization. LEFS will also be assessed at 1, 2 and 3 weeks, and 3, 6 and 12 months, these timepoints will be regarded as secondary outcomes.

The Lower extremity functional scale is a self-completed questionnaire providing a total score based on the patients subjective ankle function. The scale consists of 20 functional leg activities, each scored on a five point scale (0 impossible, 4 no difficulty), giving a minimum score of 0 (worst) to 80 (best). The questionnaire will be translated into Danish using a dual-panel approach before trial start. The LEFS will be scored online by the trial participant. This approach avoids the requirement for follow-up visits in a clinic.

Secondary outcomes

The following secondary outcomes will be measured, at baseline and the 1, 2, 3 and 4 weeks, and 3, 6 and 12 months follow-ups, unless stated otherwise. All of the secondary outcomes will be scored online by the trial participant. This approach avoids the requirement for follow-up visits in a clinic.

Pain at rest and with activity, assessed using a visual analogue scale (VAS)

The pain VAS is a unidimensional measure of pain intensity, which has been widely used in diverse adult populations[17,18]. The scale is a continuous scale comprised of a horizontal line, anchored by 2 verbal descriptors, one for each symptom extreme (0 no pain, 10 the worst imaginable pain). We will measure pain VAS at rest and pain VAS with activity.

Foot and ankle ability measure (FAAM)19

The FAAM scale is a region-specific outcome instrument divided in two separate subscales, the FAAM activities of daily living (adl) and the FAAM Sports subscales. Evidence of validity to support the use of the FAAMadl and FAAMsport is available in individuals with a wide array of ankle and foot disorders19–21. The questionnaire will be measured at 1, 2, 3 and 4 weeks, and 3, 6 and 12 month follow-ups and used in secondary analysis. The questionnaire will not be measured at baseline. The questionnaire will be translated into Danish using a dual-panel approach before trial start.

The Cumberland ankle instability tool (CAIT)[22]

The CAIT is a simple, validated, and reliable tool to measure severity of functional ankle instability[9,22]. The CAIT consists of 9 questions that are answered separately for the right and left ankle. It is scored on a 30-point scale, with lower scores indicating decreased stability. The minimal clinically important difference (MCID) for patients with chronic ankle instability is $\geq$3 points[23]. The questionnaire will be translated into Danish using a dual-panel approach before trial start.

Reinjury rates

Reinjury rates will be recorded during follow-up assessments at weeks 1-4 and 3-12 months. We endorse the definition of an ankle sprain as: *"An acute traumatic injury to the lateral ligament complex of the ankle joint as a result of excessive inversion of the rear foot or a combined plantar flexion and adduction of the foot. This usually results in some initial deficits of function and disability"*[8,9]. Reinjury will not be considered as a stopping rule for further participation in this study. Reinjures will be measured at 1, 2, 3 and 4 weeks, and 3, 6 and 12 month follow-ups and used in secondary analysis.

Quality of life (EQ-5D-3L)[24]

The EQ-5D-3L is a measure of current health status developed by the EuroQol Group for clinical and economic appraisals. The questionnaire consists of five questions assessing five dimensions

(mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension is rated on three levels: no problems, some problems and extreme problems.

Global perceived effect (GPE)[25]

Perceived effect of treatment will be measured using a transition questionnaire (TRANS-Q) on which the participants will answer if their current LAS-related health status is "unchanged", "worse" or "better" compared to their pre-LAS status. An "unchanged" equals a transition score of 0. If the participant answers "worse", he/she is asked to rate the degree of worsening on a 7 point Likert scale, and the corresponding scores range from -1 to -7. If a participant answers "better", he/she is asked to rate the degree of improvement on a 7 point Likert scale, and the corresponding scores range from 1 to 7.

Patient acceptable symptom state (PASS)[26]

The PASS is the value beyond which patients consider themselves well. Patients' opinions of their state will be recorded by answering ''Yes'' or ''No'' to the question: ''Taking into account all the activities you have during your daily life, your level of pain, and also your functional impairment, do you consider your current state is satisfactory?''.

Analgesic use

The participants self-reported use of analgesics will be collected at baseline and at follow-up week 1-4. Participants will be asked to note their use of analgesic drugs within the week before baseline and the follow-up.

Data collection methods

For consenting patients, we will at Baseline collect data on age, height, body weight, previous lateral ankle sprain, limb dominance, injured limb left/right, time since injury, education, employment, patient's contact details (Appendix 4). The information will be derived using an online platform on an Ipad available in the emergency department. Baseline data will be collected after randomization, but before treatment, E.g. in the waiting room after medical imaging.

The questionnaires will be sent to the participants in the study at 1, 2, 3 and 4 weeks and 3, 6, and 12 months. The data will be collected using an internet-based platform (Easytrial), with personal links sent to the participants on the day the window for follow-up opens. The window for completion of data registration will be small during the first 4 weeks allowing only a ±2-day registration window. At the 3, 6 and 12-month follow-up, reminders will be sent one and two weeks before and one week after the follow-up date. This will give a window of 4 weeks for completion of the assessments. See Appendix 7 for a copy of the covering letters.

To improve response rates participants will be offered the option of completing the questionnaires in paper versions to be returned by post. We will send pre-notification messages/emails/letters.

Discontinuation

Participant withdrawal

As this is a study performed in the emergency department, participants will not be able to have a 24-hour consideration period before inclusion in the study. We consider the study and its procedures to be justified from a health research ethics perspective. There are no risks or predictable harms associated with this approach.

A participant is advised to contact the investigators by telephone if they wish to withdraw from the study. A participant will be able to withdraw at any time point throughout the study period without this impacting on any future investigations and/or treatments.

If a participant withdraws from the study, the primary and secondary outcomes are sought collected before discontinuation.

Discontinuation of clinical sites

The Sponsor has the right to terminate the participation of a clinical site at any time. Reasons may include the following, but are not restricted to:

- The incidence of events at the site that indicate a potential health hazard to participants and which is not considered sporadic (i.e. events could be expected to occur at other sites as well).
- Unsatisfactory participant enrolment at the site.
- Unsatisfactory data completeness at the site.
- The incidence of protocol violations at the site which is not considered sporadic or very severe (i.e. events could be expected to occur at other sites as well).

Discontinuation of Entire Study

The Sponsor has the right to terminate this study at any time. Reasons may include the following, but are not restricted to:

- The incidence of events in this or other studies that indicate a potential health hazard to participants.
- Unsatisfactory participant enrolment.

Study procedures

Trial related clinical visits

There will be no trial-related clinical assessments. Follow-up will be done only via internet-based assessments.

Assessment windows

The assessment windows are as follows:

- Baseline measurements will be taken after randomization but before treatment in the ED.
- Outcome assessment at 1, 2, 3 and 4 weeks can be taken within ± 2 day for the scheduled assessment
- Outcome assessments at 3, 6, and 12 months can be taken within ± 2 weeks before or after the scheduled assessment.

Baseline assessment

Baseline tests and procedures must be performed and reviewed before allocation. The following information/assessments will be collected at the baseline visit:

1. Inclusion/exclusion criteria review
2. Collection of baseline information (Appendix 4)
3. Collection of primary and secondary outcomes
4. Randomization

Study completion

The end-of-study is defined as the date of the last participant's last scheduled assessment, 12 months after enrollment.

Collection of data from hospital records

All relevant information on participants will be collected using online Case Report Forms (CRF). No additional information will be collected from the included participant’s hospital records.

Determination of sample size and statistical analysis plan

Determination of Sample Size

The study will be powered to detect a difference in change of 9 points between the two groups in the primary outcome (LEFS) from baseline to 4 weeks follow-up. The 9 point change has previously been recommended and applied in similar studies as the minimal clinically important difference in LEFS[27]. To detect this difference, we will need 56 patients in each group (assuming a common SD of 17, power = 80%, alpha level = 0.05).

Participants description

Disposition of Participants

The total number of randomized participants will be summarized by site using counts and percentages. The number of patients either completing or discontinuing the study will be summarized using counts and percentages.

Study Population definitions

Intention to treat population (ITT)

The ITT population consists of all randomized patients regardless of whether the patient received study intervention or failed to comply with the study protocol, in the treatment group to which the participant was assigned (see Figure 2).

Per protocol (PP)

The per protocol population consists of participants in the ITT population with a valid baseline measurement of the variable to be analyzed.

As-observed population (AO)

The AO population consists of participants who has the outcome of interest assessed at a given time point of interest (i.e. no imputation of missing data will be done).

Data analysis considerations

The primary outcome is change from baseline in the lower extremity functional scale and will be analyzed using the ITT population.

General statistical approach

For quantitative variables we will calculate mean, standard deviation, median, range and number of missing data.

All summary tables for qualitative variables will display counts, percentages and number of missing data (if relevant) by treatment group.

All statistical tests will be two-sided and statistical significance will be claimed if the computed p-value is equal to or less than 0.05.

Concomitant medication and/or therapy

The use of concomitant medications and/or therapies (e.g. GP consultations, physiotherapy, etc.) will be summarized in each treatment group.

Primary analysis

Primary outcome analysis

The primary endpoint is the change from baseline in the lower extremity functional scale at the 4-week follow-up. The primary analysis will be done on the ITT population.

Data transformation before analysis, if any

No data transformation will be applied to raw data.

Study committees

Protocol Development Committee

Membership

The Protocol Development Committee of this study is composed of scientific, technical, and administrative persons from participating sites and other collaborating participants. There are no restrictions to the number of members in the committee.

Roles and responsibilities

This committee, led by its chairman Christian Olsen, is responsible for development, refinement, and finalization of this protocol and planning of activities related to the study.

This study was conceptualized by Christian Olsen (Study Chairman and principal investigator). The initial version of the protocol (version 1.0) was developed by Christian Olsen.

Executive Committee

The research group consists of the PhD student Christian Olsen M.Sc. in physiotherapy who will be the central study coordinator and principal investigator. Christian Olsen has experience as an ESP in the ED at Slagelse Hospital.

Marius Henriksen, Professor of Physiotherapy at the University of Copenhagen. Marius Henriksen has a special interest in research in musculoskeletal injuries and diseases and has experience with the implementation of large multicenter studies.

Søren Thorgaard Skou, PhD Physiotherapist, head of research at the Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals. Søren has experience with the design, conduct and reporting of RCT studies and coordinating large multicenter cohorts in musculoskeletal conditions.

Finn Erland Nielsen is head of Research and Chief Physician in the emergency department at Slagelse Hospital. Finn Nielsen has clinical epidemiology, register based research and emergency medicine as main interests. He has acquired a doctorate in medicine and a master degrees in applied statistics and public management. Finn Nielsen is research supervisor for doctors and medical students and has been assessor of a large number of PhD theses'.

Mikael Elsborg, physiotherapist, is managing the ESP physiotherapists working at The Regional Hospital in Horsens. He has a great interest in collection of data, and working with research projects. Mikael will be responsible for the coordination of data collection at the Horsens site in this study.

Ethics

General considerations

Prior to assessment for eligibility the trial participants will be informed, both orally and in writing, about the purpose of this trial, the overall duration and potential risks, as well as costs and benefits for participation. The leaflet "*Forsøgspersoners rettigheder i et sundhedsvidenskabeligt forskningsprojekt*" will be handed out and participants will be encouraged to read it before trial enrolment. All participants are informed of their rights to withdraw from the study. The participant may withdraw oral, written or with other clear indications about the attend to resign from the research project. If the participant withdraws their consent, this will not affect their right to present or future treatment or any other rights they may have. After the information is delivered, read and understood, voluntary informed consent is given by the participant by signing a consent form before trial participation can take place.

Oral information

When a potential participant is identified during initial assessment in the ED he/she will be given information about this trial. If further investigations are needed to determine eligibility for enrollment, the information will be given after completion of these. It will be stressed that the investigator is asking the participant to consider participation in the trial, and that the potential trial participant has the right to bring a companion to the information interview, if possible. The written information material will be handed out in the ED by the trial investigator. The participants will not be able to have a 24-hour consideration period before inclusion in the study, but will have sufficient time to consider inclusion. The oral information will be given in a language easily understood without technical or value-laden terms. The information will be given in a considerate way that is tailored to each potential trial participants. The conversation will take place without interference. It is the responsibility of the interviewer to ensure that the potential trial participant has understood all the information giving. Guidelines for the oral information are given in Appendix 6.

Written information

A written information material has been prepared and is attached this protocol as Appendix 5.

Informed consent

Consent to participation in the trial is given on the basis of the written and oral information. An informed consent form (Appendix 8) has been prepared. The form must be signed and dated by the participants prior to participation in the trial. A copy of the form is provided to the participants. The investigator or his designated delegates can receive the signed consent form.

Research ethics -the interventions

Physiotherapy

The study will be conducted in accordance with the Helsinki declaration and follow ICH9 Good Clinical Practice guidelines. We consider the study and its procedures to be justified from a health research ethics perspective. There are no risks or predictable harms associated with the physiotherapy intervention that at worst are considered harmless.

Usual care

As this is defined as usual clinical care it is not considered to be associated with research ethical issues.

Research ethics – the outcome measures

Questionnaires

Questionnaires are not considered to be associated with research ethical issues.

Research ethics approval

The study will be conducted in accordance with Danish law, the Helsinki declaration, and local research ethics committee requirements.

The Sponsor is responsible for keeping the ethical committee informed of amendments or changes to the protocol, and the progress of the study.

Case Report Form Completion

Case Report Forms

The study will use electronic CRFs using an online web-based clinical trial management application (EasyTrial). EasyTrial allows individual patients to supply data from home.

The application meets all regulatory standards, and allows management of all activities related to clinical trials that ensures optimal resource use and safety according to good clinical practice and data protection legislation.

Regulatory Standards

This study will be conducted in accordance to the Danish law: *"The Act on Processing of Personal Data".*

Notification to the Danish Data Protection Agency

Because the study is carried out at hospital emergency departments, it is regarded as "public" in accordance with the Data Protection Agency guidance. The study will be notified to the Data Protection Agency before trial start.

Financing and insurance information

The study is funded by:

The Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals.

The Research Unit at Næstved, Slagelse and Ringsted Hospital.

Publication

This study will be published in a peer-reviewed journal. In addition, the results will be presented at international conferences.

In addition, the results will be regularly presented at an Annual National Seminar on ESP physiotherapists in the emergency room, arranged by the Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals, Region Zealand.

All positive, negative or inconclusive results will be published at www.clinicaltrials.gov.

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Appendices to RCT Protocol (Appendix I)

Appendix I.A

Standard operating procedure

DS93.4	DISTORSIO REGIONIS MALLEOLI	1.° distorsion (At present the patient can bear weight): **RICE** 2.° distorsion (Pronounced limping, major pain. Able to walk 4 steps): **RICE + Pain management** 3.° distorsion (The patient cannot bear weight on the foot and walk 4 steps): **RICE+ crutches +pain management**	No follow-up Follow-up at general practitioner

Appendix I.B

Exercise program

Afdeling for Fysio- og ergoterapi

Exercise program after acute lateral ankle injury (EN)

By: Christian Olsen

It is recommended that You immediately start this training program. It is advised to exercise with pain up to, but not exceedig 5 on a pain-scale (0-10). 0 represents no pain and 10 represents the worst pain you can imagine. If you experience pain of 6 or more, You must follow the RICE principles until the pain again is below 5.

1. Information

This training program should be followed daily the first 4 weeks after your acute lateral ankle sprain. The training program is designed to be performed in the morning, at noon and in the evening.
You can use an ice bag as pain reliever. Place it directly on top of the the damaged area for 10 minutes. Pull it of and wait 10 minutes. Continue until the pain is improved.

2. Walking forward as a figure of eight movement

Walk forward and form a figure of eight. Return to starting position and repeat. Start walking in a large figure of eight, about 10 meters.
At each minute decrease the figure of eight by 1 meter, thus the last minute is only 1 meter long.
You have to walk with a speed that gives you pain corresponding to 5 or less on the 0-10 pain-scale. You are alloved to jog / run. Exercise each day in the morning, at noon and in the evening.
Sets: , Duration: 12 min 0 sec, Pain level: 5 0-10

3. One Leg Jump in Circle, Both Ways

Stand on one leg on a mat with your hands in your side. Do a 90 degrees jump on the mat and continue jumping till you have jumped all the way around yourself. Then jump 90 degrees in the opposite direction and continue till you have jumped all the way around yourself again.
Sets: , Reps: 12 , Pain level: 5 0-10

4. Single leg stand on a balance cushion (knees bent)

Stand on a pillow (or fold a mat and stand on that). Stand on one leg with the knee a little bend. Hold the other leg out in the air and grab a hold of your hips with your hands. Try to keep your balance.
Tid: 12 min, Sets: , Pain level: 5 0-10

Play Program

5. Toe lift on bench or step

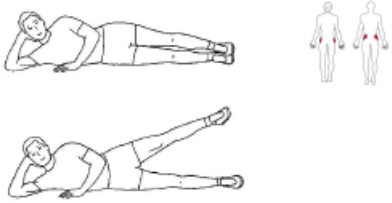
Stand on the edge of a step or a bench so that your heels are free, feet about hip-width apart. Raise your heels and push up until you are on your toes. Return to the start position and repeat. The exercise can be done with or without support.

Reps: 12 , Sets: , Pain level: 5 0-10

6. Gradual Backwards Lunge

Focus on a spot in front of you. Tighten your abdomen, place one foot on the mat and move backwards. Lower your back knee down towards the floor. Press your bottom down towards the floor, tighten abdomen and move your leg back to starting position. Perform the exercise with both legs.

Sets: , Reps: 12 , Pain level: 5 0-10



7. Side-lying single leg lift 2

Lie on your side with straight legs, supporting your head with one hand. Raise your top leg. Ensure that your toes point straight forward and that only your hip is moving. You should therefore avoid tilting your pelvis toward you or rotating your hip. Repeat the exercise with your other leg. Perform the exercise with both legs.

Sets: , Reps: 12

Appendix I.C

Outcomes

We are interested in knowing whether you are having any difficulty at all with the activities listed below because of your lower limb problem for which you are currently seeking attention. Please provide an answer for **each** activity.

Today, do you or would you have any difficulty at all with:

(Circle one number on each line)

Activities	Extreme Difficulty or Unable to Perform Activity	Quite a Bit of Difficulty	Moderate Difficulty	A Little Bit of Difficulty	No Difficulty
a. Any of your usual work, housework, or school activities.	0	1	2	3	4
b. Your usual hobbies, recreational or sporting activities.	0	1	2	3	4
c. Getting into or out of the bath.	0	1	2	3	4
d. Walking between rooms.	0	1	2	3	4
e. Putting on your shoes or socks.	0	1	2	3	4
f. Squatting.	0	1	2	3	4
g. Lifting an object, like a bag of groceries from the floor.	0	1	2	3	4
h. Performing light activities around your home.	0	1	2	3	4
i. Performing heavy activities around your home.	0	1	2	3	4
j. Getting into or out of a car.	0	1	2	3	4
k. Walking 2 blocks.	0	1	2	3	4
l. Walking a mile.	0	1	2	3	4
m. Going up or down 10 stairs (about 1 flight of stairs).	0	1	2	3	4
n. Standing for 1 hour.	0	1	2	3	4
o. Sitting for 1 hour.	0	1	2	3	4
p. Running on even ground.	0	1	2	3	4
q. Running on uneven ground.	0	1	2	3	4
r. Making sharp turns while running fast.	0	1	2	3	4
s. Hopping.	0	1	2	3	4
t. Rolling over in bed.	0	1	2	3	4
Column Totals:					

SCORE: _____/80

Figure I.C.1 - Lower extremity functional scale (English version).

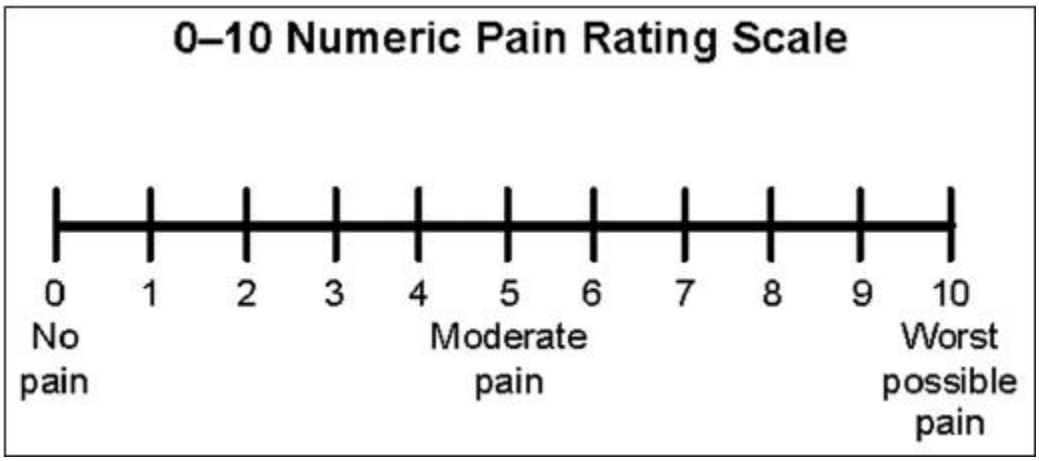


Figure I.C.2 - NRS Pain scale with rest

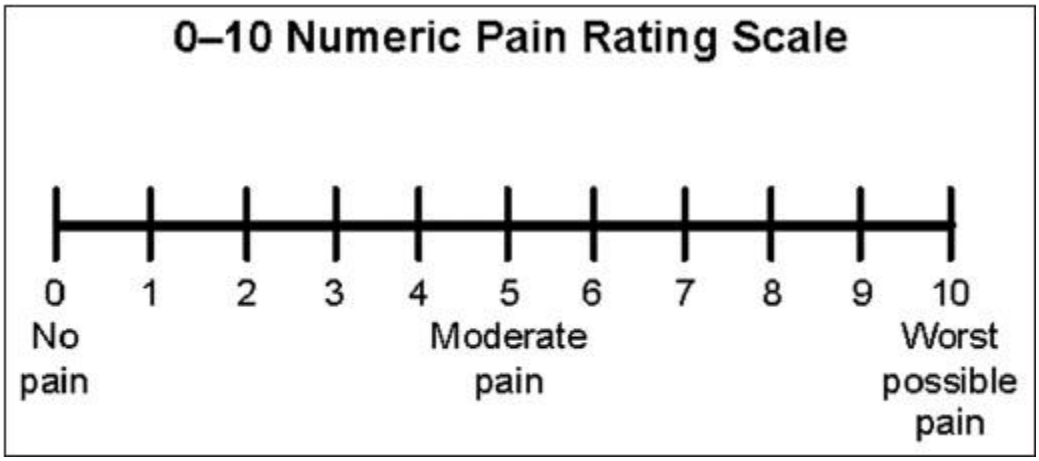


Figure I.C.3 - NRS Pain scale with activity

Foot and Ankle Ability Measure (FAAM)
Activities of Daily Living Subscale

Please Answer **every question** with **one response** that most closely describes your condition within the past week.
If the activity in question is limited by something other than your foot or ankle mark "Not Applicable" (N/A).

	No Difficulty	Slight Difficulty	Moderate Difficulty	Extreme Difficulty	Unable to do	N/A
Standing	☐	☐	☐	☐	☐	☐
Walking on even Ground	☐	☐	☐	☐	☐	☐
Walking on even ground without shoes	☐	☐	☐	☐	☐	☐
Walking up hills	☐	☐	☐	☐	☐	☐
Walking down hills	☐	☐	☐	☐	☐	☐
Going up stairs	☐	☐	☐	☐	☐	☐
Going down stairs	☐	☐	☐	☐	☐	☐
Walking on uneven ground	☐	☐	☐	☐	☐	☐
Stepping up and down curbs	☐	☐	☐	☐	☐	☐
Squatting	☐	☐	☐	☐	☐	☐
Coming up on your toes	☐	☐	☐	☐	☐	☐
Walking initially	☐	☐	☐	☐	☐	☐
Walking 5 minutes or less	☐	☐	☐	☐	☐	☐
Walking approximately 10 minutes	☐	☐	☐	☐	☐	☐
Walking 15 minutes or greater	☐	☐	☐	☐	☐	☐

Figure I.C.4 - Foot and ankle ability measure ADL subscale page 1 (English version).

Foot and Ankle Ability Measure (FAAM)
Activities of Daily Living Subscale
Page 2

Because of your foot and ankle how much difficulty do you have with:

	No Difficulty at all	Slight Difficulty	Moderate Difficulty	Extreme Difficulty	Unable to do	N/A
Home responsibilities	☐	☐	☐	☐	☐	☐
Activities of daily living	☐	☐	☐	☐	☐	☐
Personal care	☐	☐	☐	☐	☐	☐
Light to moderate work (standing, walking)	☐	☐	☐	☐	☐	☐
Heavy work (push/pulling, climbing, carrying)	☐	☐	☐	☐	☐	☐
Recreational activities	☐	☐	☐	☐	☐	☐

How would you rate your current level of function during you usual activities of daily living from 0 to 100 with 100 being your level of function prior to your foot or ankle problem and 0 being the inability to perform any of your usual daily activities.

__ __ __ . 0 %

Martin, R; Irrgang, J; Burdett, R; Conti, S; VanSwearingen, J: Evidence of Validity for the Foot and Ankle Ability Measure. Foot and Ankle International. Vol.26, No.11: 968-983, 2005.

Figure I.C.5 - Foot and ankle ability measure ADL subscale page 2 (English version).

Foot and Ankle Ability Measure (FAAM)
Sports Subscale

Because of your foot and ankle how much difficulty do you have with:

	No Difficulty at all	Slight Difficulty	Moderate Difficulty	Extreme Difficulty	Unable to do	N/A
Running	☐	☐	☐	☐	☐	☐
Jumping	☐	☐	☐	☐	☐	☐
Landing	☐	☐	☐	☐	☐	☐
Starting and stopping quickly	☐	☐	☐	☐	☐	☐
Cutting/lateral Movements	☐	☐	☐	☐	☐	☐
Ability to perform Activity with your Normal technique	☐	☐	☐	☐	☐	☐
Ability to participate In your desired sport As long as you like	☐	☐	☐	☐	☐	☐

How would you rate your current level of function during your sports related activities from 0 to 100 with 100 being your level of function prior to your foot or ankle problem and 0 being the inability to perform any of your usual daily activities?

___ . 0%

Overall, how would you rate your current level of function?

☐ Normal ☐ Nearly Normal ☐ Abnormal ☐ Severely Abnormal

Martin, R; Irrgang, J; Burdett, R; Conti, S; VanSwearingen, J: Evidence of Validity for the Foot and Ankle Ability Measure. Foot and Ankle International. Vol.26, No.11: 968-983, 2005.

Figure I.C.6 - Foot and ankle ability measure Sports subscale (English version).

APPENDIX 1: THE CAIT QUESTIONNAIRE

Please tick the ONE statement in EACH question that BEST describes your ankles.

	LEFT	RIGHT	Score
1. I have pain in my ankle			
Never	☐	☐	5
During sport	☐	☐	4
Running on uneven surfaces	☐	☐	3
Running on level surfaces	☐	☐	2
Walking on uneven surfaces	☐	☐	1
Walking on level surfaces	☐	☐	0
2. My ankle feels UNSTABLE			
Never	☐	☐	4
Sometimes during sport (not every time)	☐	☐	3
Frequently during sport (every time)	☐	☐	2
Sometimes during daily activity	☐	☐	1
Frequently during daily activity	☐	☐	0
3. When I make SHARP turns, my ankle feels UNSTABLE			
Never	☐	☐	3
Sometimes when running	☐	☐	2
Often when running	☐	☐	1
When walking	☐	☐	0
4. When going down the stairs, my ankle feels UNSTABLE			
Never	☐	☐	3
If I go fast	☐	☐	2
Occasionally	☐	☐	1
Always	☐	☐	0
5. My ankle feels UNSTABLE when standing on ONE leg			
Never	☐	☐	2
On the ball of my foot	☐	☐	1
With my foot flat	☐	☐	0
6. My ankle feels UNSTABLE when			
Never	☐	☐	3
I hop from side to side	☐	☐	2
I hop on the spot	☐	☐	1
When I jump	☐	☐	0
7. My ankle feels UNSTABLE when			
Never	☐	☐	4
I run on uneven surfaces	☐	☐	3
I jog on uneven surfaces	☐	☐	2
I walk on uneven surfaces	☐	☐	1
I walk on a flat surface	☐	☐	0
8. TYPICALLY, when I start to roll over (or "twist") on my ankle, I can stop it			
Immediately	☐	☐	3
Often	☐	☐	2
Sometimes	☐	☐	1
Never	☐	☐	0
I have never rolled over on my ankle	☐	☐	3
9. After a TYPICAL incident of my ankle rolling over, my ankle returns to "normal"			
Almost immediately	☐	☐	3
Less than one day	☐	☐	2
1–2 days	☐	☐	1
More than 2 days	☐	☐	0
I have never rolled over on my ankle	☐	☐	3

NOTE. The scoring scale is on the right. The scoring system is not visible on the subject's version.

Figure I.C.7 - The Cumberland ankle instability tool (English version)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❑

I have some problems in walking about ❑

I am confined to bed ❑

Self-Care

I have no problems with self-care ❑

I have some problems washing or dressing myself ❑

I am unable to wash or dress myself ❑

Usual Activities *(e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑

I have some problems with performing my usual activities ❑

I am unable to perform my usual activities ❑

Pain / Discomfort

I have no pain or discomfort ❑

I have moderate pain or discomfort ❑

I have extreme pain or discomfort ❑

Anxiety / Depression

I am not anxious or depressed ❑

I am moderately anxious or depressed ❑

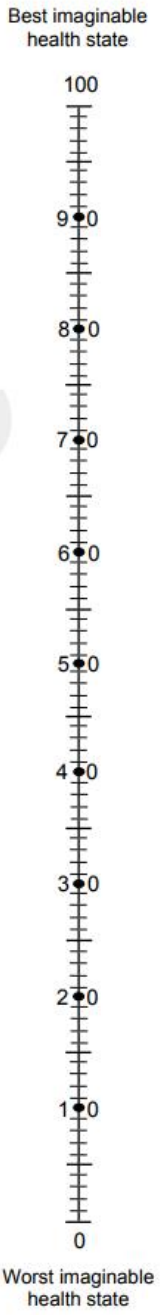
I am extremely anxious or depressed ❑

Figure I.C.8 – The EQ-5D-3L Index (English version)

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



3

Figure I.C.9 – EQ-5D-3L VAS (English version)

Appendix I.D

Baseline form

Questions	**Answers**
Date of birth	Dd/mm/YYYY
Height	Cm
Weight	Kg
Previous lateral ankle sprain in the same ankle	Yes/No
Dominant leg	Left/Wright
Site of injury	Left/Wright
Time since injury	Hours/minutes
Years of education	Years
Yearly income	DKr.
Contact information	Address, Phone number, e-mail.

Appendix I.E

Informed consent form

(S1)

Informed consent form for participation in a health science research project.

Research project title: Management of acute lateral ankle sprains: A randomized, controlled trial

Statement by the subject:

I have received written and oral information and I know enough about the purpose, method, advantages and disadvantages to say yes to participate.

I know it is voluntary to participate and that I can always withdraw my consent without losing my current or future rights to treatment.

I agree to participate in the research project and have received a copy of this consent sheet as well as a copy of the written information about the project for its own use.

The subject's name: _____

Date: _____ Signature: _____

Do you want to be informed about the results of the research project and possible consequences for you?:

Yes _____ (Mark with X) No _____ (Mark with X)

Declaration by the person giving information:

I declare that the subject has received oral and written information about the trial.

In my conviction, sufficient information has been provided for a decision to participate in the trial.

The name of the person who provided information:

Date: _____ Signature: _____

Project identification:

Human Subjects Review board number: SJ-628

Appendix II – Manuscript Study I

A prognostic evaluation by physiotherapists as a predictor of short-term outcome after treatment of minor musculoskeletal injuries in the Emergency Department: A prospective cohort study

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Abstract

Question(s): What is the overall caseload treated by the physiotherapists in the emergency department (ED)? Can physiotherapists predict the short-term outcome of patients with minor musculoskeletal (MSK) injuries managed in the ED? **Design**: Prospective cohort study. **Participants**: 432 patients managed by physiotherapists in the ED were included in the caseload study, while 109 patients with a MSK injury from the caseload study participated in the prognostic study. **Outcome measures**: At baseline, physiotherapists evaluated the 4-week prognosis for each participant on a scale from -7 (worst) to 7 (best), based on the complete session of assessment and treatment. The pre-specified outcomes: patient acceptable symptom state (PASS), pain (0-100mm VAS) and health status (EQ-5D-3L) were measured at the 4-week follow-up after ED visit. **Results**: The most common diagnoses were ankle sprains (11.3%), hand contusions (8.6%) and wrist fractures (8.6%). Prognostic scores were negatively correlated with VAS pain at rest (r_s= -0.31; *P*=0.017) and VAS pain at activity (r_s= -0.32; *P*=0.013) and positively correlated with EQ-5D index (r_s=0.36; *P*=0.004) and EQ VAS (r_s=0.32; *P*=0.012). The odds ratio for a positive answer ('yes') to the PASS question was 1.61 (95% CI 1.11 to 2.35) higher with each one-unit increase in prognostic scores. **Conclusion**: The most common diagnoses treated by physiotherapists in the ED are ankle sprains, hand contusions and wrist fractures. The physiotherapists' prognoses associate with the patients' symptomatic state four-weeks after consulting the ED due to a minor MSK injury. **Trial registration**: NCT04011917.

***Key words**: Prognosis, Physical Therapist, Musculoskeletal Diseases, Emergency Department*

Introduction

Emergency departments (EDs) are the largest providers of initial management of minor musculoskeletal (MSK) injuries, which are estimated to represent about 13% of all visits to the EDs[1,2] A correct and timely diagnosis and high-quality management of injuries is a challenge for the ED staff in a busy clinical schedule[3]. With high patient flows and increasing pressure on the healthcare system there is risk that minor injuries are given lower priorities as compared to more complicated and severe injuries and conditions.

Outside the ED, physiotherapists traditionally play an important role in the management of minor MSK injuries. Some years ago, physiotherapists were introduced as secondary contact practitioners in the ED[4,5], where they after referral from medical doctors or emergency nurse practitioners assess and manage injuries[6,7], including MSK injuries, mobility and vestibular assessments, and assist in discharge planning[4]. . In some countries, including Denmark, physiotherapists in the EDs are now autonomous practitioners, working as primary contact physiotherapists, with the same authorities as the medical doctors for the initial management of minor MSK injuries[8]. This role of primary contact physiotherapists includes independent assessment and treatment of MSK injuries: imaging prescriptions; prescription of relevant non-steroidal anti-inflammatory drugs (NSAID's); education of patients; provision of walking aids and gait training; referring of patients; and provision of bandages and orthoses[4,8,9]. The existing literature on implementation of physiotherapist to EDs have been reviewed in several studies[7,8,10,11], but the evidence is heterogenous and the roles of the physiotherapists vary between settings and studies and only a limited number of high-quality studies is found. However, physiotherapists in EDs have been shown to generate high levels of patient satisfaction[12–17], reduce length of stay[13,18–20], and have high clinical effectiveness comparable to other ED staff[12–16,21,22]. A successful implementation of physiotherapists in the ED was presented by de Gruchy et al.[2], who described the overall caseload managed by the physiotherapists in a single ED in Australia. The caseload on physiotherapists in an ED in Denmark, including the patient demographics and which diagnoses the physiotherapists manage in the EDs, has not previously been described.

In daily clinical practice at the ED, physiotherapists and other ED staff will only manage patients in a short timeframe, typically unaware of the outcome after discharge. During treatment of patients, the ED staff will have a "hunch" of how the prognosis will be for the patient. Studies using the physiotherapists "hunch" as a predictor for prognosis are scarce with the few available studies demonstrating that the physiotherapist can predict the outcome in patients with neck or low back pain[23–25]. However, it remains unknown if this "hunch" is a reliable predictor of the outcome after treatment in the ED. If the physiotherapist can predict the outcome after treatment in the ED, this

knowledge can be used to reliably identify candidates who may need referral to further treatment, thereby potentially reducing the considerable subgroup experiencing recurrent or persistent symptoms[26].

With this study we aimed to assess the caseload treated by the physiotherapists in an Danish ED and to investigate if physiotherapists managing patients with minor MSK injuries in the ED can predict the 4-weeks recovery.

Methods

We did a prospective, pragmatic cohort study with a 4-week follow-up recruiting patients over three months from July 15th, 2019 to October 15th, 2019. The study protocol was submitted to and approved by the local Health Research Ethics Committee (J.nr. 19-000067) and was registered at www.clinicaltrials.gov (NCT04011917) before commencement of the study. The study was conducted in accordance with the Helsinki Declaration and ICH Good Clinical Practice, and the reporting of this article follows the STROBE guidelines[27].

Setting

We recruited participants in the ED at Slagelse Hospital, Denmark - one of four hospitals in Region Zealand with an ED. The ED at Slagelse Hospital has a 24h service and treats approximately 49.000 patients annually. The Danish healthcare system offers equal access for all citizens. The patients are either referred by general practitioners or, if urgent, arrive on their own or by ambulance[28]. Danish privately funded hospitals have no acute patient intake[28]. The physiotherapists working in the ED are an integrated part of the staff. The physiotherapists are working in peak hours from 12.30-21.00 every day of the week, where they independently diagnose and treat patients presenting with minor MSK injuries. They are highly trained physiotherapists with comprehensive experience in the management and treatment of minor MSK injuries[29]. In Denmark the skillset of a physiotherapist working in the ED are recommended to follow the national competence profile developed by the national physiotherapy association[29]. The physiotherapists have been suggested to complete relevant courses amounting to 30 ECTS (European Credit Transfer System). Furthermore, it is advised that the EDs implement an internal certification procedure to ensure quality and patient safety, emulating the program used for the training of junior physicians.

Participants

All patients treated in the ED by a physiotherapist as primary or in a joined effort role during the 3-month period were included in the caseload study.

From the population of patients included in the caseload study, patients diagnosed and treated by a physiotherapist (primary contact) for a minor MSK injury in the ED, aged >18 years and with an e-mail address were invited to participate in the prediction cohort study. Patients under the influence of drugs or alcohol, or a condition that, in the opinion of the investigator, would preclude participation in the study (e.g., not having access to the internet, cognitive impairments etc.) were excluded. Patients received oral and written information about the study procedures before giving oral and written informed consent.

Baseline characteristics

In the prediction cohort study, gender, age, height, weight, educational level, and the International Statistical Classification of Diseases and Related Health Problems 10 (ICD-10) codes for the injury on which the patient sought treatment were registered by the physiotherapist based on the examination, while only gender, age and ICD-10 codes and the reason for not being included in the prediction cohort study were collected in the caseload study.

The follow-up assessment in the prediction cohort was conducted using an internet-based platform (Research Electronic Data Capture; REDCap), with personal links sent via email to the participants. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing: 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources. Via REDCap, individual internet-hyperlinks were emailed to the participants four weeks after the ED visit. The hyperlinks led to a secured web-page on which the patients answered questionnaires. The participant-submitted responses were automatically registered in a secured database[30,31]. The follow-up assessments were performed at 4-weeks after enrolment and up to three reminders were sent every other days, if the participant did not respond.

Physiotherapists' prognosis score

The physiotherapists were asked to estimate each participant's outcome four weeks after the visit to the ED, based on the complete session including triage, history, examination, treatment and discharge in the ED. The physiotherapists were instructed to score each participant on a 15-points numerical rating scale ranging from -7 (suggesting a very poor projected outcome) to 7 (suggesting an excellent projected outcome). They scored each participant after their complete experience with them in the ED, including triaging, patient history, physical examination, treatment, personality, discharge and more. The patients were kept blinded to the prognostic scores.

Pain

At baseline (in the ED) and after 4 weeks, current pain intensity was assessed using a 100 mm visual analogue scale (VAS), which has been widely used in many adult populations[32,33]. The scale is a unidimensional continuous scale comprised of a horizontal line, anchored by two verbal descriptors, one for each symptom extreme (0 = "no pain", 100 = "worst imaginable pain"). Self-reported VAS pain in rest and during activity was recorded at baseline and follow-up.

Health status and quality of life survey (EQ-5D-3L)

At the 4-week follow-up the EQ-5D-3L was measured. The EQ-5D[34,35] is a measure of current health status developed by the EuroQol Group for clinical and economic appraisals. The questionnaire consists of a descriptive system and an EQ Visual Analogue Scale (EQ VAS). The descriptive system comprises of five questions assessing five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension was rated by the participants on three levels: no problems, some problems, and extreme problems. From the answers an EQ-5D index score is calculated based on Danish normative values[36]. The index ranges from -0.624 (worst) to 1.000 (best). The EQ VAS was used to record the participants self-rated health at 4-week follow-up on a horizontal 100 mm VAS with endpoints labelled *'best imaginable health state'* and *'worst imaginable health state'*. The EQ-5D-3L was only collected at follow-up.

Patient Acceptable Symptom State (PASS)

At the 4-week follow-up Patient Acceptable Symptom State was evaluated at follow-up using a single item with response categories ''Yes'' or ''No'': *''Taking into account all the activities you have during your daily life, your level of pain, and also your functional impairment, do you consider your current [injury site]-state following your 4-weeks-old injury to be satisfactory?''*. Injury site was automatically replaced with the site of injury reported at baseline.

Protocol deviations

We pre-specified the global perceived effect questionnaire as the primary outcome. Unfortunately, the participants were not able to answer the question satisfactorily. The question aimed at assessing the participants' change following treatment compared to their pre-injury health status on a 15-points numerical rating scale ranging from -7 (much worse) to 7 (much better) relating to pre-injury state. As the patients were in the ED with acute MSK injuries, most patients were expected to score ≤0, as 0 would represent their habitual health status for most people. However, this was not the case as most patients reported above 0, suggesting that they had a better overall health compared to before their injury. Because of this unexpected deviation, we choose to disregard the prespecified primary outcome and analyse only the other outcome measures as a representation of the 4-week follow-up status.

Statistics

For the caseload study we present patient demographics and diagnoses seen by the physiotherapists. To assess the association between the physiotherapists' prognostic scores and the 4-week outcomes we first performed Spearman's bivariate correlations. For the analyses of the dichotomous PASS question, we analysed differences in the baseline prognosis between participants answering 'yes' and 'no' to PASS using un-paired t-tests.

We used logistic regression analyses to calculate odds ratios (OR) with 95% confidence intervals (CI) for reporting a positive answer ('yes') on the PASS at the 4-week follow-up with higher prognostic scores. P-values of <0.05 were considered statistically significant. None of the underlying statistical assumptions of the logistic regression analysis were violated.

Results

Caseload study

In total, the physiotherapists in the ED managed and treated 432 patients during the 3-month inclusion period (Figure II.A). Most of the patients, 339 (78.47%) were treated with the physiotherapists working as the primary contact health professional. The most common diagnoses treated by the physiotherapists in the ED were: ankle sprains(11.3%), hand contusions(8.6%) and wrist fractures(8.6%) (Table II.A).

Prediction cohort study

One-hundred-nine patients (55% females) were included in the prediction cohort study. The mean age was 40.3 years (SD 16.3), and mean BMI was 26.4 (SD 5.1). In the ED, the patients reported pain with activity of 72.5 mm (SD 20.2) and pain at rest of 36.5 mm (SD 22.2). At the 4-week follow-up, 61 participants (56%) answered the follow-up questionnaires. Except for the proportion of females, the responders and non-responders were similar at baseline (Table II.B).

At the 4-week follow-up, the average VAS pain with activity had decreased to 40.9 mm (SD 28.8) and the average VAS pain with rest had decreased to 23.5 mm (SD 22.6).

The physiotherapists' prognostic scores ranged from -7 to 2 (mean -1.92).

The physiotherapists' prognostic scores were significantly and negatively correlated with VAS pain at rest (r_s= -0.31; *P*=0.017) and at activity (r_s= -0.32; *P*=0.013). The prognostic scores were positively correlated with EQ-5D index (r_s=0.36; *P*=0.004) and EQ VAS (r_s=0.32; *P*=0.012) at the 4-week follow-up. Altogether the results suggest that a higher prognostic score at baseline is associated with a better outcome after four weeks.

At the 4-week follow-up 23 (38.3%) participants answered ‘yes’ to the PASS and had an average baseline prognostic score at baseline of -1.2 (SD 1.6). Thirty-seven participants (62.7%) answered ‘no’ and had an average baseline prognostic score of -2.4 (SD 1.7). There was a statistically significant difference in the baseline prognostic scores between participants who answered ‘yes’ and ‘no’ to the PASS questions at the 4-week follow-up (mean difference: 1.2 points (95% CI 0.3 to 2.1).

The prognostic scores were statistically significantly associated with the PASS question as the logistic regression analyses resulted in an odds of a positive answer (‘yes’) of 1.61 (95% CI 1.11 to 2.35; P=0.013) with each one-unit increase in prognostic scores.

Discussion

We found that the most common diagnoses treated by the physiotherapists in the ED are ankle sprains, hand contusions and wrist fractures and that the physiotherapists’ prognoses associate with the patients’ symptomatic state four weeks after consulting the ED due to a minor MSK injury.

As demonstrated, physiotherapists in the ED are managing and treating a broad range of diagnoses, thus contributing to the overall workflow. Comparing our overall caseload to that of de Gruchy et al.[2], relatively fewer patients with injuries to the lumbar region were treated by physiotherapists in our study. This difference is likely due to national differences in the physiotherapists’ scope of practice and therefore susceptible to change in the future as physiotherapists have competences in treating injuries to the lumbar region. Another important difference between this study and the study by de Gruchy et al.[2] is the overall caseload of patients that the physiotherapists managed independently: In the study by de Gruchy et al[2], 46.5% were independently managed; in our study the physiotherapists managed 78.5%. This indicates a high confidence in physiotherapists that, over a short period, have become an integrated part of the ED staff being able to treat most patients independently.

Participants failed to score the pre-specified primary outcome GPE. We suspect that the confusion for the scoring of the instrument is because patients failed to understand that the scoring should have been based upon their pre-injury status, not their baseline status. Future studies investigating change in patients’ health status are advised to use one-directional scales to avoid this problem.

Our study is the first on the ability of physiotherapists to predict the short-term outcomes in patients treated for a minor MSK injury in the ED. Our results show that physiotherapists were able to differentiate between patients that would have an acceptable symptom state at the 4-week follow-up and those who would not. This may help physiotherapists working in the ED in identifying patients

who would benefit from referral to specialized assessment, rehabilitation or other treatments. Other studies investigating physiotherapists' predictions have found similar results for patients with neck or low back pain[23,25]. In these studies, the physiotherapists managed and treated the patient's multiple times over 2 weeks, thus giving the therapist significantly more time with the patients before making their prognosis. Working in an ED is associated with a high patient flow, short encounters and no follow-up visits: The physiotherapists in our study made their projected prognosis based on a very time-limited consultation with the patient. This suggests that trained physiotherapists can predict outcomes even after short consultations with their patients and that they can make a valid initial screen of patients that might need additional specialized assessment and treatment after leaving the ED to avoid long-term symptoms.

Limitations

There are a number of limitations to the present study. First, the study was limited to a single center. Although presentations to the ED may be comparable to other EDs, variations in the scope of practice will exist due to different healthcare authorization legislations and local hospital policies. Furthermore, patients presenting outside normal working hours of the physiotherapists were not included in this cohort study (12.30-21.00). This may compromise the generalizability of the results gathered in our study. The flow of patients in a Danish ED peak at around 11.00 o'clock and continues to be high throughout the day to around 20.00/21.00 o'clock[37]. Further studies are needed to clarify the distribution of patients arriving at the ED outside normal working hours of the physiotherapists. This could provide knowledge about the need for implementing physiotherapists in the ED outside patients peak-hours, as patients outside the peak-hours categorized as triage blue constitute patients relevant for treatment by primary contact physiotherapists. Secondly, the physiotherapists in this study were highly trained, which is a requirement for independent roles in an ED, but at the same time limits the generalizability to other settings without highly trained physiotherapists. Thirdly, the distinct nature of some injuries may influence the physiotherapists' prediction as 4-week follow-up will not sufficiently represent end of recovery for some injuries. We did not assess the prognostic results within specific diagnoses due to a limited study sample, but speculate that for some injuries longer follow-up is needed to evaluate prediction of full recovery. However, the 4-week time frame may have been incorporated in the physiotherapists' prognoses of these patients, thus resulting in lower prognostic scores for these patients. Further, other types of information could have been useful in identification of potentially modifiable factors that associate with the prognoses. Such information could have helped identifying the underlying factors that the physiotherapists based their prognoses on and used to propose interventions to mitigate negative outcomes. Finally, the low response rate (56%) to the 4-week follow-up survey is a limitation,

although only the distribution of females was significantly different between responders and non-responders.

Implications for Physiotherapy Practice

The demand on EDs throughout Denmark is increasing. Physiotherapists were introduced in the ED to improve the flow of patients and ensure quality in treatment of patients with minor MSK injuries. The role of the physiotherapist has now evolved into a primary contact role, where the physiotherapists have the same authorities as physicians for treatment of minor MSK injuries. With this study we show that the caseload treated by physiotherapists in the EDs is high, making it relevant for all EDs to consider to withstand the increasing number of patients attending the EDs and to accommodate the shortage of physicians and nurse practitioners.

In conclusion, this study found that the most common diagnoses treated by the physiotherapists in the ED are ankle sprains, hand contusions and wrist fractures. Furthermore, it demonstrated that the physiotherapists' prognoses associate with the patients' symptomatic state four weeks after consulting the ED due to a minor MSK injury.

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Tables

Table II.A – Overall caseload managed by the physiotherapist in the emergency department

	Fracture	Contusion	Ligament sprain	Ligament rupture	Dislocation	Other	Total
Knee	21	18	22	6	5	3	75 (17.4%)
Ankle	3	11	49	7	0	1	71(16.4%)
Foot	26	28	10	1	1	0	66 (15.3%)
Hand	15	37	12	2	0	0	66 (15.3%)
Wrist	37	11	3	0	0	0	51 (11.8%)
Shoulder	10	6	6	1	5	1	29 (6.7%)
Elbow	9	12	2	0	4	0	27 (6.3%)
Hip	3	11	0	2	2	2	20 (4.6%)
Lumbar	7	2	0	0	0	1	10 (2.3%)
Cervical	5	0	0	0	0	1	6 (1.4%)
Thoracic	3	2	0	0	0	0	5 (1.2%)
Pelvis	1	0	0	0	0	0	1 (0.2%)
Multiple sites	0	0	0	0	0	1	1 (0.2%)
Other	0	0	0	0	1	3	4 (0.9%)
Total	140 (32.4%)	138 (31.9%)	104 (24.1%)	19 (4.4%)	18 (4.2%)	13 (3.0%)	432 (100%)

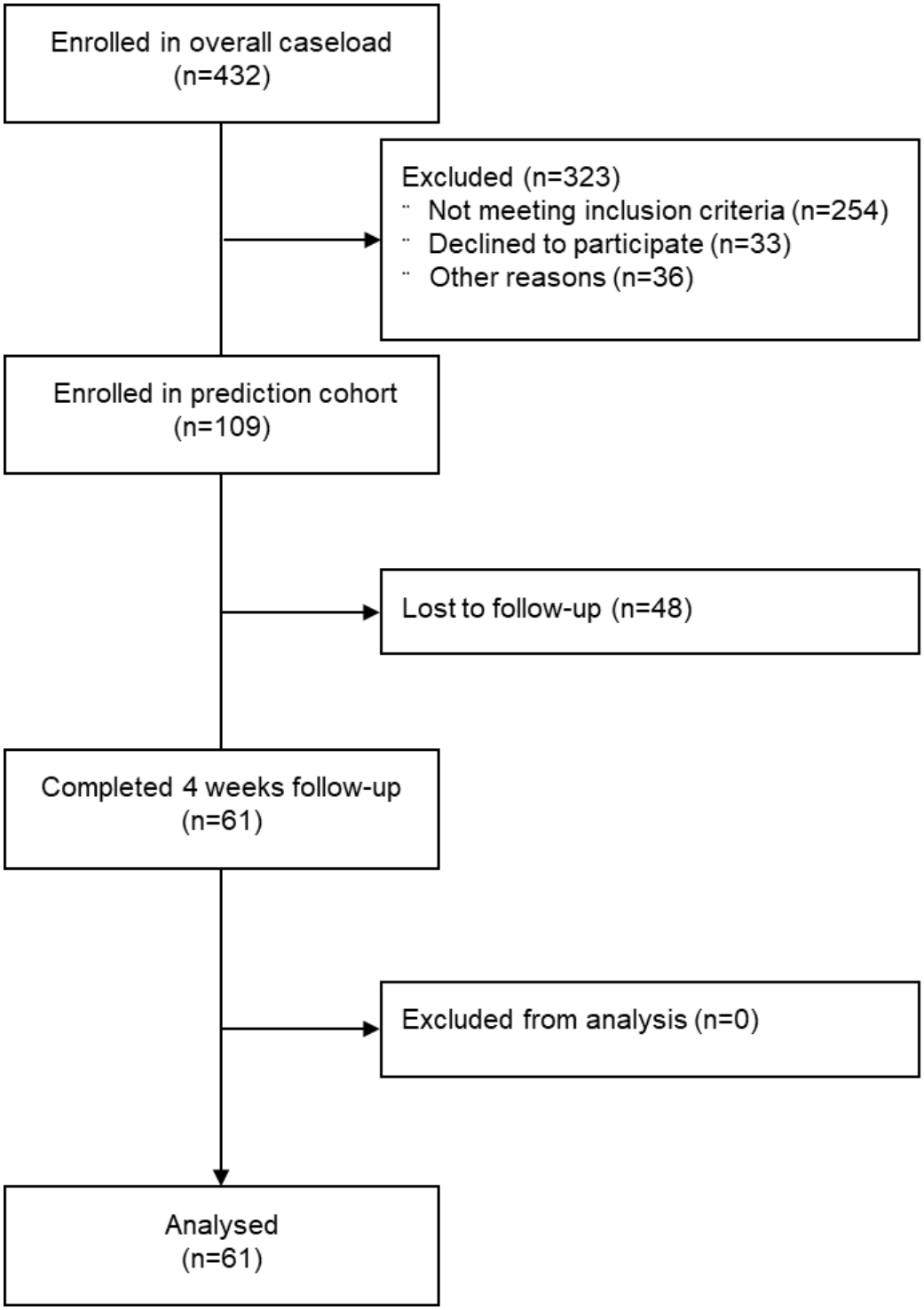
Table II.B – Participant characteristics in prediction cohort at baseline

	All (n=109)	Responders (n=61)	Non-responders (n= 48)
Age, Mean (SD)	40.3 (16.3)	42.2 (16.8)	37.8 (15.4)
Female, n (%)	60 (55%)	40 (66.7%)	20 (33.3%)
VASpain activity, mean (SD)	72.5 (20.2)	74.8 (20.0)	69.6 (20.3)
VASpain rest, mean (SD)	36.5 (22.2)	38.3 (21.2)	34.3 (23.4)
BMI, Mean (SD)	26.4 (5.2)	26.3 (5.4)	26.6 (4.9)
Injury site, n (%)			
• **Foot**	34 (31.2%)	21 (34.4%)	13 (27.1%)
• **Ankle**	19 (17.4%)	7 (11.5%)	12 (25.0%)
• **Wrist**	17 (15.6%)	11 (18.0%)	6 (12.5%)
• **Knee**	14 (12.8%)	8 (13.1%)	6 (12.5%)
• **Finger**	13 (11.9%)	5 (8.2%)	8 (16.7%)
• **Shoulder**	9 (8.3%)	6 (9.8%)	3 (6.3%)
• **Elbow**	3 (2.8%)	3 (4.92%)	0 (0.0%)
Injury type, n (%)			
• **Contusion**	39 (35.8%)	24 (39.3%)	15 (31.3%)
• **Fracture**	30 (27.5%)	18 (29.5%)	12 (25.0%)
• **Ligament sprain**	31 (28.4%)	14 (23.0%)	17 (35.4%)
• **Ligament rupture**	5 (4.6%)	3 (4.9%)	2 (4.2%)
• **Dislocation**	2 (1.8%)	2 (3.3%)	0 (0.0%)
• **Other**	2 (1.8%)	0 (0.0%)	2 (4.2%)

SD = Standard deviation; VAS = Visual analogue scale; BMI = Body mass index

Figures

Figure II.A - Study flow chart



Appendix III - Manuscript Study II

Dual-panel translation and cross-cultural adaptation of the Danish Version of the Cumberland Ankle Instability Tool, Foot and Ankle Ability Measure, and Lower Extremity Functional Scale

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Abstract

Background: In the assessment of ankle injuries or ankle disorders, Cumberland Ankle Instability Tool (CAIT), Foot and Ankle Ability Measure (FAAM) and Lower Extremity Functional Scale (LEFS) are well known patient reported outcome measures (PROMs) that are widely used for measuring lower limb functional status in clinical research. A translation of the PROMs is important for use in daily clinical practice as well as in the implementation of international research studies. **Aim of study:** The aim of this study was to translate the CAIT, FAAM, and LEFS questionnaires from English too Danish and too cross-culturally adapt the Danish versions of the questionnaires. **Method:** The LEFS, CAIT and FAAM questionnaires was translated using a dual-panel approach. **Results and discussion:** The LEFS, QAIT and FAAM were successfully translated into Danish and cross-culturally adapted into Danish. A major limitation to this study was that no assessment of the psychometric properties of the Danish version of the three questionnaires was done. **Conclusion:** The translation of the LEFS, QAIT and FAAM into Danish and its cross-cultural adaptation to a Danish speaking population were done carefully and without any major inconsistencies. Future studies should aim at examining the questionnaires validity, reliability and responsiveness following the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist.

Introduction

Injuries causes a great economic burden on society due to the combination of treatments costs and reduced level of function, thus loss of productivity. The term injuries covers a very wide spectrum of injuries and diagnoses, but one of the most common reasons for patients to seek health care are musculoskeletal injuries and complaints, which have been found to account for 13.8% of all visits in emergency departments (ED)[1]. When divided into regions, extremity injuries represent the greatest proportion of injuries in the ED, with the lower extremity being the primary body region injured[2]. It has previously been found that from all visits in ED in the U.S. over a year, 14,6% of the visits were for lower extremity injuries[3]. Sprains and strains have been found to account for more than one third of the lower extremity injuries in patients seeking health care in emergency departments in U.S, and fractures account for 18%[3]. The incidence of musculoskeletal injuries in the lower extremities is, however estimated to be much higher, as the numbers from the ED only show their rate of patients. Many patients with musculoskeletal injuries are expected to seek treatment elsewhere, e.g. at their general practitioner or therapist[4].

In evidence-based medicine, treatment and rehabilitation, clinical tests and scales, measuring pain, joint motion and functional level, have previously been the primary tools for monitoring changes in

patient responses and evaluating treatment[5]. For the assessment of function in the lower extremity, numerous rating scales have been developed. Around 140 different assessment tools have been described in research in relation to function in just the lower leg[6]. Combined with rating scales, the importance of monitoring the patients perspective has become more recognized. It is used increasingly, as it is a significant criterion for evaluating effectiveness of interventions and treatment[5,7]. Patient reported outcome measures (PROMs) consider the patients perspective on participation, restrictions and decreased quality of life, thus they are recommended as primary outcome measures over clinician-rated measures[8]. PROMs exist as both generic, or more region- and disease specific assessment tools. In the assessment of ankle injuries or ankle disorders, Cumberland Ankle Instability Tool (CAIT), Foot and Ankle Ability Measure (FAAM) and Lower Extremity Functional Scale (LEFS) are well known measurement tools that are widely used for measuring lower limb functional status in clinical research[9,10]. LEFS[11–13], FAAM[14–23]. and CAIT[14,22,24–28] have been used in numerous RCT studies related to acute LAS or CAI (see Table III.A for overview)**.**

The CAIT, FAAM and LEFT questionnaires have not been translated into Danish. A translation of the questionnaires is important for use in daily clinical practice as well as in the implementation of international research studies. Therefore, the aim of this Study was to translate the CAIT, FAAM, and LEFS questionnaires from English too Danish and too cross-cultural adapt the Danish versions of the questionnaires.

Methods

In this combined translation of three ankle specific questionnaires, we used a pragmatic design approach. The translation process followed existing guidelines for all of the questionnaires. The translation steps were combined to ensure efficiency throughout the study.

Figure III.A: Dual-Panel translation process:

The LEFS, CAIT and FAAM questionnaires were translated using a dual-panel approach (see Figure 1 for overview of the process). Two panels, a bilingual panel (panel 1) and a panel consisting of laymen (panel 2), conducted the translation process. Panel 1 consisted of 3 Danish bilingual persons with extensive English language competences. Each bilingual person independently provided translations of all the questionnaires. The questionnaires were then condensed into one single draft by one of the group members (CPO). The bilingual panel approved the draft. If there

were any disagreements regarding the translations, this was discussed until consensus was reached via online feedback.

The Danish translations of the questionnaires were reviewed and revised by a second panel consisting of Danish laymen (panel 2) who were blinded to the original version of the questionnaire. This panel was instructed to ensure that the average Danish person would understand the wording of the translated questionnaires. The panel consisted of 6 persons (3 women and 3 men) with an average level of education and no previous history of ankle injuries. After reviewing the questionnaires independently, a focus group-interview was held with all panel 2 members present. At the focus group interview all suggestions for alternate wording were discussed in plenum, until the panelists agreed on the specific wording.

Variables

LEFS

LEFS is a self-reported questionnaire that measures the patient's subjective lower extremity function through 20 items on functional level. Every item is rated on a 5-point scale, indicating whether the patient is unable to perform the activity (0 points) or able to perform the activity without difficulties (4 points). Highest achievable score shows a high functional level[29]. LEFS was originally developed in English, and has been found to be valid and reliable, with an excellent test-retest reliability, in many different clinical patient groups with musculoskeletal disorders in their foot or lower leg[9]. LEFS has also been translated and validated in several languages, including Finnish[30], Arabic[31], Persian[32], Spanish[33], Brazilian Portuguese[34], Taiwan Chinese[35], Dutch[36], Italian[37], and German[38].

CAIT

CAIT is a simple reliable and validated questionnaire that identifies and measures the severity of functional ankle instability. CAIT can also be useful in monitoring progress and effect of treatment[39]. CAIT consists of 9 items designed to assess several aspects of functional ankle instability. All questions are answered separately for the right and left ankle. The total score of the 9 items ranges from 0, indicating severe ankle instability, to 30, indicating normal ankle stability[10,39]. The English version of CAIT was found to have excellent correlation to LEFS and VAS, acceptable construct validity and internal reliability was found with a Cronbach $\alpha = .83$, together with an excellent test-retest reliability with an intraclass correlation coefficient type 2,1 (ICC) = 0.96[39]. CAIT has previously been translated and validated in Japanese[40], Arabic[41], Persian[42], Korean[43], Spanish[44], French[45] and Portugese[46].

FAAM

FAAM is a region-specific questionnaire designed to measure limitations and restrictions in participation in patients with foot and ankle disorders. The questionnaire consists of 29 items divided into two subscales regarding activities of daily living (ADL) in 21 items, and Sports in 8 items. Each item is scored on a 5-point Likert scale ranging from 0 (unable to do) to 4 (no difficulties at all) with a lower score representing a lower level of physical function[47]. The use of FAAM has been found to be valid in the assessment of the ability in patients with a wide array of ankle and foot disorders[48,49]. FAAM has been found to be a reliable measurement with an intraclass correlation coefficient 2,1 at .89 for the ADL subscale and 0.87 for the Sports Subscale, respectively, and to be valid and responsive. FAAM has previously been translated and validated in Japanese[50], German[51], Chinese[52], Brazil[53], French[54] and Persian[42].

Results

During the translation process, the two panels provided feedback that resulted in adjustments in the final version of the translated questionnaires (Table III.B, III.C and III.D). The participants in both panels found no difficulty in understanding most of the items. In general, they found the LEFS short and easy to understand; the QAIT questionnaire to be long and difficult to fill out; and the FAAM to be long but very relevant for patients with acute ankle injuries.

Discussion

The LEFS, CAIT and FAAM questionnaires assesses self-reported function in the lower extremity in various aspects. Creating a Danish version of the instruments is empirically useful as it facilitates comparison of cross-national research. Moreover, it gives clinicians a useful toolbox of instruments to use when treating patients with injuries in the lower extremity. The questionnaires all measure self-reported function in the lower extremity, but have different aspects and focuses' in the questionnaires, which is why this combined translation and cross-cultural adaptation was feasibly.

The LEFS have a specific focus in patients with lower extremity musculoskeletal injuries; the CAIT has a specific focus in patients with functional ankle instability and the FAAM has a specific focus in patients with foot and ankle musculoskeletal disorders[47,55,56]. Because of the interrelations of the three questionnaires we used this combined translation method, to reduce discrepancies to a minimum. This method ensured a uniform translation.

Patient-reported outcome measures often refer to questionnaires that are used in clinical setting and in clinical trial. Due to the international nature of many clinical studies and trials it is often necessary to produce several language versions of specific measures[57]. The translated version of the

questionnaire needs to be conceptually equivalent which emphases the importance of a cross-cultural adaptation.

Traditionally, forward-backward translation of questionnaires has been the recommended methodology[58–60]. Forward-backward translation consist of obtaining one or several forward translations by independent translator. The translated questionnaires are afterwards back-translated to the source language. The two versions of the questionnaire in the source language are then compared and discrepancies are highlighted. However, this method has several drawbacks and is very time consuming, and even if a translation is good, the back-translation may look nothing like the source questionnaire[57].

An alternative to the forward-backward method is the dual-panel method. This method has been widely and successfully used in several studies in the adaptation of questionnaires[61–67]. Using this method, you avoid the drawback of back-translation, but the method is highly dependent on the panels used to produce the translations[68]. Translating is never a straightforward process. In practice the process is very dependent on the wording and cannot be viewed as a task of "just" finding equivalents of words and stringing them together[57]. Different languages have different and specific ways of putting life into words depending on the context. Using the dual-panel approach, the process of producing a version of a specific questionnaire in another language is considered a process of adaptation rather than translation[57], which is why the dual-panel approach was chosen in this study.

When we compared the translation process of LEFS to other studies we found similar difficulties. We encountered cultural differences in the adaptation process. In Denmark we do not use city blocks to describe distances, therefore item 11 was changed to "Walking 200 meters" by the bilingual panel. Cruz-Díaz et al. used "250 meters", Repo et al. "200 meters" and Hoogeboom et al. "250 meters"[30,33,36]. In addition, as Denmark does not use British imperial miles, the bilingual panel consented to use the metric system in item 12 by changing ''Walking a mile'' to ''Walking 2 km''. The panel considered an even number more suitable instead of the "correct" translation of "1.6 km". Cruz-Díaz et al. used "1 km", Repo et al. "2 km" and Hoogeboom et al. "1.5 km"[30,33,36]. When we compared the translation process of CAIT to other studies we found similar difficulties. The bilingual panel translated item 5 "On the ball of my foot" to "On the forefoot". Noronha et al. changed it to "At the tip of the foot", Cruz-diaz et al. used "the foot pad"[44,46]. When we compared the translation process of FAAM to other studies we found similar difficulties. The bilingual panel translated item 10 of the ADL subscale to "go down into a squat", indicating a movement not holding a static position. The same approach was made in the German translation, who changed it to "in die Hocke gehen"[51].

A major limitation to this study is that no assessment of the psychometric properties of the Danish version of the three questionnaires was done. Psychometric properties refer to the validity and reliability of the questionnaire. To state that a questionnaire is reliable and valid, the psychometric properties must be evaluated extensively. Due to limited time and resources, this was not done with the questionnaires, but should be done in a future study, before the questionnaires can be used in the clinic. This study is a first step towards a full validation of the three questionnaires in Danish. The findings from this translation study most go through rigorous testing before generalisability is established. Testing the generated questionnaires validity, reliability and responsiveness following the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist is advised[69].

Conclusion

The translation of the LEFS, QAIT and FAAM into Danish and its cross-cultural adaptation to a Danish speaking population were done carefully and without any major inconsistencies. Future studies should aim at examining the questionnaires validity, reliability and responsiveness following the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist[69].

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Tables

TABLE III.A - The use of LEFS, FAAM and CAIT in RCT studies related to acute LAS or CAI across the published literature.

Participants	Objective	Design	Setting	PROM	Conclusion	Reference
101 patients with an acute grade 1 or 2 ankle sprain.	Compare early therapeutic exercise after acute LAS with RICE	RCT	Accident and emergency department and university-based sports injury clinic	LEFS	An accelerated exercise protocol during the first week after ankle sprain improved ankle function; the group receiving this intervention was more active during that week than the group receiving standard care.	Bleakley et al. [13]
74 patients with acute LAS	Compare the effectiveness of manual therapy and exercise (MTEX) to a home exercise program (HEP) in the management of individuals with acute LAS	RCT	Four physical therapy clinics	LEFS, FAAM-ADL FAAM-Sports NRS	A MTEX approach is superior to an HEP in the treatment of inversion ankle sprains.	Cleland et al. [12].
37 patients with severe ancle sprain	Compare patient function in patients receiving standard therapy IV Platelet-rich plasma and patients who receive standard therapy plus sham injection (placebo).	Prospecti ve, randomiz ed, double-blinded, placebo-controlled trial.	Emergency department	LEFS, VAS	No statistically significant difference in VAS and LEFS scores between groups	Rowden et al. [11]
43 patients with CAI	Compare the effectiveness of three rehabilitation programs on clinical measures of balance and self-reported function in individuals with CAI	RCT	Laboratory setting	FAAM-ADL CAIT	All 3 rehabilitation groups demonstrated improvement compared with the control group. Evidence was too limited to support a superior intervention.	Cain et al. [14]
40 patients with CAI	Investigate the effect of corrective exercises on functional movement patterns, sensorimotor function, self-reported function, and fatigue	RCT	Laboratory setting	FAAM-ADL	Eight weeks of corrective exercises enhanced movement efficiency, sensorimotor function, and self-reported function in collegiate athletes with	Bagherian et al. [15]

	sensitivity in athletes with CAI				CAI.	
10 patients with CAI	Investigate the effects of joint mobilization timing during a four-week calf stretching intervention in individuals with CAI	Randomized two-group pretest posttest design	Laboratory setting	FAAM-ADL DPA FABQ	Timing of joint mobilization in conjunction with calf stretching does not effect treatment efficacy. The combination of joint mobilization and calf stretching can improve dorsiflexion ROM and self-reported function in individuals with CAI.	Feldbrugge et al. [16]
18 patients with CAI	Investigate the effects of progressive hop-to-stabilization balance (PHSB) program compared with a single-limb balance (SLB) program in individuals with CAI.	RCT	Laboratory setting	FAAM-ADL FAAM-Sports	A four-week PHSB or SLB can be used in athletes with CAI to improve self-reported function, dynamic postural control, and joint position sense	Anguish et al. [17]
39 patients with CAI	Determine the improvement of patient-reported outcomes after balance- and strength-training and control protocols among individuals with CAI.	RCT	Laboratory setting	FAAM-ADL DPA FABQ VAS	Participants in both the balance- and strength-training–protocol and control groups improved in global and regional health-related quality of life.	Hall et al. [18]
50 patients with CAI	Investigate the effectiveness of specific collagen peptide supplementation (SCP) to improve ankle stability in athletes with CAI.	Randomized, double-blinded and placebo-controlled study	Laboratory setting	CAIT FAAM-ADL	Specific collagen peptide supplementation in athletes with CAI results in significant improvements in subjective perceived ankle stability	Dressler et al. [19]
26 patients with CAI	Determine the effects of hip strengthening on clinical and self-reported outcomes in patients with CAI	RCT	Laboratory setting	FAAM-ADL FAAM-Sports	The training group displayed significantly improved clinical and patient-reported outcomes	Smith et al. [70]
80 patients with CAI	Determine the effects of two weeks of sensory-	RCT	Laboratory setting	FAAM-ADL	All STARS groups improved patient-oriented outcomes	McKoen et al. [71]

	targeted rehabilitation strategies (STARS) on patient- and clinician-oriented outcomes in individuals CAI			FAAM_Sports	with joint mobilization having the most meaningful effect immediately after the intervention and plantar massage at the one-month follow up	
84 patients with CAI	Determine the comparative efficacy of two ankle rehabilitation techniques: wobble-board balance training and ankle strengthening using resistance tubing in individuals with CAI.	RCT	Laboratory setting	FAAM-ADL FAAM_Sports ADL SF-36 GFR	A single-exercise four-week intervention can improve patient- and clinician-oriented outcomes.	Wright et al. [22]
26 patients with CAI	Compare the effect of a four-week rehabilitation program that includes destabilization devices to rehabilitation without devices in patients with CAI	RCT	Laboratory setting	FAAM-ADL	Both groups had large improvements in self-reported function and ankle strength. No differences between the no-device and device groups for any measure.	Donovan et al. [23]
70 patients with CAI	Determine and compare the influence of adding self-mobilization of the ankle joint to CrossFit training versus CrossFit alone or no intervention in patients with CAI	RCT	Laboratory setting	CAIT	Ankle-joint self-mobilization and CrossFit training were effective in improving ankle Ankle-dorsiflexion range of motion, dynamic postural control and self-reported instability in patients with CAI.	Cruz-Diaz et al. [24]
22 patients with CAI	Examine the effect of therapeutic exercise performed on sea sand on pain, fatigue, and balance ability in patients with CAI.	RCT	Laboratory setting	CAIT VAS	Therapeutic exercise on sea sand effectively improved balance and decreased pain and fatigue.	Shin et al.[72]
30 patients with CAI	Assess improvement of quantitative neurosensory indicators after short-foot exercise and to determine	RCT	Laboratory setting	CAIT	SFE is more effective than PSE for treating ankle sprain patients.	Lee et al. [73]

	the effect of proprioceptive sensory exercise in patients with CAI.					
70 patients with CAI	Determine the effectiveness of a six-week balance training program on patients with CAI	RCT	Laboratory setting	CAIT	Exercise therapy training based on multi-station balance tasks led to significant improvements in dynamic balance and self-reported sensation of instability in patients with CAI.	Cruz-Diaz et al. [27]
90 patients with CAI	Evaluate the effects of joint mobilization, in which movement is applied to the ankle's dorsiflexion, on patients with CAI	A double-blind, placebo-controlled, randomized trial	Laboratory setting	CAIT	Joint mobilization techniques applied to subjects suffering from CAI were able to improve ankle Dorsiflexion Range of Motion, postural control, and self-reported instability.	Cruz-Diaz et al. [74]

Table III.B - The LEFS questionnaires instructions, title, translations and adjustments based on consensus. [Items marked: * Difficult to translate; + adjusted by bilingual panel; # adjusted by laymen panel]

Original version Lower extremity functional scale	**Adjustments**
Questionnaire title	*#
Questionnaire instructions	*# "for which you are currently seeking attention" Changed to "for which you are seeking contact" – *"som du har henvendt dig med".*
a. Any of your usual work, housework, or school activities	
b. Your usual hobbies, recreational or sporting activities	
c. Getting into or out of the bath	*
d. Walking between rooms	*+ Changed to "go from one room to another" – *"Gå fra et værelse til et andet".*
e. Putting on your shoes or socks	
f. Squatting	*
g. Lifting an object, like a bag of groceries from the floor	
h. Performing light activities around your home	

i. Performing heavy activities around your home	
j. Getting into or out of a car	*# Changed to “Getting in to or out of a car” – “*Komme ind eller ud af en bil”.*
k. Walking 2 blocks	*# Changed to “Walk 200 meters” – *“Gå 200 m”.*
l. Walking a mile	*# Changed to “Walk 1.5 km” – *“Gå 1,5 km”.*
m. Going up or down 10 stairs (about 1 flight of stairs)	*# Changed to “Going up or down 10 stairs (ABT. 1 floor)” – *“Gå op eller ned af 10 trappetrin (ca. 1 etage)”.*
n. Standing for 1 hour	
o. Sitting for 1 hour	
p. Running on even ground	*
q. Running on uneven ground	*
r. Making sharp turns while running fast	
s. Hopping	
t. Rolling over in bed	*# Changed to “Turning over in bed” – *“Vende dig i sengen”*

Tabel III.C - The CAIT questionnaires instructions, title, translations and adjustments based on consensus. [Items marked: * Difficult to translate; + adjusted by bilingual panel; # adjusted by laymen panel]

Original version CAIT questionnaire	**Adjustments**
Questionnaire title	*
Questionnaire instructions	*+# Changed to, ”Please tick the ONE statement for EVERY question that BEST describes each of your ankles”. ”Sæt venligst kryds i det ENE udsagn for HVERT spørgsmål som BEDST beskriver hver af dine ankler”.
I have pain in my ankle	
• **Never**	
• **During sport**	
• **Running on uneven surface**	*+ Changed to ”When i run on uneven surface” - ”Når jeg løber på ujævnt underlag”.
• **Runing on level surface**	*+ Changed to ”When i run on even surface” - ”Når jeg løber på en plan overfalde”.
• **Walking on uneven surface**	*+ Changed to ”When i walk on uneven surface” - ”Når jeg går på ujævnt underlag”.
• **Walking on level surfaces**	*+ Changed to ”When i walk on even surface” - ”Når jeg går

	på en plan overfalde".
My ankle feels UNSTABLE	
• **Never**	
• **Sometimes during sport (not every time)**	
• **Frequently during sport (every time)**	
• **Sometimes during daily activity**	
• **Frequently during daily activity**	
When I make SHARP turns, my ankle feels UNSTABLE	*+ Changed to "My ankle feels USTABLE when I make SHARP turns" - "Min ankel føles USTABIL, når jeg laver SKARPE retningsskift"
• **Never**	
• **Sometimes when running**	
• **Often when running**	
• **When walking**	
When going down the stairs, my ankle feels UNSTABLE	
• **Never**	
• **If I go fast**	*+ Changed to " If I walk fast" - "Hvis jeg går hurtigt"
• **Occasionally**	
• **Always**	
My ankle feels UNSTABLE when standing on ONE leg	
• **Never**	
• **On the ball of my foot**	*+ Changed to "On the forefoot" - "På forfoden"
• **With my foot flat**	
My ankle feels UNSTABLE when	
• **Never**	
• **I hop from side to side**	
• **I hop on the spot**	
• **When I jump**	
My ankle feels UNSTABLE when	
• **Never**	
• **I run on uneven surfaces**	

• **I jog on uneven surfaces**	
• **I walk on uneven surfaces**	
• **I walk on a flat surface**	
TYPICALLY, when I start to roll (or "twist") on my ankle, I can stop it	*+ Changed to "If I am about to twist my ankle, I can TYPICALLY stop it" - "Hvis jeg er ved at vride om på min ankel, kan jeg TYPISK stoppe det".
• **Immediately**	
• **Often**	
• **Sometimes**	
• **Never**	
• **I have never rolled over on my ankle**	
After a TYPICAL incident of my ankle rolling over, my ankle returns to "normal"	*+ Changed to "When I twist my ankle, it returns to "normal"" - "Når jeg har vredet om på min ankel, vender den tilbage til "normal"".
• **Almost immediately**	
• **Less than one day**	
• **1-2 days**	
• **More than 2 days**	
• **I have never rolled over on my ankle**	

Table III.D - The FAAM questionnaires instructions, title, translations and adjustments based on consensus. [Items marked: * Difficult to translate; + adjusted by bilingual panel; # adjusted by laymen panel]

Original version FAAM questionnaire	Adjustments
Questionnaire title	*+ Changed to "Questionnaire for measuring function in the foot and ankle" – "Spørgeskema til måling af funktion i fod og ankel".
Questionnaire instructions	*# "condition" changed to "health condition" – helbredstilstand.
• **No Difficulty**	
• **Slight Difficulty**	*+# Changed to "Minor problems" "Mindre problemer"
• **Moderate Difficulty**	
• **Extreme Difficulty**	
• **Unable to do**	
• **N/A**	*+ "Not relevant" - "Ikke relevant"

Standing	
Walking on even ground	
Walking on even ground without shoes	
Walking up hills	
Walking down hills	
Going up stairs	
Going down stairs	
Walking on uneven ground	
Stepping up and down curbs	*+# ”Changed to ”Step up and down from a curb” - ”Træde op og ned fra en kantsten”
Squatting	*+# Changed to “go down into squatting” - “Gå ned i hug”
Coming up on your toes	*+# “Stand on your toes” – “Stå på tæer”
Walking initially	*+# “From (still)standing to walking” – “Fra stillestående til gående”
Walking 5 minutes or less	
Walking approximately 10 minutes	
Walking 15 minutes or greater	
Home responsibilities	
Activities of daily living	
Personal care	
Light to moderate work (standing, walking)	*
Heavy work (push/pulling, climbing, carrying)	*
Recreational activities	
How would you rate your current level of function during you usual activities of daily living from 0 to 100 with 100 being your level of function prior to your foot or ankle problem and 0 being the inability to perform any of your usual daily activities.	*+# Changed to “How do you rate your current level of functioning during your usual daily activities from 0 to 100; where 100 is your level of function before your foot or ankle problem and 0 is the inability to perform your usual daily activities”. ”Hvordan vurderer du dit nuværende funktionsniveau under dine sædvanlige dagligdags aktiviteter fra 0 til 100; hvor 100 er dit funktionsniveau inden dit fod- eller ankelproblem og 0 er manglende evne til at udføre nogle af dine sædvanlige daglige aktiviteter”.
Sports Subscale	*+# Changed to “Part 2 Sports related activities” - “Del 2 Sportsrelaterede aktiviteter”.

Running	
Jumping	
Landing	
Starting and stopping quickly	
Cutting/lateral Movements	*
Low impact activities	*
Ability to perform activity with your normal technique	*+# Changed to ”Perform activities with your usual technique” - ”Udføre aktiviteter med din vanlige teknik”.
Ability to participate in your desired sport as long as you like	*+# Changed to ”Participate in your favorite sport for as long as you like” - ”Deltage i din foretrukne sport så længe du har lyst”.
How would you rate your current level of function during your sports related activities from 0 to 100 with 100 being your level of function prior to your foot or ankle problem and 0 being the inability to perform any of your usual daily activities?	+ Changed to “sports related activities” –“sædvanlige sportsrelaterede aktiviteter”.

Appendix IV - Manuscript Study III

A randomised trial of pain-guided early rehabilitation of acute lateral ankle sprains delivered by physiotherapists in the emergency department

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Abstract

Background: Lateral ankle sprain (LAS) is a common musculoskeletal injury and often results in the development of chronic ankle instability (CAI). Previous studies have suggested that early and targeted interventions for providing optimal loading in the acute phase may be beneficial to increase the functional status early after injury and mitigate the risk of developing CAI. We therefore hypothesized that a low activity level in the early stages after a LAS results in impairments in ankle function and increase the risk of CAI. **Objective:** The objective of this study was to compare the functional outcomes following acute LAS managed by usual care (RICE) or by a treatment approach consisting of pain-guided early rehabilitation in a randomized controlled trial. **Setting:** Emergency department. **Study design:** RCT. **Method:** 77 patients with acute LAS were included. The patients were randomly allocated to pain-guided early rehabilitation or usual care (RICE). The primary outcome, self-reported ancle function, was assessed using LEFS at baseline, at 1-, 2-, 3-, 4-week follow-up and at 3-, 6-, and 12-month follow-up. **Results:** No statistical difference between the groups were found in the primary outcome at the primary endpoint 4-week follow-up. In the 4-week follow-up period, 8/39 (21%) participants in the pain-guided group and 14/38 (37%) in the usual care group reported a re-injury of the same ankle, with no significant difference between the two trial arms (P=0.14). However, the attrition rates were very high. This precluded statistical comparisons at the 3-, 6- and 12-month follow-up. **Conclusion:** This trial showed no additional short-term effect in ankle function of a pain-guided early rehabilitation approach compared to usual care (RICE) for the treatment of acute LAS in the ED. Unfortunately, the retention was very low, and the study results must be interpreted very cautiously.

Introduction

Lateral ankle sprain (LAS) is a common musculoskeletal injury in the general population[1] and in sports and recreational activities[2]. Acute LAS is defined by Delahunt et al.[3] and endorsed by the International Ankle Consortium (IAC)[4] as: *"An acute traumatic injury to the lateral ligament complex of the ankle joint as a result of excessive inversion of the rear foot or a combined plantar flexion and adduction of the foot."* Acute LAS is common in the Emergency Department (ED) representing between 3-5% of the overall attendances[5], with incidence rates expected to be considerably higher in the general population[6]. The treatment of acute LAS in the ED consists of initial assessment and acute management of the injured foot, traditionally done by a physician or emergency nurse practitioner. The Ottawa ankle foot rule is used to determine the patients' need for radiography and ultimately to rule out fractures[7,8].

Different management strategies for acute ankle injuries outside the ED have been assessed in randomised controlled trials (RCTs) with mixed results. Most regimes are typically composed of a treatment approach consisting of Rest, Ice, Compression and Elevation (RICE), with advice about complete rest the first 48-72 hours after injury[9]. The more recent POLICE guidelines follow the same core treatments with the addition of protection (P) and optimal loading (L), although optimal loading is not well defined[9]. Bleakley et al.[10] showed favorable results towards an accelerated functional treatment approach, while Brison et al.[11] did not demonstrate a greater improvement in outcome with the addition of supervised physiotherapy to usual care.

One of the main concerns related to LAS is the development of chronic ankle instability (CAI). Doherty et al 2016 showed that poor functional status within the initial two weeks after injury is predictive of CAI[12]. The study showed that motor control deficits within two weeks of a first-time LAS and poorer dynamic postural control and lower self-reported function six months after a first-time LAS were predictive of eventual CAI outcome[12]. A study by Hultman et al.[13] incorporated a treatment regime with early physiotherapy instructed exercises and showed that early physiotherapy intervention has an positive effect on patient reported ancle function after acute LAS[13]. This suggests that early and targeted interventions for providing optimal loading in the acute phase by physiotherapists in the EDs may be beneficial to increase the functional status early after injury and mitigate the risk of developing CAI. Consequently, the aim of this study was to compare whether pain-guided early rehabilitation provided by physiotherapists was superior to advice and instructions in RICE following standard operating procedures provided by a physician (usual care) in improving self-reported functional outcome in patients with acute, non-fracture LAS presenting in the ED.

The study hypothesis was that pain guided early rehabilitation would be superior to usual care with respect to improvement in 4-week ankle function.

Methods

We did a multicenter open-label, two-arm, parallel-group, superiority, RCT, with the primary endpoint at four weeks. The protocol was submitted to and approved by the local Data Protection Agency (REG-141-2017), the Health Research Ethics Committee in Region Zealand (SJ-628) and was registered at www.clinicaltrials.gov (NCT03527121) before commencement of the trial. The trial was conducted in accordance with the Helsinki Declaration and ICH Good Clinical Practice (GCP). This article follows the CONSORT reporting guidelines for RCTs[14,15].

Setting and eligibility criteria

We recruited participants between May 2018 and January 2020 from the ED at Slagelse Hospital and Horsens Hospital in Denmark. Patients aged >18 years were included if they had a grade 1 or 2 ankle sprain sustained within 24 hours of randomisation. Patients were excluded if they were unable to bear weight on the affected foot for four steps with/without pronounced limping; were diagnosed with CAI on the affected limb[3,4]; had a fracture diagnosed by X-ray; had previous enrollment in the same study; had major lower limb surgery or other severe lower extremity injury in the past three months on the affected limb; were under the influence of drugs or alcohol; or had a condition that, in the opinion of the investigator, would preclude participation in the study (e.g. not having access to the internet, immobilization etc.).

Procedures

Potentially eligible participants were identified in the ED and received oral and written information about the study and study procedures and underwent a screening examination to assess eligibility. All included participants gave oral and written informed consent.

Descriptive data (age, height, body weight, previous lateral ankle sprain, limb dominance, injured limb left/right, time since injury, education, employment, contact details) were recorded in the ED. All follow-up assessments were collected using an internet-based survey platform (Easytrial), with personal links sent via email to the participants. The online follow-up assessments were performed prior to randomization (at baseline), at 1-, 2-, 3- and 4-week follow-up and at 3-, 6-, and 12-month follow-up. The windows for completion were ± two days (week one-four) and +/- two weeks (three, six and 12 months).

Randomisation and treatment allocation

After inclusion in the ED, the participants were randomised to either pain-guided early rehabilitation or usual care. The online data management program Easytrial produced the blinded randomisation sequence, only revealing treatment allocation of the individual participant to the physiotherapist working in the ED after informed consent and after baseline assessment had been completed. Patients were enrolled allocating participants in permuted blocks of 2 to 6 to either the pain-guided early rehabilitation or usual care group (1:1).

Treatments

Participants allocated to usual care followed standard guidelines consisting of advice about Rest, Ice, Compression and Elevation (RICE) provided by the physician at work. The advice also included avoidance of activities with risk of re-injury for a few months, and gradually putting more weight on the ankle, with slow progression to running and twisting. The treatment in the usual care group followed the S.O.P. but may differ from patient to patient. We do not know the extent of the information the patient in this study received at the ED.

Participants allocated to pain guided early weight bearing received instructions from a physiotherapist on how to manage their acute LAS together with a written homebased exercise program. The participants received advice and instructions in accelerated and early weight bearing, commencing at discharge. It was advised to load and exercise the ankle joint and accepting pain (during loading/exercising) up to, but not exceeding 5 on a 0-10 verbal rating scale (VRS). The written homebased exercise program was initiated at discharge from the hospital. If patients experienced pain exceeding VRS 5, they should follow the same guidelines as the usual care group consisting of Rest, Ice, Compression and Elevation. This approach was initiated to guide optimal loading following the acute LAS. Compression, with an elastic bandage, was administered in the ED and instructions on how to apply and manage the bandage correctly were given. The bandage should be worn all day, including during nighttime for three weeks. The elastic bandage should also be used as protection when performing exercises and activities with increased the risk of reinjury for at least three months after the initial injury. Participants were instructed to follow the home exercise program three times each day from discharge to the 4-wees follow-up. It consisted of ankle rehabilitation exercises focusing on walking with full weight bearing, neuromuscular training, balance training, muscle strengthening and jumping (details in Appendix IV.A). The physiotherapists in the ED had received specific training in the treatment protocol and instructed the participants in the home exercise program.

Outcome measurements

As we expected maximal clinical effects on ankle function after four weeks , the primary outcome was chosen as the self-reported ankle function, assessed using the lower extremity functional scale (LEFS)[19] at the 4-week follow-up. The LEFS is a patient reported outcome measure providing a total score based on the patient's subjective ankle function. The scale consists of 20 functional leg activities, each scored on a five-point Likert-like scale (0 impossible, 4 no difficulty), giving a total score of 0 (worst) to 80 (best)[16].

Secondary outcomes included pain at rest and with activity, assessed using 0-10 (NRS)[17,18]; the foot and ankle ability measure (FAAM) that is divided in two subscales: the FAAM activities of daily living and the FAAM Sports subscales[19]; the Cumberland ankle instability tool[20]; recurrent sprain experienced within last follow up (dichotomized as yes/no); and the EuroQol Health-related quality of life (EQ-5D-3L) questionnaire[21]. Furthermore, global perceived effect (GPE) of treatment was assessed using a transition questionnaire on which the participants would answer if their current LAS-related health status was "unchanged", "worse" or "better" compared to their pre-LAS status[22]. Also, the patient acceptable symptom state (PASS) was assessed by the answer (yes/no) to the question: ''*Taking into account all the activities you have during your daily life, your level of pain, and also your functional impairment, do you consider your current state is satisfactory?*''[23].

Sample size

The study was powered to assess superiority in a comparison between the participants allocated to pain-guided early rehabilitation and those allocated to receive RICE. Assuming that pain-guided early rehabilitation would produce a LEFS score at week 4 that was 9 points larger than the usual care, with a standard deviation of 17 points, we calculated that we would need 112 patients in the intention-to-treat (ITT) population (56:56) to test a two tailed hypothesis with more than 80% power (91%) at a 5% statistical significance level. The 9 point change in LEFS score were based on the systematic review published by Mehta et al.[24], which concluded that the MCID was 9 points in patients with lower extremity musculoskeletal conditions. The SD of 17 points were obtained from the article presented by Bleakley et al.[10]. Although we also investigated effects on other secondary outcomes, we did not power the trial for this because we had no a priori assumptions about effect sizes, and a larger trial may be needed to reliably detect these.

Statistical analysis

Statistical analyses were done on the ITT population, including all randomized participants in the analysis, all retained in the group to which they were allocated. A blinded investigator (CPO) did the initial data handling and all hypothesis testing.

We analyzed continuous outcomes using repeated measures mixed linear models including participants as a random effect, with group (2 levels) and week (4 levels: week 1, 2, 3, and 4) as fixed factors with the corresponding interactions. To assess the adequacy of the linear model(s) describing the observed data - as well as checking the assumptions for both the systematic and the random parts of the models - we investigated the model features via the predicted values and the studentized residuals, i.e. the residuals had to be normally distributed (around zero), and be independent of the predicted values. Results are expressed as estimates of the between group differences in the outcomes at week 1, 2, 3, and 4 visits with 95% confidence intervals (CI) to represent the precision of the estimates. Missing data were not imputed but were handled implicitly by the mixed models (maximum likelihood) approach.

Dichotomous outcomes were analyzed using Chi-square statistics or Fisher's Exact test. Results are expressed as number and proportions in each group at week 1, 2, 3 and 4.

We set the statistical significance for hypothesis tests at the conventional level of 0.05. All analyses were done using SAS statistical software (version 9.4).

RESULTS

Between May 2018 and January 2020, 77 patients were included in this study to receive either usual care (n=38) or pain-guided early rehabilitation (n=39). 33 (43%) participants (20 usual care; 13 pain-guided early rehabilitation) completed the 4-week assessment. Figure IV.A summarizes the recruitment, randomization, and follow-up rates. Table IV.A summaries the baseline demographic and clinical characteristics of the participants and Table IV.B and Table IV.C the primary and secondary outcomes.

Except for the GPE (Mean difference -1.96; 95% CI [-3.51 to -0.41]) and FAAM Sport (Mean difference 13.84; 95% CI [0.58 to 27.1]), all in favor of the usual care group, there were no statistically significant group differences at the 4-week follow-up (Table IV.A and IV.B). The statistically significant group differences in GPE and FAAM-Sport at the 4-week follow-up favoring usual care correspond to effect sizes of 0.57 and 0.47, respectively, indicating moderate effects.

In the 4-week follow-up period, 8/39 (21%) participants in the pain-guided early rehabilitation group and 14/38 (37%) in the usual care group reported a re-injury of the same ankle, with no significant difference between the two trial arms (P=0.14).

Unfortunately, there were high attrition rates at the 3-, 6- and 12-months follow-ups, which precluded statistical comparisons. For completeness of reporting, we therefore present raw data across all follow-ups as Appendix IV.B.

DISCUSSION

Principal findings

This pragmatic RCT showed no significant between-group difference in short-term ankle function of a pain-guided early rehabilitation approach, compared to usual care (RICE). The usual care group reported a significantly better outcome on the FAAM Sport subscale, and GPE after four weeks, as compared to the pain-guided early rehabilitation group. The pain-guided early rehabilitation group experienced nearly half as many recurrent sprains compared to the usual care group, 8 vs. 14 respectively during the four follow-ups.

Interpretation of findings

Based on the precision of the between-group difference estimate (95% CI) it cannot be ruled out that there could be a clinically relevant difference in favor of the usual care treatment. This is supported by the group differences in the FAAM Sport and the GPE favoring the usual care group. On the other hand, nearly twice as many participants in the usual care group reported a recurrent sprain to the ankle, which is an important predictor of development of CAI and could suggest long-term benefits of an early pain-guided loading strategy. An inherent part of the early pain-guided loading strategy is that the participants are encouraged to experience pain. This may also explain the lack of short-term efficacy over usual care. We managed to include only 69% (77 of 112) of the estimated number of patients needed, resulting in low statistical power. Because of the study being underpowered, the results cannot be generalised to the greater patient population.

Comparison with other studies

The inclusion and exclusion criteria used in this study for identifying participants with acute LAS corresponds to the minimum standard of clinical diagnostic assessment presented in the ROAST guidelines, except for the clinical assessment of ligaments[25]. We used the S.O.P. at the ED to differentiate between grade 1, 2 and 3 ankle sprains. The ROAST guidelines recommends that patients be scheduled four to six days after injury for clinical stability tests of the ankle joint ligaments. Because of the lack of delayed injury grading in this study, some patients included to the study might have been patients with a grade 3 ankle sprain.

Ankle sprains are the most common minor musculoskeletal injury treated in the ED[26,27], yet high levels of patients experience recurrent symptoms or CAI[28]. The current optimal treatment approach for the prevention of chronicity and reinjury consists of exercise therapy and bracing/ taping[29].

Exercise therapy and bracing/ taping is difficult to implement in an ED as the clinicians only manage the initial phase of the injury. Furthermore, this approach is not current practice in the Danish EDs and would not be feasibly to adapt to a Danish context. In this study, we investigated the effect of one session of treatment and advice regarding pain-guided early rehabilitation from a physiotherapist in the ED. One session with a physiotherapist at the ED only provides a very small timeframe for advice and might not be sufficient to improve patient function following treatment. One or more follow-up visits could be one approach to address and adapt the program to the individual as described by Vuurberg et al.[30].

A study providing an overview of the existing literature on the epidemiology of acute ankle sprains stated that the proportion of recurrent ankle sprains are reported between 12%-47%[31]. Thus, highlighting the need for research into the time-dependent measure as a predictor of recurrent ankle sprain. In this study, we followed patients for 12 months after inclusion, unfortunately due to high attrition rates in both groups no clear conclusion can be made on the long-term effects of the two allocated treatment regimes. For future epidemiological studies we however note that within the 12-month follow-up period 32/77(42%) participants reported a minimum of one recurrent sprain of the same ankle (See Appendix IV.B for details).

The treatment approach delivered in this study was based on existing literature indicating that an accelerated approach is favorable for short- and long-term patient outcomes[10]. We wanted to use an aggressive approach with training and full weight bearing already at discharge. This approach has not been tested before and is controversial in regards to the proposed approach of RICE[32], PRICE[11], POLICE[9] and PEACE and LOVE[33]. All other approaches apply rest/unloading of the injured ankle for the first 0-48/72 hours after injury. We used the patients NRS pain to guide them in how much rest/unloading they should use (optimal loading). One other study has used NRS pain as guidance for progression, but only used it to guide progression in exercises when training[13].

We included 53.8% patients with a history of previous ankle sprain. In a study conducted by Bleakley et al.[10] 73.1% of the patients included, reported to have a previous ankle sprain and a similar study by Brison et al.[11] 59.5%. The exclusion of patients with CAI in our study could explain the variance observed between the baseline characteristics 53.8% vs. 73.1% and 59.5%. The exclusion of patients with CAI were done as studies have shown difference in expected outcome between acute LAS and recurrent CAI patients[29].

The strengths of this study include the pragmatic approach, in which we aimed to test interventions in a real-world setting. Also, the two groups were comparable at baseline, suggesting that the random distribution of unknown confounders were successful. There are also several limitations to the study. . Importantly, we experienced a relatively high attrition rate across all follow-ups week one to four. The reasons for this are unknown, but fortunately, the attrition is equally distributed across both groups of the study. We used a pragmatic approach in this study and did not choose to incorporate clinical follow-up visits with a physiotherapist, as this is not current practice. Other studies investigating patients treated in the ED have shown similar difficulties with high attrition rates[34]. The high attrition rate may cause bias, positive or negative, and poses a serious risk for the studies external validity. Also, an important limitation is that we did not survey the participants' adherence to the allocated treatment strategies. The lack of between-group differences could be speculated to reflect a low adherence to the early pain guided loading strategy, although adherence was not evaluated. Finally, as we did not receive our pre-defined sample size, further confirmatory trials are needed.

CONCLUSION

This trial showed no additional short-term (four weeks) effect in ankle function of a pain-guided early rehabilitation approach, compared to usual care (RICE) for the treatment of acute LAS in the ED. The pain-guided early rehabilitation group experienced fever recurrent sprains compared to the usual care group within the first four weeks after injury.

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Figure IV.A - Study flow chart

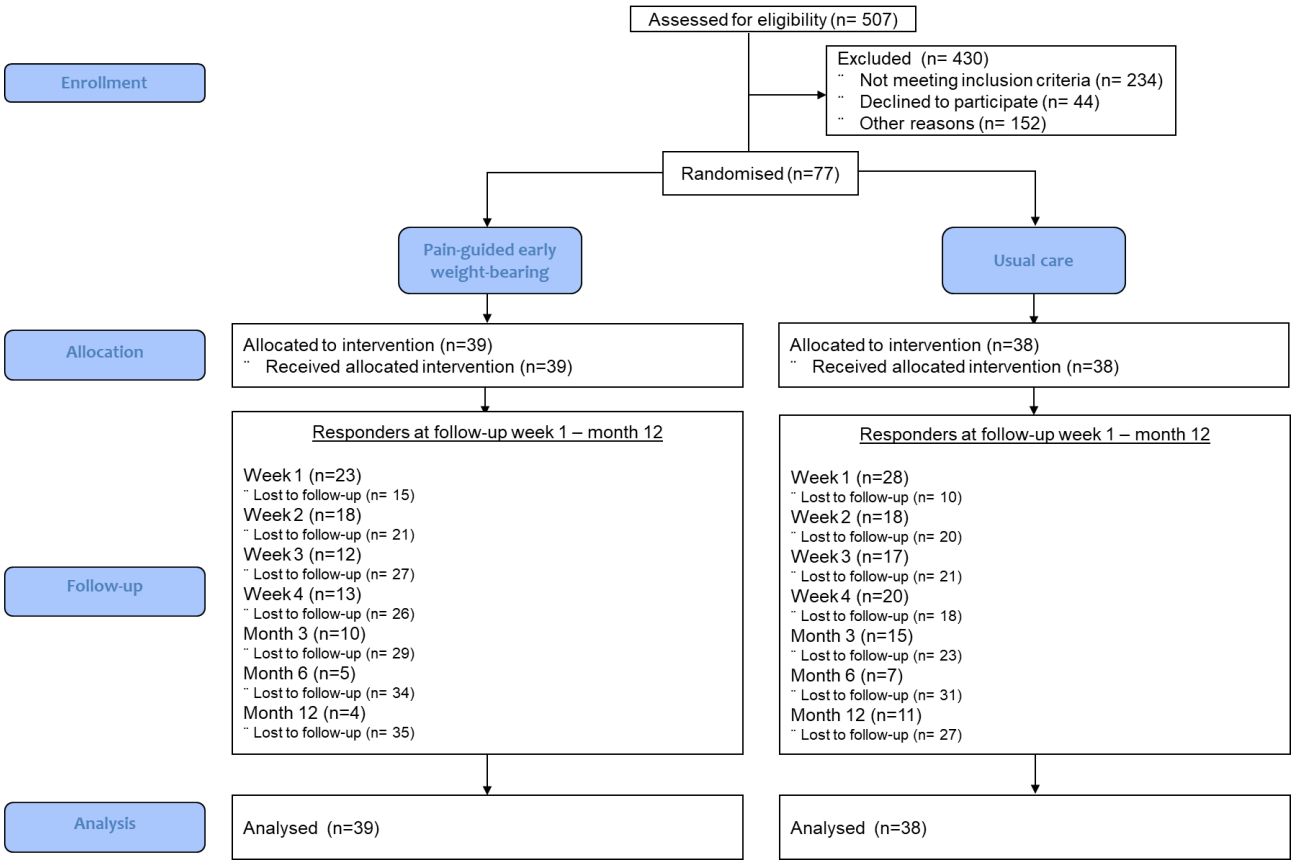


Table IV.A - Baseline demographic and clinical characteristics

	Pain-guided early rehabilitation **n= 39**	**Usual care** **n= 38**
Age, mean (SD)	30.8 (12.1)	32.9 (12.0)
Females, n (%)	23 (58.8%)	20 (52.6%)
Height, cm (SD)	173.3 (8.9)	174.6 (8.6)
Weight, kg (SD)	82.3 (16.2)	88.8 (21.4)
BMI (SD)	27.4 (4.9)	29.0 (6.2)
Educational level, n (%)		
➢ **Lower secondary school / academy preparatory education**	5 (6.5%)	2 (2.6%)
➢ **Upper secondary education / vocational education**	17 (22.1%)	18 (23.4%)
➢ **Short-cycle higher education**	5 (6.49%)	5 (6.5%)
➢ **Medium-cycle higher education**	9 (11.7%)	11 (14.3%)
➢ **Long-cycle higher education**	3 (3.9%)	2 (2.6%)
Income, n (%)		
➢ **<100.000 DKK**	7 (9.1%)	4 (5.2%)
➢ **100.000 - 199.999**	4 (5.2%)	4 (5.2%)
➢ **200.000 - 299.999**	6 (7.8%)	9 (11.7%)
➢ **300.000 - 399.999**	4 (5.2%)	10 (13.0%)
➢ **400.000 - 499.999**	5 (6.5%)	5 (6.5%)
➢ **500.000 - 749.999**	3 (3.9%)	2 (2.6%)
➢ **Declined to State**	10 (13.0%)	4 (5.2%)
Time from injury, n (%)		
➢ **0 - 2 Hours**	3 (3.9%)	2 (2.6%)
➢ **2 - 4 Hours**	8 (10.4%)	8 (10.4%)
➢ **4 - 6 Hours**	6 (7.8%)	8 (10.4%)
➢ **6 - 8 Hours**	2 (2.6%)	7 (9.1%)
➢ **8- 10 Hours**	5 (6.5%)	3 (3.9%)
➢ **10 - 12 Hours**	5 (6.5%)	0 (0.0%)
➢ **12 - 16 Hours**	4 (5.2%)	2 (2.6%)
➢ **16 - 20 Hours**	1 (1.3%)	2 (2.6%)
➢ **20 - 24 Hours**	5 (6.49%)	6 (7.8%)
Dominant side injured, n (%)	20 (51.3%)	17 (44.7%)
Previous ankle sprain (Yes), n (%)	21 (53.9%)	21 (55.3%)
LEFS, Mean (SD)	27.6 (14.1)	32.8 (15.8)
CAIT Injured leg, Mean (SD)	7.6 (8.1)	9.2 (9.0)

CAIT Uninjured leg, Mean (SD)	26.0 (4.9)	27.5 (2.9)
Eq5d-3L index, Mean (SD)	0.6 (0.2)	0.6 (0.2)
Eq5d-3L VAS, Mean (SD)	70.4 (27.0)	66.7 (25.8)
NRS Pain with rest, Mean (SD)	5.2 (2.6)	4.7 (2.5)
NRS Pain with activity, Mean (SD)	6.0 (3.1)	6.4 (2.9)
PASS (No), n (%)	33 (84.6%)	33 (86.8%)
Analgesic use past week (Yes), n (%)	21 (53.8%)	19 (50%)

Table IV.B - Change from baseline to 4 weeks.

	Pain-guided early rehabilitation		**Usual care**		**Diff**		
	Mean change	SE	Mean change	SE	Mean change	95%CI	
Primary outcome							
LEFS	31.01	3.26	35.04	2.67	-4.79	-12.33	4.27
Secondary outcomes							
NRS pain with rest	-3.33	0.49	-3.44	0.39	0.11	-1.13	1.34
NRS pain with activity	-3.71	0.56	-4.30	0.45	0.59	-0.82	2.00
CAIT injured leg	8.53	1.73	8.82	1.42	-0.29	-4.70	4.13
Eq5d-3L index	0.18	0.04	0.21	0.03	-0.03	-0.12	0.06
GPE	1.95	0.60	3.91	0.51	-1.96	-3.51	-0.41
FAAM adl	-28.63	3.07	-32.58	2.26	3.95	-3.59	11.49
FAAM sport	-31.01	5.30	-44.85	4.07	13.84	0.58	27.10

Table IV.C - Between-group difference at 4-week follow-up in analgesic use, PASS and TF.

	Pain-guided early rehabilitation	**Usual care**	**Fisher's P**
Analgesic use past week (Yes), n (%)	3 (23.1 %)	0 (0 %)	0.05
PASS (No), n (%)	10 (30.3 %)	12 (36.4 %)	0.46
TF (No), n (%)	8 (36.4 %)	10 (45.5 %)	1.00

Appendix IV.A

Exercise program

Afdeling for Fysio- og ergoterapi

Exercise program after acute lateral ankle injury (EN)

By: Christian Olsen

It is recommended that You immediately start this training program. It is advised to exercise with pain up to, but not exceedig 5 on a pain-scale (0-10). 0 represents no pain and 10 represents the worst pain you can imagine. If you experience pain of 6 or more, You must follow the RICE principles until the pain again is below 5.

1. Information

This training program should be followed daily the first 4 weeks after your acute lateral ankle sprain. The training program is designed to be performed in the morning, at noon and in the evening.
You can use an ice bag as pain reliever. Place it directly on top of the the damaged area for 10 minutes. Pull it of and wait 10 minutes. Continue until the pain is improved.

2. Walking forward as a figure of eight movement

Walk forward and form a figure of eight. Return to starting position and repeat. Start walking in a large figure of eight, about 10 meters.
At each minute decrease the figure of eight by 1 meter, thus the last minute is only 1 meter long.
You have to walk with a speed that gives you pain corresponding to 5 or less on the 0-10 pain-scale. You are alloved to jog / run. Exercise each day in the morning, at noon and in the evening.

Sets: , Duration: 12 min 0 sec, Pain level: 5 0-10

3. One Leg Jump in Circle, Both Ways

Stand on one leg on a mat with your hands in your side. Do a 90 degrees jump on the mat and continue jumping till you have jumped all the way around yourself. Then jump 90 degrees in the opposite direction and continue till you have jumped all the way around yourself again.

Sets: , Reps: 12 , Pain level: 5 0-10

4. Single leg stand on a balance cushion (knees bent)

Stand on a pillow (or fold a mat and stand on that). Stand on one leg with the knee a little bend. Hold the other leg out in the air and grab a hold of your hips with your hands. Try to keep your balance.

Tid: 12 min, Sets: , Pain level: 5 0-10

Afdeling for Fysio- og ergoterapi

Exercise program after acute lateral ankle injury (EN)

By: Christian Olsen

5. Toe lift on bench or step

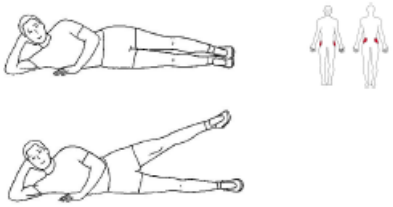
Stand on the edge of a step or a bench so that your heels are free, feet about hip-width apart. Raise your heels and push up until you are on your toes. Return to the start position and repeat. The exercise can be done with or without support.

Reps: 12 , Sets: , Pain level: 5 0-10

6. Gradual Backwards Lunge

Focus on a spot in front of you. Tighten your abdomen, place one foot on the mat and move backwards. Lower your back knee down towards the floor. Press your bottom down towards the floor, tighten abdomen and move your leg back to starting position. Perform the exercise with both legs.

Sets: , Reps: 12 , Pain level: 5 0-10



7. Side-lying single leg lift 2

Lie on your side with straight legs, supporting your head with one hand. Raise your top leg. Ensure that your toes point straight forward and that only your hip is moving. You should therefore avoid tilting your pelvis toward you or rotating your hip. Repeat the exercise with your other leg. Perform the exercise with both legs.

Sets: , Reps: 12

Appendix IV.B

Raw data from baseline to all follow-ups

LEFS scores

	Pain-guided early rehabilitation group								Usual care (RICE)							
	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	23	18	12	13	10	5	4	38	28	18	17	20	15	7	11
Mean	27,6	46,0	50,6	62,8	62,1	73,1	75,2	75,8	32,8	40,3	55,1	64,3	67,3	71,3	77,0	70,5
Median	25	46	54	65,5	66	76,5	75	79	31,5	40	56	68	72,5	76	80	78
Min	0	17	10	30	21	58	68	65	10	15	31	41	37	30	70	33
Max	62	79	80	80	77	80	80	80	80	69	76	80	80	80	80	80
SD	14,1	16,8	21,4	13,7	15,8	7,8	5,1	7,2	15,8	17,1	13,7	13,9	13,5	13,0	4,1	15,5

FAAM_ADL scores

	Pain-guided early rehabilitation group							Usual care (RICE)						
	1. week	2. week	3. week	4. week	3 month	6 month	12 month	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	22	18	11	13	10	4	4	26	18	16	20	13	6	11
Mean	59,6	66,1	80,2	78,9	93,3	95,5	94,3	53,5	72,8	87,0	87,1	94,5	99,2	88,4
Median	64,9	72,6	88,1	79,8	97,6	97,6	96,4	53,6	70,2	94,6	95,8	95,2	100,0	100,0
Min	15,5	19,0	41,7	7,9	79,8	86,9	84,5	20,0	45,2	53,6	50,0	85,7	96,4	48,8
Max	100,0	100,0	100,0	98,8	100,0	100,0	100,0	100,0	96,4	100,0	100,0	100,0	100,0	100,0
SD	21,3	25,0	19,6	24,7	7,8	6,2	7,4	18,5	17,2	14,9	15,3	5,4	1,4	18,6

FAAM_ADL_VAS

	Pain-guided early rehabilitation group							Usual care (RICE)						
	1. week	2. week	3. week	4. week	3 month	6 month	12 month	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	22	18	11	13	10	4	4	26	18	17	20	13	6	11
Mean	62,7	59,1	76,8	77,2	92,3	97,5	98,8	57,8	68,3	82,8	84,7	88,0	93,7	88,2
Median	65	69	80	75	95	98	100	69	75	90	90	90	99	100
Min	5	1	50	39	70	95	95	0	10	50	35	60	75	40
Max	99	99	100	99	100	100	100	85	100	100	100	100	100	100
SD	20,7	29,8	15,7	17,6	9,9	2,9	2,5	23,2	24,8	14,8	16,6	12,1	9,9	18,5

FAAM_SPORT

	Pain-guided early rehabilitation group							Usual care (RICE)						
	1. week	2. week	3. week	4. week	3 month	6 month	12 month	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	21	18	11	13	10	4	4	26	18	15	20	12	6	11
Mean	31,2	40,3	55,5	61,4	80,1	88,4	83,0	24,6	39,5	66,9	65,7	73,8	86,9	76,0
Median	28,6	33,9	75,0	67,9	87,5	89,3	91,1	19,6	39,3	75,0	75,0	78,6	96,4	92,9
Min	0,0	0,0	0,0	21,4	35,7	75,0	50,0	0,0	0,0	0,0	0,0	21,4	46,4	7,1
Max	100,0	100,0	100,0	96,4	100,0	100,0	100,0	64,3	78,6	100,0	100,0	100,0	100,0	100,0
SD	27,3	32,8	34,2	25,6	23,9	11,8	23,6	20,4	25,4	28,6	30,8	25,4	21,0	32,7

FAAM_SPORT_VAS

	Pain-guided early rehabilitation group							Usual care (RICE)						
	1. week	2. week	3. week	4. week	3 month	6 month	12 month	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	21	18	11	13	10	4	4	26	18	17	20	13	6	11
Mean	37,9	46,0	60,0	63,8	73,6	96,0	87,5	26,7	52,6	63,9	73,3	73,6	84,8	76,1
Median	30,0	55,0	80,0	75,0	90,0	97,0	95,0	22,5	62,0	75,0	82,5	80,0	89,5	90,0
Min	0	0	0	10	0	90	60	0	0	0	10	25	60	0
Max	95	99	92	95	100	100	100	80	90	100	100	100	100	100
SD	28,8	35,1	32,4	30,0	34,6	4,5	18,9	21,4	27,7	30,8	26,2	25,5	14,8	34,6

FAAM_Overall_Function

	Pain-guided early rehabilitation group							Usual care (RICE)						
	1. week	2. week	3. week	4. week	3 month	6 month	12 month	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	22	18	11	13	10	4	4	26	18	17	20	13	6	11
Normal (%)	5%	6%	0%	8%	30%	50%	50%	0%	0%	12%	20%	23%	50%	45%
Nearly normal (%)	18%	50%	64%	54%	70%	50%	25%	35%	50%	59%	60%	54%	33%	36%
Abnormal (%)	64%	39%	36%	38%	0%	0%	25%	46%	39%	29%	20%	23%	17%	9%
Severly abnormal (%)	14%	6%	0%	0%	0%	0%	0%	19%	11%	0%	0%	0%	0%	9%

CAIT_INJURED

	Pain-guided early rehabilitation group								Usual care (RICE)							
	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	23	18	12	13	10	5	6	38	27	18	17	20	13	6	9
Mean	7,6	9,1	10,8	13,9	14,8	19,1	20,6	20,2	9,2	6,8	9,7	14,4	16,1	20,5	25,5	21,3
Median	4	7	9	16	14	24	23	23	5	6	9	13	18	24	28	26
Min	0	1	1	1	4	5	7	4	0	0	2	6	1	8	19	4
Max	30	26	26	24	24	30	30	30	29	26	24	26	27	30	30	30
SD	8,1	7,1	9,2	7,9	7,4	10,0	9,9	10,7	9,0	5,5	6,2	7,8	8,0	7,1	4,8	10,3

CAIT_UNINJURED

	Pain-guided early rehabilitation group								Usual care (RICE)							
	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	23	17	12	11	10	4	9	38	27	19	17	22	13	7	6
Mean	26,0	26,5	28,4	27,2	28,3	28,5	29,8	27,0	27,5	27,2	28,2	27,9	27,4	27,8	28,7	27,5
Median	27	27	30	29	30	30	30	30	29	29	30	30	30	30	29	30
Min	10	8	25	14	21	25	29	10	19	13	20	17	14	17	26	20
Max	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30
SD	4,9	4,9	2,0	4,6	2,8	2,2	0,5	6,5	2,9	4,6	2,9	4,1	4,5	3,8	1,4	4,0

EQ-5D-3L Index

	Pain-guided early rehabilitation group								Usual care (RICE)							
	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	23	18	12	13	10	5	4	38	27	18	17	20	13	6	11
Mean	0,6	0,7	0,7	0,8	0,8	0,9	0,9	1,0	0,6	0,7	0,7	0,8	0,8	0,9	0,9	0,8
Median	0,7	0,7	0,7	0,7	0,8	0,8	1,0	1,0	0,6	0,7	0,7	0,8	0,8	1,0	0,8	1,0
Min	0,1	0,4	0,2	0,5	0,6	0,7	0,8	0,8	0,2	0,3	0,6	0,7	0,7	0,7	0,8	0,5
Max	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
SD	0,2	0,1	0,2	0,1	0,2	0,1	0,1	0,1	0,2	0,1	0,1	0,1	0,1	0,1	0,1	0,2

EQ-5D_3L VAS

	Pain-guided early rehabilitation group								Usual care (RICE)							
	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	23	18	12	13	10	5	4	38	27	18	17	20	13	6	11
Mean	70,4	76,6	80,1	80,8	84,7	92,0	96,2	91,8	66,7	67,5	73,7	84,1	75,4	88,2	80,5	89,8
Median	76	81	86	84	90	95	95	97	71	75	77	87	85	90	92	95
Min	2	30	49	45	52	75	94	75	5	15	7	59	10	60	20	70
Max	100	100	100	100	100	100	100	98	100	98	97	98	100	100	100	100
SD	27,0	19,2	17,7	14,8	14,0	8,3	2,7	11,2	25,8	22,0	21,0	12,0	26,7	12,2	30,1	9,5

NRS_PAIN_REST

	Pain-guided early rehabilitation group								Usual care (RICE)							
	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	24	18	12	13	10	5	4	38	28	18	17	20	14	7	11
Mean	5,2	3,6	2,5	2,2	2,2	0,7	0,3	1,0	4,7	3,6	2,0	1,5	1,5	0,8	1,0	0,8
Median	5,5	3,5	2,0	1,3	2,0	0,8	0,0	1,0	5,0	3,3	1,0	1,0	1,0	0,5	0,5	0,5
Min	0,0	0,0	0,0	0,0	0,5	0,0	0,0	0,0	0,0	1,0	0,0	0,0	0,0	0,0	0,0	0,0
Max	10,0	9,0	8,5	8,5	7,5	1,5	1,0	2,0	9,5	7,0	5,5	5,0	5,0	3,5	3,5	4,5
SD	2,6	2,3	2,4	2,3	1,9	0,6	0,4	0,8	2,5	1,9	1,6	1,6	1,4	1,0	1,2	1,3

NRS_PAIN_ACTIVITY

	Pain-guided early rehabilitation group								Usual care (RICE)							
	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	23	18	12	13	10	5	4	38	27	18	17	20	13	7	11
Mean	6,0	5,7	4,9	3,3	3,1	1,4	1,0	1,0	6,4	5,2	3,6	2,5	2,3	1,5	2,4	1,8
Median	7,5	6,0	5,0	2,8	2,0	1,0	1,0	1,0	7,5	5,0	3,5	2,5	2,0	1,0	1,0	1,0
Min	0	1	0	2	1	0	0	0	0	2	2	0	0	0	0	0
Max	10	9	9	8	10	4	3	2	10	9	6	5	6	3	6	8
SD	3,1	2,2	2,5	1,9	2,7	1,5	1,2	0,8	2,9	1,8	1,4	1,4	1,9	1,2	2,4	2,4

Global Perceived Effect_GPE

	Pain-guided early rehabilitation group							Usual care (RICE)						
	1. week	2. week	3. week	4. week	3 month	6 month	12 month	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	23	18	12	13	10	5	4	27	18	17	20	13	6	11
Mean	1,7	0,4	1,4	1,5	3,8	2,0	1,8	1,8	2,9	3,8	4,0	4,3	2,5	3,0
Median	2,0	0,0	1,5	0,0	5,0	0,0	1,5	2,0	3,0	4,0	5,0	5,0	2,0	4,0
Min	-4	-4	-5	-2	0	-1	0	-4	-2	0	0	-2	-1	-1
Max	6	4	5	6	6	6	4	6	6	6	6	6	6	6
SD	2,8	2,2	2,9	3,1	2,7	3,2	2,1	2,5	1,9	2,0	1,7	2,5	3,2	2,8

Patient Acceptable Symptom State_PASS

	Pain-guided early rehabilitation group								Usual care (RICE)							
	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	23	18	12	13	10	5	4	38	27	18	17	20	13	6	11
PASS No (n)	33	16	15	8	10	6	2	0	33	26	12	9	12	5	2	4
PASS No (%)	84,6	69,6	83,3	66,7	76,9	60,0	40,0	0,0	86,8	96,3	66,7	52,9	60,0	38,5	33,3	36,4

Treatment Failure

	Pain-guided early rehabilitation group								Usual care (RICE)							
	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month	Baseline	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	33	16	15	8	10	6	2	0	33	26	12	9	12	5	2	4
TF No (n)	31	14	13	6	8	5	1	0	26	21	10	9	10	4	1	3
TF No (%)	93,9	87,5	86,7	75,0	80,0	83,3	50,0		78,8	80,8	83,3	100,0	83,3	80,0	50,0	75,0

Recurrent sprain

	Pain-guided early rehabilitation group							Usual care (RICE)						
	1. week	2. week	3. week	4. week	3 month	6 month	12 month	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	23	18	12	13	10	5	4	27	18	17	20	13	6	11
Recurrent Sprain Yes(n)	4	3	2	3	2	1	2	6	6	3	3	6	4	8
Recurrent_Sprain Yes(%)	17%	17%	17%	23%	20%	20%	50%	22%	33%	18%	15%	46%	67%	73%

Recurrent sprain total new cases in ITT

	Pain-guided early rehabilitation group							Usual care (RICE)						
	1. week	2. week	3. week	4. week	3 month	6 month	12 month	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	39	39	39	39	39	39	38	38	38	38	38	38	38
Recurrent Sprain Total Yes(n)	4	6	6	8	10	10	11	6	12	14	14	16	19	21
Recurrent Sprain Total Yes(%)	10%	15%	15%	21%	26%	26%	28%	16%	32%	37%	37%	42%	50%	55%

Analgesic use

	Pain-guided early rehabilitation group							Usual care (RICE)						
	1. week	2. week	3. week	4. week	3 month	6 month	12 month	1. week	2. week	3. week	4. week	3 month	6 month	12 month
No. of patients	39	24	18	12	13	10	5	4	38	28	18	17	20	14
Analgesic Use Yes (n)	21	16	8	2	3	0	0	0	19	17	5	3	0	0
Analgesic Use Yes (%)	54%	67%	44%	17%	23%	0%	0%	0%	50%	61%	28%	18%	0%	0%

Co-authorship declarations

GRADUATE SCHOOL OF HEALTH AND MEDICAL SCIENCES
UNIVERSITY OF COPENHAGEN

PHD-THESIS
DECLARATION OF CO-AUTHORSHIP

The declaration is for PhD students and must be completed for each conjointly authored article. Please note that if a manuscript or published paper has ten or less co-authors, all co-authors must sign the declaration of co-authorship. If it has more than ten co-authors, declarations of co-authorship from the corresponding author(s), the senior author and the principal supervisor (if relevant) are a minimum requirement.

1. Declaration by	
Name of PhD student	Christian Pilely Olsen
E-mail	Chrol@regionsjaelland.dk
Name of principal supervisor	Marius Henriksen
Title of the PhD thesis	Physiotherapy for minor musculoskeletal injuries in hospital emergency departments

2. The declaration applies to the following article	
Title of article	**Physiotherapists' prognosis as a predictor of short**-term outcome after treatment of minor musculoskeletal injuries in the Emergency Department: A prospective cohort study
Article status	
Published ☐ Date:	Accepted for publication ☐ Date:
Manuscript submitted ☒ Date: 29 March 2020	Manuscript not submitted ☐
If the article is published or accepted for publication, please state the name of journal, year, volume, page and DOI (if you have the information).	

3. The PhD student's contribution to the article ***(please use the scale A-F as benchmark)*** Benchmark scale of the PhD-student's contribution to the article **A.** Has essentially done all the work (> 90 %) **B.** Has done most of the work (60-90 %) **C.** Has contributed considerably (30-60 %) **D.** Has contributed (10-30 %) **E.** No or little contribution (<10 %) **F.** Not relevant	**A, B, C, D, E, F**
1. Formulation/identification of the scientific problem	B
2. Development of the key methods	B
3. Planning of the experiments and methodology design and development	A
4. Conducting the experimental work/clinical studies/data collection/obtaining access to data	A
5. Conducting the analysis of data	B
6. Interpretation of the results	A
7. Writing of the first draft of the manuscript	A
8. Finalisation of the manuscript and submission	A
Provide a short description of the PhD student´s specific contribution to the article.[1] In collaboration wit his supervisors, Christian has developed the protocol. Then Christian has organised the data collection, collected data and processed the data for analyses. The analyses was done in collaboration with his supervisors. Manuscript preparation was done by Christian, and after revisions from his suprvisors, Christian has submitted it for publication.	

Latest update of the declaration: December 2018

4. Material from another thesis / dissertation[ii]	
Does the article contain work which has also formed part of another thesis, e.g. master's thesis, PhD thesis or doctoral dissertation (the PhD student's or another person's)?	Yes: ☐ No: ☒
If yes, please state name of the author and title of thesis / dissertation.	
If the article is part of another author's academic degree, please describe the PhD student's and the author's contributions to the article so that the individual contributions are clearly distinguishable from one another.	

5. Signatures of the co-authors[iii]

	Date	Name	Title	Signature
1.	17/04/2020	Marius Henriksen	Professor	
2.	19/4-20	Søren T. Skou	Professor	
3.	27/4-20	Finn E. Nielsen	Senior researcher	
4.				
5.				
6.				
7.				
8.				
9.				
10.				

6. Signature of the principal supervisor

I solemnly declare that the information provided in this declaration is accurate to the best of my knowledge.
Date: 17-4-2020
Principal supervisor:

7. Signature of the PhD student

I solemnly declare that the information provided in this declaration is accurate to the best of my knowledge.
Date: 09-05-2020
PhD student: Christian Pilely Olsen

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[i] This can be supplemented with an additional letter if needed.
[ii] Please see Ministerial Order on the PhD Programme at the Universities and Certain Higher Artistic Educational Institutions (PhD Order) § 12 (4):
"Any articles included in the thesis may be written in cooperation with others, provided that each of the co-authors submits a written declaration stating the PhD student's or the author's contribution to the work."
[iii] If more signatures are needed please add an extra sheet.

PHD-THESIS
DECLARATION OF CO-AUTHORSHIP

The declaration is for PhD students and must be completed for each conjointly authored article. Please note that if a manuscript or published paper has ten or less co-authors, all co-authors must sign the declaration of co-authorship. If it has more than ten co-authors, declarations of co-authorship from the corresponding author(s), the senior author and the principal supervisor (if relevant) are a minimum requirement.

1. Declaration by	
Name of PhD student	Christian Pilely Olsen
E-mail	Chrol@regionsjaelland.dk
Name of principal supervisor	Marius Henriksen
Title of the PhD thesis	Physiotherapy for minor musculoskeletal injuries in hospital emergency departments

2. The declaration applies to the following article	
Title of article	Dual-panel translation and cross-cultural adaptation of the Danish Version of the Cumberland Ankle Instability Tool, Foot and Ankle Ability Measure & Lower Extremity Functional Scale.
Article status	
Published ☐ Date:	Accepted for publication ☐ Date:
Manuscript submitted ☐ Date:	Manuscript not submitted ☒
If the article is published or accepted for publication, please state the name of journal, year, volume, page and DOI (if you have the information).	

3. The PhD student's contribution to the article ***(please use the scale A-F as benchmark)*** Benchmark scale of the PhD-student's contribution to the article **A.** Has essentially done all the work (> 90 %) **B.** Has done most of the work (60-90 %) **C.** Has contributed considerably (30-60 %) **D.** Has contributed (10-30 %) **E.** No or little contribution (<10 %) **F.** Not relevant	**A, B, C, D, E, F**
1. Formulation/identification of the scientific problem	A
2. Development of the key methods	A
3. Planning of the experiments and methodology design and development	A
4. Conducting the experimental work/clinical studies/data collection/obtaining access to data	A
5. Conducting the analysis of data	F
6. Interpretation of the results	F
7. Writing of the first draft of the manuscript	A
8. Finalisation of the manuscript and submission	A
Provide a short description of the PhD student´s specific contribution to the article.[1] Christian has protocolised, prepared, organised and participated in the data collection. Christian has written the first manuscript draft and finalised it for publication after comments from his co-authors.	

Latest update of the declaration: December 2018

4. Material from another thesis / dissertation[v]	
Does the article contain work which has also formed part of another thesis, e.g. master's thesis, PhD thesis or doctoral dissertation (the PhD student's or another person's)?	Yes: ☐ No: ☒
If yes, please state name of the author and title of thesis / dissertation.	
If the article is part of another author's academic degree, please describe the PhD student's and the author's contributions to the article so that the individual contributions are clearly distinguishable from one another.	

5. Signatures of the co-authors[vi]				
	Date	Name	Title	Signature
1.	17-4-2020	Marius Henriksen	Professor	
2.	19/4-20	Søren T. Skou	Professor	
3.	27/4-2020	Finn E. Nielsen	Senior researcher	
4.				
5.				
6.				
7.				
8.				
9.				
10.				

6. Signature of the principal supervisor
I solemnly declare that the information provided in this declaration is accurate to the best of my knowledge. Date: 17-4-2020 Principal supervisor:

7. Signature of the PhD student
I solemnly declare that the information provided in this declaration is accurate to the best of my knowledge. Date: 09-05-2020 PhD student: Christian Pilely Olsen

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PHD-THESIS
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1. Declaration by	
Name of PhD student	Christian Pilely Olsen
E-mail	Chrol@regionsjaelland.dk
Name of principal supervisor	Marius Henriksen
Title of the PhD thesis	Physiotherapy for minor musculoskeletal injuries in hospital emergency departments

2. The declaration applies to the following article	
Title of article	A randomised trial of pain guided early rehabilitation of acute lateral ankle sprains delivered by physiotherapists in the emergency department
Article status	
Published ☐ Date:	Accepted for publication ☐ Date:
Manuscript submitted ☐ Date:	Manuscript not submitted ☒
If the article is published or accepted for publication, please state the name of journal, year, volume, page and DOI (if you have the information).	

3. The PhD student's contribution to the article ***(please use the scale A-F as benchmark)*** Benchmark scale of the PhD-student's contribution to the article **A**. Has essentially done all the work (> 90 %) **B**. Has done most of the work (60-90 %) **C**. Has contributed considerably (30-60 %) **D**. Has contributed (10-30 %) **E**. No or little contribution (<10 %) **F**. Not relevant	**A, B, C, D, E, F**
1. Formulation/identification of the scientific problem	A
2. Development of the key methods	B
3. Planning of the experiments and methodology design and development	A
4. Conducting the experimental work/clinical studies/data collection/obtaining access to data	A
5. Conducting the analysis of data	A
6. Interpretation of the results	B
7. Writing of the first draft of the manuscript	A
8. Finalisation of the manuscript and submission	A
Provide a short description of the PhD student´s specific contribution to the article.[i] Christian has conceptualised the study, writtne the protocol and prepared and organised the collection of data. He has analysed the data and in collaboration with co-authors interpreted the results. Christian has written the first manuscript draft and revised it according to comments and suggestions from his co-authors. Christian has finalised and submitted the manuscript for publication.	

Latest update of the declaration: December 2018

4. Material from another thesis / dissertation[ii]	
Does the article contain work which has also formed part of another thesis, e.g. master's thesis, PhD thesis or doctoral dissertation (the PhD student's or another person's)?	Yes: ☐ No: ☒
If yes, please state name of the author and title of thesis / dissertation.	
If the article is part of another author's academic degree, please describe the PhD student´s and the author´s contributions to the article so that the individual contributions are clearly distinguishable from one another.	

5. Signatures of the co-authors[iii]				
	Date	Name	Title	Signature
1.	17-4-2020	Marius Henriksen	Professor	
2.	19/4-20	Søren T. Skou	Professor	
3.	27/4-20	Finn E. Nielsen	Senior researcher	
4.				
5.				
6.				
7.				
8.				
9.				
10.				

6. Signature of the principal supervisor

I solemnly declare that the information provided in this declaration is accurate to the best of my knowledge.

Date: 17-4-2020

Principal supervisor:

7. Signature of the PhD student

I solemnly declare that the information provided in this declaration is accurate to the best of my knowledge.

Date: 09-05-2020

PhD student: Christian Pilely Olsen

Please learn more about responsible conduct of research on the Faculty of Health and Medical Sciences' website.

[i] This can be supplemented with an additional letter if needed.
[ii] Please see Ministerial Order on the PhD Programme at the Universities and Certain Higher Artistic Educational Institutions (PhD Order) § 12 (4):
"Any articles included in the thesis may be written in cooperation with others, provided that each of the co-authors submits a written declaration stating the PhD student's or the author's contribution to the work."
[iii] If more signatures are needed please add an extra sheet.