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PhD thesis

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Measuring Symptoms, Function, and Psychosocial Consequences in Patients with Anterior Cruciate Ligament Rupture

Development and Validation of a Patient-related Outcome Questionnaire

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Ph.D. Dissertation

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1. Preface and Acknowledgements

The *Guidelines for the PhD Programme* of the Faculty of Health Science, University of Copenhagen[1] stipulate that when a PhD a thesis incorporates more than one scientific paper submitted for publication, the written structure of the articles should be accompanied by an "extended summary" of approximately 30 pages. The summary is normally structured as follows:

- A brief, general presentation of the research hypotheses presented in the included articles;
- A brief presentation of the results achieved with an assessment of the methods applied and a critical review of the conclusions that can be drawn from the results;
- A comparison with and assessment of other researchers' published results to the extent that this is relevant to the presentation of the author's contribution to the analysis of the research hypothesis;
- A summary conclusion

The Guidelines also state that the scientific articles/manuscripts can be included as chapters instead of the brief presentation of the methods applied and the main findings.

The form of the present thesis adheres to the above-described structure. The thesis is based on three scientific papers, which have been submitted for peer-review, and an accompanying summary consisting of an introduction, background, and objectives, followed by the three manuscripts submitted for publication. Each paper is followed by a discussion of the major findings, assessment of methods, justification of conclusions, and contribution to current knowledge.

The studies performed in this thesis were carried out from 2009 to 2012 in a collaborative effort between the Department of Sports Traumatology, Institute of Orthopedics and Internal Medicine, Faculty of Health Science, at the University of Copenhagen, and the Department and Research Unit of General Practice, Institute of Public Health, Faculty of Health Science, University of Copenhagen.

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Origins of project

It was by chance that I met my supervisor, John Brodersen, at a private dinner party in 2004. John, an MD and specialist in general practice, was approaching the end of his own PhD study concerning the psychosocial consequences of false-positive breast cancer screening. He had developed a questionnaire to measure these consequences, and had used an advanced statistical method called Rasch analysis to validate the instrument. I had heard of Rasch analysis, and I was aware that some of the world's leading experts, such as Svend Kreiner, were at the University of Copenhagen. I was working closely at that time with my other supervisor, Chief Surgeon Michael Krogsgaard, in rehabilitation of patients with knee injuries. It was a common occurrence that my patients complained of difficulty answering some of the questions in our standardized questionnaires. Therefore, John, Michael, Senior Scientist and fellow physical therapist Nina Beyer, and I planned to investigate the measurement performance of the questionnaires using Rasch analysis. We published our results in 2008.[2] The present PhD is a direct consequence of that study.

Originally, this PhD project consisted of two major stages. Phase 1 was the development and validation of a condition-specific patient-related outcome (PRO) questionnaire for patients with anterior cruciate ligament (ACL) deficiency pre- and post-ACL reconstruction. The instrument would be subjected to psychometric validation using the Rasch model of item-response theory (IRT).

Phase 2 was to involve computer-generated three-dimensional biomechanical analysis of a cohort of these patients, and the results were subsequently to be compared in a regression analysis using structural equation or log linear chain-graph modeling techniques.

The research process did not progress exactly as planned. The biomechanical analyses are not included in this thesis for two reasons: 1) the timeframe of the development and validation of the condition-specific PRO questionnaire extended beyond the allotted three-year period of the PhD program, and 2) the biomechanical test laboratory, where the testing was to take place, had a technical permanent malfunction of its infrared optical tracking cameras. This rendered viable motion capture impossible.

Acknowledgements

I am grateful for my collaboration with Tine Alkjær and Erik Simonson from the Department of Biomechanics, Panum Institute - University of Copenhagen. From Bispebjerg Hospital, I want to thank Jes Bruun Lauritzen, Nina Beyer, Monika Bayer, Christian Couppé, Pia Andersen, and all the staff and the surgeons at the Department of Sports Traumatology. Also thanks to all my colleagues at Sahva, in particular Christer Levin.

I want to thank my dear friends and colleagues at the Research Unit and Section of General Practice, particularly in the UPPS group.

Special thanks to Hanne Thorsen (for getting this ball rolling, long before I knew it existed, and then passing it on to John Brodersen) and Klaus Witt. Also thanks to Olivia Spalletta and David Stodolsky for editorial assistance and scientific discussions.

Very special thanks to Svend Kreiner and Volkert Siersma. I do not think humans can get much brighter or kinder (imperviously kind!), as is the case with most everyone in the Matilda Bay Club, which is a group of statisticians and scientists, led by David Andrich, committed to using Rasch models for various measurement applications.

Finally, I want most specially to thank my supervisors Michael Krogsgaard and John Brodersen. What can I say about these two fellows? Great minds, great hearts, great clinicians. It is a privilege simply to be associated with them. While Michael is the best surgeon I have had the fortune to work with, John's insight into the human condition, and the challenges we face as clinicians in the justification of our actions, is unsurpassed. In addition, his ability to grasp the fundamental concepts of Rasch analysis, and even more important, employ these together with qualitative concepts to generate useful metrics is nothing short of brilliant. Words cannot express my gratitude.

My intention with this project has been to be as efficient as possible; however, as my friend Timothy Dunne, a mathematics and statistics professor from South Africa, so poignantly stated, "Efficiency without compassion approaches abuse".[1]

This thesis is dedicated to my wife Eva, my sons Niklas and Max, and my family in the United States (my mother, brother, sisters, and particularly to my father, the late Dr. Arnold C. Comins).

[1] Tim Dunne spontaneously uttered this phrase in response to a comment by John Brodersen on the current trend to streamline, at all costs, healthcare systems in Western societies. This was while attending the Fifth International Conference on Probabilistic Models for Measurement in Perth Australia in January 2012, eating breakfast in the 40-C° summer heat (and no air conditioning).

2. Summary

The objective of this PhD study was to construct and validate a questionnaire that can be used to measure the effect of treatment in patients with ACL deficiency. This process was divided into separate studies described in the three articles presented in this thesis.

Study 1 encompassed a literature search to find all questionnaires used to assess outcome in the targeted patient group. The objective was to identify item content deemed suitable for these patients by clinical experts; that is, items that possess face validity. The next step was to translate all “non-Danish” items into Danish and consolidate items with redundant content. Different questionnaires ask many of the same questions. Thus, item reduction was performed retaining only items with unique content. The literature search included 31 PROs, which yielded 539 items in four languages. Because the majority of items were not in Danish, translation was carried out by extracting just the meaningful content of the item. For example, an item such as “In the past week, I have had difficulty walking down a flight of stairs” would be truncated to “difficulty walking down stairs”. These truncated items were then translated to Danish and assessed for content redundancy. The final number of truncated items with unique content was 157. This process was the substantive part of Paper 1. The article was submitted for publication and is now under revision.

The second study involved focus group interviews with patients with ACL rupture, pre- and postoperatively. Each item from the literature search was discussed on an item-by-item basis to ascertain the content relevance for these patients. Thirty-eight items from the initial item pool, five modified items, and twelve items with new content were confirmed to be relevant by the patients in three focus groups and seven single interviews. The result was a 55-item pilot questionnaire with six proposed functional measurement domains. This process is described in Paper 2, which has been submitted for publication and is in review.

In the third study, 242 patients consisting of patients prior to and subsequent to ACL reconstruction were recruited from the ACL registry list at Bispebjerg Hospital. The patients completed the 55-item draft questionnaire. The subjects consisted of three groups: 62 subjects in the pre-operative group, 87 subjects in the first post-operative group (four to 16 months post-op), and 93 subjects in the third post-operative group (at least 28 months post-operative). The responses were analyzed using Partial-Credit and Graphical Loglinear Rasch models. Forty-one items exhibited fit to the Rasch model and thus possess unidimensional measurement characteristics as applied to patients, pre- and post- ACL reconstruction. The items were

distributed across seven constructs and not six as proposed *a priori*. This was because one proposed domain was found to consist of two separate constructs. The seven scales comprise the newly formed condition-specific PRO questionnaire entitled the *Knee Numeric Entity Evaluation Score – ACL (KNEES-ACL).*[2] This scale validation study is described in Article 3, which is included in this thesis. The paper has been finalized and is in the process of being submitted for peer-review.

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[2] Definition of acronym: KNEES – ACL

When an item fits a Rasch model, and thus can be used in numeric comparisons, the output score can be considered a numeric-entity, representing the individual's level of the attribute. The acronym Knee-Numeric-Entity-Evaluation-Score came about through a philosophical discussion of measurement theory with David Stodolsky, PhD. He is thanked for his input in this regard.

3. Resumé (Danish Summary)

Formålet med dette projekt var at konstruere et spørgeskema til måling af behandlingseffekt på patienter med forreste korsbåndsinsufficiens. Processen bestod af 3 studier, som er beskrevne i denne afhandling.

Studie 1 omfattede en systematisk litteratursøgning, som skulle finde frem til alle potentielt relevante spørgeskemaer, der anvendes til at vurdere effekten af behandling af den pågældende patientgruppe. Dette var for at identificere de items og begreber, som kliniske eksperter har skønnet, er egnet til disse patienter. Det næste skridt var at oversætte alle de "ikke-danske" items til dansk. Dette var for at kunne vurdere, hvorvidt indholdet af items overlappede (item redundans). Derefter skulle relevansen af items undersøges i forhold til målgruppen gennem fokusgruppe-interviews for at identificere, hvilke elementer der var kvalitativt relevante i forhold til disse patienter. I litteratursøgningen identificerede vi 31 spørgeskemaer anvendt på patienter med sygdom i knæet, der opfyldte inklusionskriterierne. Det blev til i alt 539 items fordelt over fire sprog. Meget få af disse items var oversat til dansk, og derfor blev den planlagte 2-panels oversættelse af logistisk årsager ikke mulig at gennemføre. Derfor valgte mine vejledere og jeg at udføre oversættelsesprocessen på en anden måde. Vi fjernede sætningsstrukturen i hvert item og isolerede det meningsfyldte indhold. For eksempel, et item som "I den forløbne uge, har jeg haft svært ved at gå ned ad en trappe" ville blive til "svært ved at gå ned ad trappen". Derefter oversatte vi disse forkortede items til dansk og vurderede dem for indholdsredundans, hvilket medførte, at det endelige antal trunkerede items blev reduceret til 157. Denne proces er beskrevet i en videnskabelig artikel og indsendt med henblik på publicering i et videnskabeligt tidsskrift.

I Studie 2 blev fokusgruppe-interviews med præ- og postoperative patienter med ACL-ruptur/ACL-rekonstruktion gennemført. Hvert item fra litteratursøgningen blev vurderet i en én efter én analyse for at fastslå indholdsrelevansen for vores målgruppe. Ud af de 157 items blev 38 items direkte anerkendt som relevante for deltagerne, 5 items blev modificerede og 12 items med nyt indhold blev bekræftet som relevante af interviewdeltagerne. Dette resulterede i sammensætningen af et 55-item testspørgeskema, som skulle felt-testes på en kohorte af de samme typer patienter. De kvalitative interviews og processen vedrørende spørgeskemaets konstruktion er beskrevet i artikel II, som er blevet indsendt med henblik på videnskabelig bedømmelse.

I det tredje studie blev 242 patienter fra Bispebjerg Hospitals database over præoperative og postoperative ACL-rekonstruktioner bedt om at udfylde det 55-item testspørgeskema udviklet i

forbindelse med Studie I og Studie II. Deltagerne bestod af tre grupper: 63 i den præoperative gruppe, 87 i den første postoperative gruppe (4 til 16 måneder efter operation), og 94 i den tredje postoperative gruppe (mindst 28 måneder efter operation). Svarene blev analyseret statistisk ved hjælp af loglinear Rasch-modellen, og 41 items fordelt over 7 skalaer fittede en både en Partial-Credit og en Grafisk Loglinear Rasch model. Disse 7 skalaer udgør det nye sygdomsspecifikke spørgeskema, der benævnes *the Knee Numeric Entity Evaluation Score – ACL (KNEES-ACL).* Manuskriptet er under udarbejdelse mhp. publicering, og bliver indsendt til *peer-review* inden den 30. juni, 2012.

4. Introduction

4.1 Who needs surgery?

What is the most effective strategy for the treatment of anterior cruciate ligament (ACL) deficiency, and what do patients with ACL-deficiency experience as the most significant problems due to their knee injury? Is ACL reconstructive surgery the best way to prevent osteoarthritis in these patients? Alternatively, is non-surgical physical therapy sufficient, or even superior? After forty years of highly sophisticated surgical techniques to reconstruct the ligament using augmentation techniques, a variety of autografts and allografts, a multitude of physical therapeutic modalities, and conflicting evidence that between 14 percent [3] and 70 percent [4] of these patients can regain pre-injury levels of function through non-surgical treatment; the evidence is still not clear.[5-7] A randomized clinical trial showed there was no difference between patients treated surgically and those treated non-surgically at two years follow-up.[8] However, these results have been questioned due to doubts as to the validity of the outcome measure.[6, 9, 10] A fundamental requirement in order to answer such questions is the use of valid outcome measures. With appropriate measurement methods, it should indeed be possible to identify which patients will most likely benefit from surgical versus non-surgical treatment, and thus which of these modalities is most efficacious for the patient with ACL deficiency.

4.2 Anterior Cruciate Ligament Deficiency

4.2.1 Mechanisms of injury

The primary function of the ACL is to restrain the forward translation of the tibia relative to the femur as well as to restrict axial rotation between these two long bones during weight bearing. Multiple mechanisms and risk factors for anterior ACL deficiency have been described and as the focus on general participation in sports has increased in modern society, the mechanisms responsible for ACL deficiency have been the subject of intense scrutiny.[11-19] The majority of lesions to the ACL are incurred during running, cutting (twisting), jumping, and landing maneuvers in connection with sports where the knee is subjected to excessive valgus and axial rotational moments near extension.[11, 20-22] While there is a distinction between *non-contact* and *contact* injuries, the vast majority of ruptures occur in conjunction with some form of contact with the ground. Thus, the *ground reaction force* (GRF) is ultimately the external force responsible for rupturing the ACL, due to increased inter-segmental valgus/rotation torques. More specifically, the lateral femoral chondyle twists and glides on the lateral tibial plateau, which creates a fulcrum between the femur and tibia that cannot be mechanically constrained by the ACL. Numerous factors increase the risk of ACL deficiency.[14, 23, 24] Extrinsic factors include weather conditions, type of contact surface, shoe type, and interactions between these factors. Intrinsic factors include anthropometric aspects (such as femoral and tibial length, increased Q-angle, and interchondylar notch width), gender, hypermobility, body mass index, hormonal, and neuromuscular mechanisms.[5, 19, 23-26]

Figure 1 shows an ACL rupture.

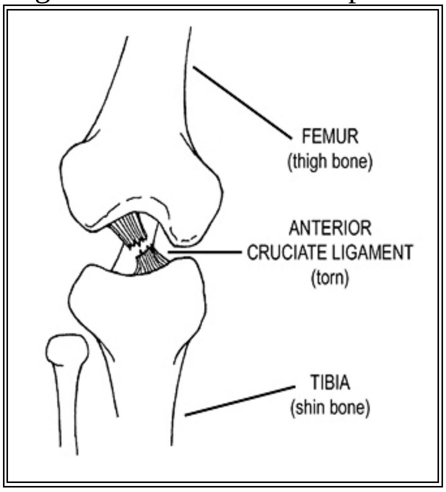
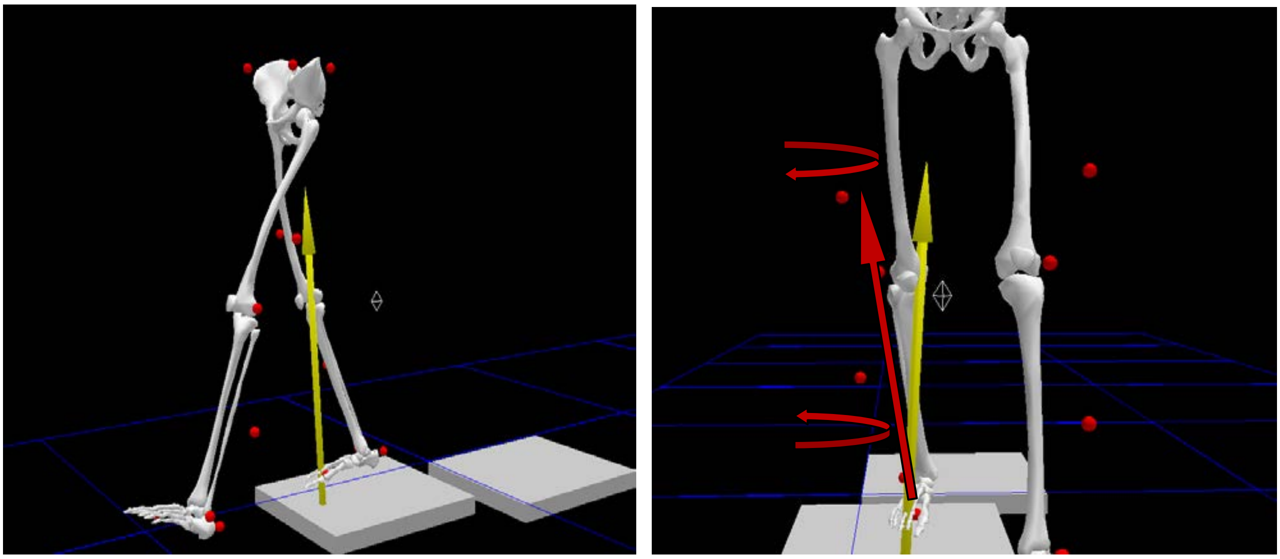


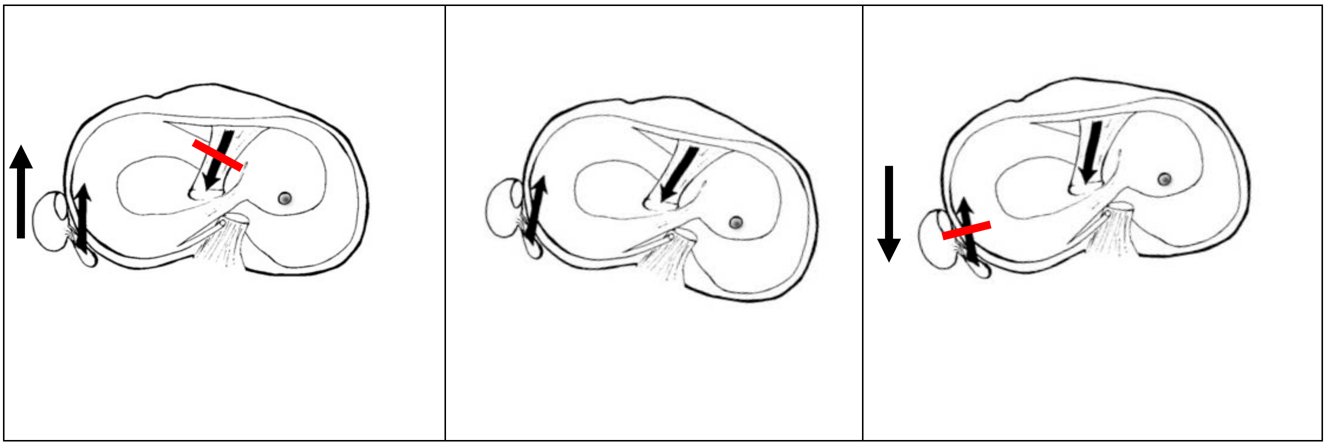
Figure 1 shows the relationship between the femur, tibia, and the ACL. Figure 2 illustrates how the longitudinal rotational axis of the knee passes through the medial compartment and the mechanisms of rotational instability. Secondary constraints to tibio-femoral excursion include capsular and neuromuscular contributions from the popliteus and hamstrings musculotendinous structures.[27, 28] Thus, the causal mechanisms contributing to functional instability are highly multifactorial, depending on anatomical, biomechanical, neuromuscular, as well as psychological input.

Figure 2.



The figures show normal GRF vectors (yellow) relative to the knee joint center of rotation. For ACL rupture to occur, the GRF will be lateral to the center of knee rotation in the coronal plane in combination with oppositely directed axial tibio-femoral rotations at near extension (red arrows).

Figure 3.



The rotation of the lateral compartment is controlled by the ACL, the popliteofibular ligaments, and the popliteus tendon. ACL deficiency results in internal tibial rotation (left). Rupture of the popliteofibular ligaments and the popliteus tendon results in external tibial rotation (right). One or both of these lesions can result in functional rotational instability and subluxation of the lateral femoral condyle on the lateral tibial plateau.[29] (Illustration from Krogsgaard, 2007)[29]

4.2.2 Incidence and socioeconomic aspects of ACL deficiency

Trauma of the ACL is one of the most common injuries to the knee joint in industrialized society.[5, 29-31] Incidence rates per 100,000 person-years are reported to be around 1200,[32] which corresponds to 1.2 percent per year. These numbers seem to be consistent in Western countries, in general.[33] Incidence rates in high-risk activities and sports, such as soccer and football, are increased by as much as a factor of ten.[34, 35] Between 3000 and 3500 ACL reconstructions are performed annually in Denmark, a country of five million inhabitants.[36, 37] The economic impact of ACL deficiency has not been determined in Denmark. However, in the United States, approximately 200,000 ACL reconstructions are performed annually, costing around $3 billion.[18] ACL deficiency is known to increase the risk of knee osteoarthritis [38-40] and is present in around twenty-three percent of these patients.[39] The prevalence of knee osteoarthritis in industrialized countries is ten percent and affects roughly thirty percent of persons aged seventy.[40-42] The socioeconomic impact (total direct and indirect costs) of osteoarthritis is estimated at 0.3% of the gross national product,[42] which corresponds annually to nearly $8 billion in Denmark.

4.2.3 Diagnosis of ACL deficiency

The diagnosis of ACL deficiency is dependent on the history of injury, clinical evaluation, and paraclinical confirmatory analyses. The patient presenting with an ACL deficiency will describe injury events, which correspond with the mechanisms touched upon in Figures 1 and 2: Buckling of the knee during directional change of motion, most often in a sporting situation, and usually with an external valgus moment imparted on the knee. The patient reports there was immediate swelling of the knee, inability to continue the activity, and possibly an “audible pop.” Depending on the acuteness of the injury, the level of activity and the degree of mechanical instability, the patient may exhibit continued swelling and giving way during weight-bearing tasks. Rotational instability is the most common cause of symptoms during functional activities.[29] A clinical diagnosis is confirmed by Lachman’s test, Anterior Drawer test, and Pivot Shift test. Lachman’s test is the Gold Standard of clinical tests with high sensitivity and specificity (eighty-five and ninety-two percent respectively). The Pivot shift test, with a sensitivity of twenty-four percent, is not adequate to reveal ACL deficiency; however with specificity of ninety-eight percent, the test combined with Lachmans is very useful.[43] Magnetic resonance imaging (MRI) can also be used to confirm diagnosis; however, sensitivity and specificity is not enhanced relative to clinical examination. MRI is clearly warranted for assessment of multiple injuries to concomitant knee structures such as meniscus or cartilage lesions.[44, 45]

4.2.4 Quantifying diagnostic efficiency - sensitivity, specificity, and predictive values

Sensitivity, specificity, and the positive and negative predictive values of diagnostic tests are important from a socioeconomic perspective. They are the foundation for choice of action, that is, whether and how to treat. The objective of diagnostic tests is to identify pathology in patients who present with symptoms that might indicate the presence of pathology (sensitivity) or exclude patients without the condition (specificity). For example, persons who might at some point have experienced a swollen knee after some traumatic event, and who test positive for having ACL deficiency, may in fact have an intact ACL (false positive), and persons with normal test results may in fact have a rupture (false negative). See table 1.

Table 1. Diagnostic tests.

	Persons with rupture	Persons without rupture	Total persons
Positive test	A (TP)	B (FP)	A + B
Negative test	C (FN)	D (TN)	C + D
Total tests	A + C	B + D	A+B+C+D

Sensitivity: A/(A+C);
Specificity: D/(B+D)
Positive predictive value (PPV): A/(A+B)
Negative predictive value (NPV): D/(C+D)
TP: True Positive finding, FP: False Positive finding
FN: False Negative finding, TN: True Negative finding

Possible outcomes of tests: “A” is the number of persons with ACL deficiency identified by the test, the true positives. In contrast, “C” is the number of persons with ACL deficiency that the test misses (i.e., the false negatives). “B” is the number of normally functioning persons with an abnormal test result, the false positives. “D” is number of normally function persons with a negative test result, the so-called true negatives.

The positive predictive value (PPV) of a test is simply the proportion of persons with a positive test who, in fact, have the condition relative to the total number of positive tests. This will depend on the particular group to which the test is being applied, as the prevalence of ACL deficiency will invariably be higher in soccer and basketball players than in a group of rowers and in the general population at large. The prevalence is the total number of persons in a population who have the condition. Thus, the PPV of the test will be significantly greater for field and indoor court sportsmen than rowers and cyclists. Conversely, the negative predictive value (NPV) is the number of individuals who in fact do not have the condition relative to the total number of negative tests. The NPV will thus decrease in groups of patients with increased prevalence, such as soccer and basketball players.

In practical terms for the clinician, these concepts can be used to assess the probability of a patient actually having a certain condition, such as ACL deficiency. Using Fagan’s Nomogram of Bayesian statistics,[46] a clinician who knows the base rate of a condition in a certain population (e.g., the incidence of ACL deficiency in female basketball players) can use the prevalence (or alternatively, the likelihood ratio in Fagan’s Nomogram)[46] to calculate the probability of the person having the condition.

4.2.5 Copers verus Non-copers

Individuals classified as having ACL deficiency have been categorized as Copers and Non-copers.[47-51] Copers achieve asymptomatic pre-injury levels of activity despite ACL deficiency and represent between 23 and 33 percent of these patients.[18, 52] The treatment for Copers is strictly non-surgical, primarily consisting of proprioceptive-, progressive resistive strengthening-, and agility exercises. Non-copers will most often receive the same non-surgical treatment regimen; however, as they experience knee instability even during basic functional tasks, this usually warrants surgical intervention.[29] The importance of the terms Copers and Non-copers becomes apparent when deciding when a diagnosis of ACL deficiency is clinically significant, that is, represents a condition, which is meaningful for the patient. Non-copers are, as the name implies, unable to cope with the condition of their knee. This indicates that they are unable to function at a level that is satisfactory for them. This fact is important to consider when applying diagnostic tests and screening for patients who may be deemed to benefit from a specific intervention, such as surgery or physical therapy, since the objective of such treatment is to ensure a satisfactory level of function. The concept of satisfactory function, and exactly what this entails, is important. As Copers function normally, one could claim that they are functionally without disease, which may imply that the concepts of ACL deficiency and Non-copers are synonymous. However, compounding the problem is the fact that there are three overlapping diagnostic constructs involved: ACL deficiency, Non-copers, and the anatomic ACL rupture. The degree to which these converge is not very clear.

4.3 Treatment Strategies for ACL Deficiency

In Denmark, the general practitioner, when treating a patient who presents with a knee injury, may choose a “wait and see” strategy, refer the patient to physical therapy, or refer the patient directly to an orthopaedic specialist. Individuals with acutely severe symptoms or patients with persisting symptoms despite physical therapy (Non-copers) are at some point referred to an orthopaedic specialist. These Non-copers receive two options in the attempt to move into the “healthy” category: Non-surgical treatment, consisting of physical therapy, or surgical reconstruction of the ACL. The decision to reconstruct or not is primarily based on the degree of functional impairment experienced by the patient and the expected or desired level of functional activity.[33, 53] Moknes et al.[4] found that in a group of patients with ACL deficiency classified as Non-copers, 70 percent of these patients could be reclassified as Copers, after an aggressive physical therapy regimen and thus were able to forego ACL reconstruction. The patients included in the study were diagnosed using *Magnetic Resonance Imaging* (MRI), had at least 3 mm anterior tibial translation in a

Lachmans test, participated regularly in high-level activities and sports, and had history of a knee injury. However, risk factors for ACL deficiency in different sports are quite heterogeneous [34] and depending on which MRI criteria are used, the sensitivity, specificity, and accuracy of MRI to confirm ACL deficiency (and thus Non-copers) are quite divergent.[44, 45]

4.3.1 Non-surgical treatment

The course of treatment after the acute knee injury in Denmark is:

- The patient is most often seen by a general practitioner (GP) or at the emergency room where the general diagnosis knee sprain is given. The patient can receive a knee brace, possibly crutches, and is instructed to apply the principles of RICE (Rest, Ice, Compression, and Elevation), and paracetamol and/or non-steroid anti-inflammatory drugs can be prescribed.

- If pain and swelling persist more than two weeks, the patient can be referred by the GP to an orthopaedic specialist for knee assessment. Diagnostic tests of ligament instability will be performed and the patient is often referred to physical therapy.

- In physical therapy, a progressive rehabilitation regimen is instigated. The objectives of rehabilitation are to manage pain, reduce swelling, re-establish normal range of motion, normalize strength and balance, and above all restore the sensation of a normally functioning knee, specifically considering the patient's habitual level of activity and goals for treatment.

4.3.2 Surgical intervention (ACL reconstruction)

Treatment intervention will consist of ACL reconstruction for patients classified as Non-copers, that is, patients with positive diagnostic test results and non-responders to physical therapy. Most often autologous graft material harvested from the patellar tendon, the quadriceps tendon, or the hamstring tendons (semitendosis-gracilis) of the patient are used, although allografts are also commonly used for multi-ligament injuries or revision surgery. Reconstruction can be anatomic or non-anatomic single or double bundle depending on surgical preferences and a number of other factors. Postoperative rehabilitation regimens vary to a degree between hospitals and between the private and public sectors in Denmark. Most patients complete a two to four month rehabilitation trajectory under the supervision of physical therapists. Accelerated rehabilitation ad modem Shelbourne is the most prevalent method of progression, where aggressive range of motion, early weight bearing, progressive resistive strengthening, and functional exercises are emphasized.[54]

4.4 Measuring Outcome in Patients with ACL Deficiency

Valid outcome measurement is paramount for assessment of treatment effect. The goal is accurate evaluation of changes in end-point variables compared with the baseline status of the patient. When looking into the effect of intervention for ACL deficiency, the success criterion must be the degree of "normalization of function" (or absence of dysfunction). Thus, the concept of function must be operationalized in order to measure the degree of success of a given intervention.

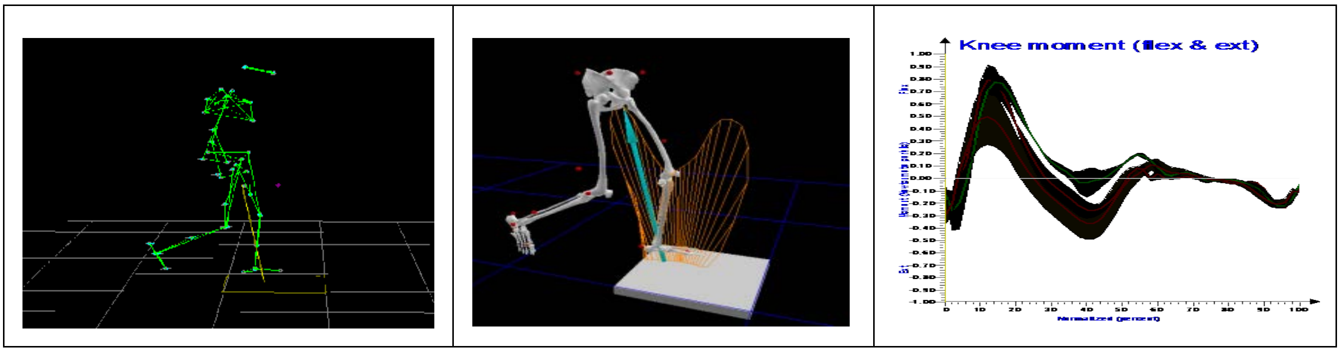
4.4.1 Physical function

General outcome assessment of ACL deficiency includes the diagnostic tests as mentioned in section 4.2.4. Typically, the physical therapist will apply a "return-to-sport" functional criterion assessment.[55] A general rule has been that if the isokinetic or isometric thigh strength, rate of force development, various balance or proprioceptive tasks, running, cutting, and hop tests for distance are at least 80 percent, as compared with the uninvolved side, then the patient is ready for re-entry into pre-injury participation in sporting activities.[22, 53, 55, 56] The cut-off ratio of 80 percent is apparently arbitrary, but seems useful for practical purposes despite recent criticism of the concept.[57] Together, these tests can help guide the patient back towards normalized function and activity level. However, the tests yield rather gross estimates of function and are non-specific in terms of objectively quantifying knee function.

4.4.2 Biomechanical measures of function

Increasingly, video-based instrumented 3-dimensional (3-D) motion capture analysis is being applied clinically to quantify biomechanical knee function and is commonly used in clinical research.[58-62] The method has been used in healthy subjects to identify loading patterns, which can place individuals at risk for ACL injury,[22, 63] and it has been suggested for clinical assessment of patients with ACL deficiency and ACL reconstruction attempting to re-enter competitive level sports activities.[22] This method makes it possible to quantify physically detailed components of knee function.[60] The technique involves placing retro-reflective markers on specific anatomical landmarks of the body. With the use of special infrared cameras, computer software, and synchronisation algorithms, the 2-dimensional coordinates of the markers are reconstructed as 3-D coordinates in space. The 3-D motion data combined with anthropometric parameters from the major body segments is used to construct a biomechanical link-segment model (Figure 3).[62] Using raw data derived from 3-D force plates and inverse dynamic equations of motion,[62] net forces and moments of force about each joint can be calculated.[47, 62, 64, 65] Advantages of the method include the extraction of parameters such as peak knee moment of force at a specific instant in time during the gait cycle, and it has been used to quantify biomechanical deficits during functional tasks in ACL deficiency patients.[47, 49-52] Non-copers and patients with ACL reconstruction were found to have diminished peak knee flexion and significantly reduced extension moments during gait.[49, 66] Inverse dynamic analysis of forward lunge has also revealed temporal and kinetic differences between Copers and Non-copers.[47] These methods are promising; however, there are some drawbacks in relation to the clinical setting. The equipment is costly. Time-consuming aspects include placement of the retro-reflective markers, the acquisition of motion capture data, and the treatment and analysis of the data. Furthermore, there is a degree of kinematic artefact due to marker movement, depending on the type of functional activity that is recorded, as well as considerations concerning biomechanical modelling algorithms and tri-planar axes of joint rotation.[67-70] However, the method does yield quantitative data of functional activities and substantial advances have been made to rectify some of the above-mentioned disadvantages.[69, 70]

Figure 3.



Three-dimensional biomechanical analysis of functional tasks can quantify functional anomalies. The figure to the left shows the 3-D link segment model and the curves to the right are internal knee moments.

4.4.3 Patient-related outcome (PRO)

While physical and biomechanical measures of outcome can help quantify a patient's level of function from the perspective of the clinician, they do not take into consideration how patients experience, feel, and interpret their own level of functional capacity, or success of the treatment. PRO questionnaires have become an integral component of functional evaluation to determine the effects of surgical intervention, and PROs have attained a level of importance comparable to physical examination.[71] Most PROs are reported to have been validated in some manner,[72, 73] which implies that they can quantify the degree of functional change. Numerous PROs have been developed to evaluate health outcome from the perspective of the patient for a variety of conditions.[73] Some instruments combine individual question-response scores to produce a single over-all index (a sum score), while others yield multiple sub-scores for separate functional domains.[74] Comparisons of different scoring instruments reveal discrepancies in how each self-assessed parameter is reflected in the score.[75-80]

PRO questionnaires can be defined as "any report coming directly from subjects without interpretation of the physician or others about how they function overall or feel in relation to a condition and its therapy."[81] Thus, PROs address the patient's own perception of function, treatment satisfaction, and other aspects deemed relevant by the patient in relation to a certain condition.[82-84] PRO data are most often collected via standardized questionnaires designed to assess underlying constructs not directly measurable, such as pain (or other symptoms), or the ability to carry out functional tasks. Such underlying constructs are referred to in psychometric theory as *latent traits* or *latent variables*. Individual items (an item is a question and its response categories) are grouped into one or more domains, depending on the concept they represent. Table 2 exemplifies items and their response options in a small hypothetical activity scale. A scale in this context is defined as the sum of at least two item-response scores. The item statement is the qualitative content or theme of the item and the response options are the categorical choices representing the endorsement of the item theme. Items with dichotomous response options, such as "Agree/Disagree" or Yes/No", address only whether the item is endorsed or not. If the item has a polytomous response structure as seen in Table 2, then the amount of that endorsement is also addressed. Each option represents a number (e.g., "Not at all" is scored as 0, "A bit" as 1, and so on). This item-response score signifies the amount of item content the person possesses. These response scores are added together and the summary score represents the level of activity for the person who completes the questionnaire. Conceptually, this is the basis of what is known as a *total score* or *sum score*. Thus, the range of possible sum scores in the scale in Table 2 is zero through nine, that is, from least to most functionally impaired.

Table 2.

Item statement	Response options			
	Not at all	A bit	Quite a bit	A lot
1. I have difficulty walking.	☐	☐	☐	☐
2. I have difficulty running.	☐	☐	☐	☐
3. I have difficulty jumping.	☐	☐	☐	☐

A hypothetical 3-item activity scale as an example of a PRO

4.4.4 PROs versus "surrogate" measures

The current rise in popularity of PROs in the health sciences may be attributed to the American Food and Drug Administration (FDA), which emphasizes the use of PROs stating that "physical examination and performance testing is not sufficient to measure what may be most important from the patients perspective."[85] Editor in Chief of the British Medical Journal, Fiona Godlee, expresses that endpoints stemming from the patient, such as visual impairments or quality of life, are "hard outcomes that matter to the patient" and should be prioritized over "surrogate end-points", such as biomarkers. Surrogates will often show much larger and faster responses to treatment and thus are preferred by the biomedical industry.[86] Clinical and surrogate measures are important to confirm diagnoses and establish treatment strategies. However, the most clinically relevant outcomes must be those, which address the patient's perceived response to the condition or the treatment. The clinician can record an objectively perfect result; however, in order to utilize this positive outcome, the patient must endorse the perceived result. Thomée and colleagues [57] stress that despite achieving acceptable levels of physical function as dictated by common return-to-sport criteria, many athletes never reach the goal of actually returning to sport. The authors argue that patient-reported themes such as fear of re-injury should be specifically emphasized, and that physical measures are insufficient to address the demands of high-level activity. Furthermore, physical performance measures do not necessarily correlate well with PROs, as has been demonstrated in numerous studies.[53, 87-89] For example, a recent study compared various hop tests with the *International Knee Documentation Committee* (IKDC) and the *Knee-injury and Osteoarthritis Outcome Score* (KOOS) questionnaires and found low associations in three of the five subscales of KOOS.[90] Interestingly, these same subscales were found to lack unidimensionality in a Rasch model (see section 4.6.12 for more on Rasch analysis) when applied to patients 4-6 months after ACL reconstruction.[2] Conversely, Fuchs et al. found significant correlations between the *Knee Society Score* and sagittal plane knee range of motion and coronal plane knee moments derived from inverse dynamics,[91] and Grindem et al. recorded that a single hop test significantly predicted self-reported knee function in patients with ACL deficiency.[92] A methodologically strong study by Mizner et al. comparing physical performance test outcomes with widely used patient-related measures found that the outcome results did not reflect each other after total knee replacement.[93]

4.5 Measuring Outcome in Danish Patients with ACL Deficiency

4.5.1 Physical performance assessment

The Danish National Registry for Cruciate Ligament Injury has stipulated that certain tests should be used to measure outcome in ACL reconstruction. As a routine protocol at the Copenhagen University Hospital – Bispebjerg, patients scheduled for ACL reconstruction complete a series of tests to assess physical performance pre- and postoperatively. These tests include single-leg hop tests for distance, instrumented thigh strength, measure of thigh girth, and other balance–related measures. The tests are well defined, widely used worldwide, and are considered a gold standard.[51, 53, 94-97] One advantage with physical tests is that they are convenient to perform and standardize, and the data are easy to acquire, process, and tabulate. They are also easily understood by the patient. The downside is that the resultant score does not necessarily reflect the spectrum of relevant outcome from the perspective of the patient.[81]

4.5.2 PRO assessment

The Danish ACL registry requires that all hospitals and private clinics in Denmark, where ACL reconstructive surgery is performed, report the results of the *Tegner Activity Scale* and the KOOS questionnaire preoperatively and at 1, 5, and 10 years post-surgery.[98] Prior to 2008, physical therapists at Bispebjerg were manually responsible for the administration and scoring of these PROs. A common occurrence among physical therapists at Bispebjerg Hospital was that patients complained of not understanding the content of certain questions, for example, in KOOS, or patients could be confused as to which response option to choose.[2]

4.5.3 Ambiguous items

Responses to items are more likely to yield spurious reflections of the patient's condition when the respondents are confused by the item content.[83, 99-102] An example of an item patients with ACL deficiency found difficult to complete in KOOS was: "Do you feel grinding, hear clicking or any other type of noise when your knee moves?" The response options are "Never", "Rarely", "Sometimes", "Often", and "Always". What is the correct response if the patient experiences clicking but not grinding, or other noises, but not clicking? There is only one response option available to answer the question. Items of this type are referred to as *double-barreled* or *ambiguous items* and should be avoided, or at least rephrased and/or split into separate items in the questionnaire development phase.[2, 102] Physical therapists at Bispebjerg were instructed to tell the patient to complete the response that "fits best" when the patient was ambivalent as to an item. Another problematic item in KOOS was "Can you straighten your knee fully?" with the same five response categories as above. Patients responded often that they either could or could not straighten the knee fully, so they had difficulty choosing the appropriate response category. Intuitively, these items should be dealt with in a qualitative manner to ease their use for the specific patients they are intended for, particularly because they are an integral part of a measurement tool. However, the ambivalence patients experience when responding to such ambiguous items is also quantitatively detectable using certain statistical methods.[103, 104]

4.5.4 Analysis of problem items

A closer look at the origin of KOOS can explain why such items were included in the instrument. From its inception, KOOS was designed to measure patient-related function in individuals with an acute knee injury as well as patients with degenerative knee disease.[105] This was in order to capture functional deficits in the acute phase of injury and to track the progression of functional problems in patients with chronic development of osteoarthritis of the knee. The strategy for creating KOOS involved the inclusion of the entire 33-item *Western Ontario and McMasters Osteoarthritis Index* (WOMAC)[3] and the addition of nine new items, which addressed issues pertaining to sport/recreational activities and quality of life. Thus, KOOS is a generic instrument generated from items targeting chronic degenerative osteoarthritis, acute injury, and multiple joints. An investigation into the psychometric properties of KOOS revealed that three of the five proposed scales in the instrument did not fulfill the requirements of a measurement scale.[2] The study showed that the WOMAC subscales of *Knee Symptoms, Pain,* and *Activities of Daily Living* were not appropriate measurement constructs for patients who were 20 weeks post ACL reconstruction. Table 3 shows the results of the overall fit to the partial-credit Rasch model for polytomous items as described in Comins et al. (2008).[2] The asterisks demarcate the WOMAC domains. The concepts in Table 3 are explained more thoroughly in section 4.7 of this thesis.

Table 3.

Dimensions (Number of items)	WP-χ^2	DF	*p*	PSI	α
Knee Symptoms (7)	24.65	14	0.038*	0.70	0.63
Pain (9)	36.11	18	0.007*	0.81	0.80
ADL (17)	67.16	34	0.001*	0.87	0.91
Sport/Rec (5)	9.17	10	0.516	0.81	0.80
QoL (4)	2.91	8	0.940	0.75	0.75

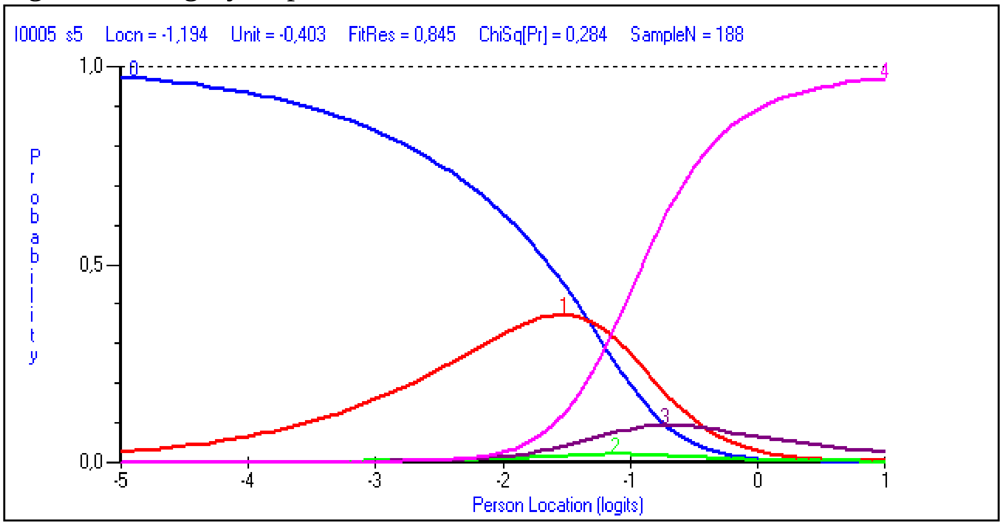
Wright-Panchapakesan (WP) fit statistics, Person Separation Index, and the Cronbach's alpha of five dimensions in the KOOS.[2] The asterisk* indicates significant chi-square misfit.

Rasch analysis revealed that the ambiguous items for patients in the clinical setting were also statistically problematic. For example, the response options of "Sometimes" and "Rarely" in the item: "Can you straighten your knee fully?" were found to be insufficient for patients with ACL reconstruction (see Figure 4). These are the two flattened-out curves at the bottom of the graph. Furthermore, the response category "Often" (the red curve "1" in Figure 4) was qualitatively

[3] The WOMAC is one of the most widely used questionnaires for assessment of osteoarthritis of the knee and hip joints.[106]

problematic, for how "often" can a person be expected to be able to straighten the knee "fully?" Full extension would most expectedly be either possible or not possible for ACL deficient individuals, and therefore a question of this type might be more appropriate if the response options were "Yes" and "No."

Figure 4. Category response curves of an item.



Category Probability Curves of item S5 "Can you bend your knee fully?" The scale from -4 to +1 symbolises the latent trait of knee symptoms, with the severity of symptoms increasing towards the right. Response categories: 0 "Always", 1 "Often", 2 "Sometimes", 3 "Rarely" and 4 "Never".

4.6 Constructing PRO Questionnaires

Many aspects must be considered when developing questionnaires for use as measurement scales.[100] Most importantly, the specific patient group targeted for assessment and the specific condition to be measured must be thoroughly contemplated.

4.6.1 Condition-specific versus generic questionnaires

PROs can be developed to address specific conditions, or more general health concerns, so-called *condition-specific* and *generic* questionnaires.[107] Proponents of generic PROs cite the fact that they are reported to have well-established validity and, therefore, often are used as criterion measures for validation of new instruments.[108] Moreover, they are promoted as a means of comparing the impact of disease and treatment across populations, or to compare acquired patient data with normative values.[100] However, this practice has been criticized, as the use of generic questionnaires for cross-disease comparisons is scientifically questionable because items can have different meanings in different patient groups.[100, 109] Furthermore, a number of studies show that the results are inconsistent when such scales are applied across patient populations.[2, 110-112] Generic

PROs are not designed to capture issues of concern for the specific patient groups and, thus, are more likely to inquire about irrelevant themes. This can increase the likelihood of respondent alienation and missing data, particularly in more severely affected patients.[2, 113, 114]

PRO questionnaires developed for generic applications are often used in condition-specific studies. Such instruments as the Short Form 36 (SF-36)[115] and the EuroQoL (Eq-5D)[116] can be used in any number of ways. Pitfalls associated with the application of generic PROs have led to an increase in the development and use of condition-specific questionnaires.[100, 101, 117-119] Condition-specific PROs are developed to assess aspects of outcome that are important for specific patient populations. Condition-specificity entails qualitatively deriving the content of items directly from the targeted patient populations (see section 4.5.6). Condition-specific PROs have the advantage that they provide more detailed information than generic questionnaires and are thus more likely to be sensitive to disease- or treatment-specific effects.[100, 119]

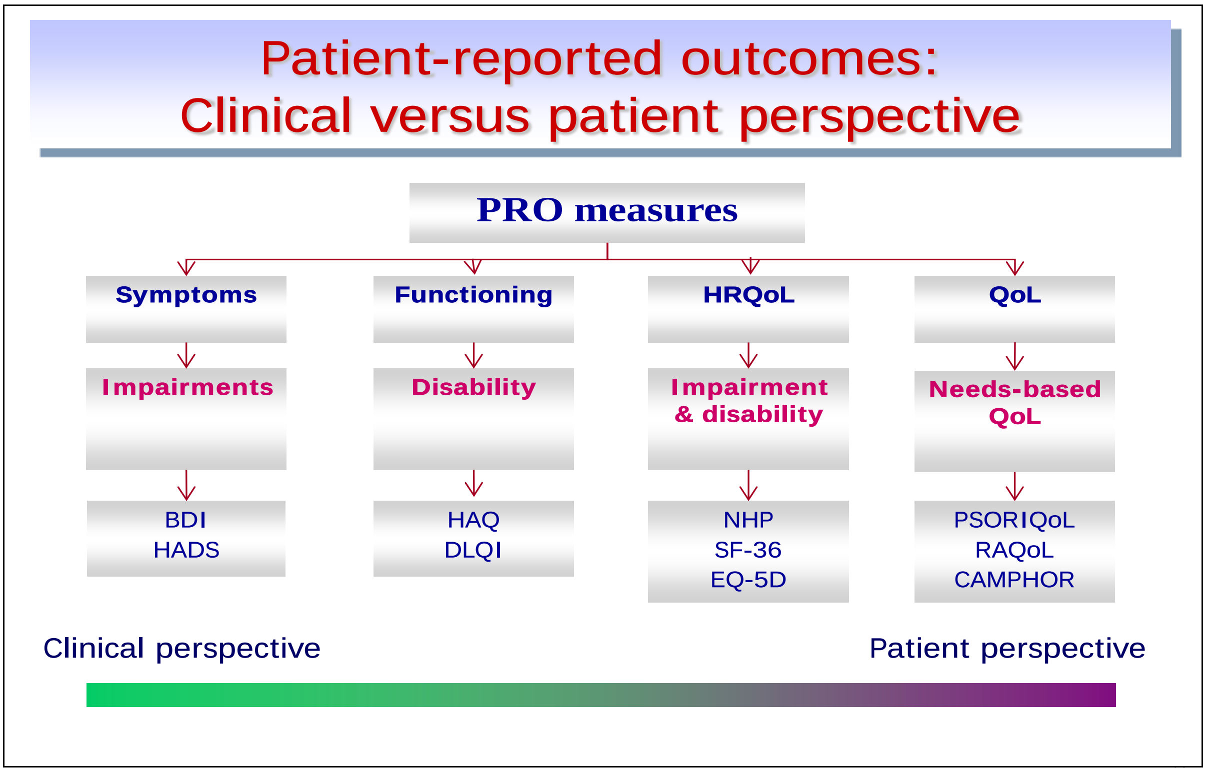
4.6.2 Assembling the questionnaire

Depending on which constructs are deemed relevant, a theoretical model to address the appropriate item content in relation to the targeted patient population must be chosen in order to establish a viable frame of reference to achieve measurement. A myriad of PROs exist for different types of clinical assessment. The most common constructs are measures of:

- Impairment (symptoms)
- Activity limitations (functioning)
- Participation restrictions
- Health status / Health-related Quality of Life (HRQL)
- Quality of Life
- Treatment satisfaction

The constructs of impairments (symptoms), activity (limitations) and participation (restrictions) have been clearly defined in the International Classification of Functioning, Disability and Health (ICF; WHO, 2001) and are widely accepted. These constructs are particularly relevant for PROs used in clinical research, where measures targeting bodily function, activity level, and participation in life’s situations are particularly useful. Figure 5 shows the continuum between at the one end clinically related conditions, where patients with musculoskeletal pathology such as ACL deficiency are more appropriately targeted within the ICF categorizations (Impairment, Activity, and Participation). At the other end of the spectrum, the Needs-based model may be better suited to address constructs such as Quality of Life or satisfaction with life’s general conditions, for example, in connection with life-threatening diseases.

Figure 5.



Conceptual model of function and disability (with permission from Brodersen)[100]

4.6.3 *Item content generation*

Item content must be generated once the frame of reference and the model have been established. There are essentially two sources of item content: a) the clinician (or clinical expert), and b) the patient.

4.6.4 *Face validity*

Item content derived from the clinical expert will according to Mosier[120, 121] possess *face validity*, in that the instrument will be "considered to be valid, if the sample of items appears to the subject matter experts to represent adequately the total universe of appropriate test questions." This item content can be derived through individual- and focus group- interviews of clinicians or from assembling items from existing PROs created and used by clinical experts.[100, 122-125] The main purpose of collecting item content from the perspective of the clinician is to identify possibly relevant constructs for the patient, based on the fact that the clinical expert has extensive diagnostic and treatment experience relative to the particular patient group.

4.6.5 *Content validity*

Content derived from the clinician may or may not be relevant for the patient. There is only one method to confirm content relevance, and that is through direct patient confrontation.[84, 100, 118, 126] Thus, after item generation from the clinician, the next step is to confront the specific patient groups with the assembled items and ascertain which items can be endorsed in order to ensure well-functioning items that will be perceived as relevant and comprehendible by the target group.[100, 126] This can be accomplished in single or focus group interviews where content relevance and content coverage can be assessed. Content relevance is addressed through item endorsement. Content coverage, also termed comprehensiveness, addresses the emergence of new items, themes, and constructs that were not previously identified by, say, previous analysis of pre-existing instruments. In practical terms, this really involves the assessment of the saturation of themes patients find relevant, where verbatim comments from the participants can be used to define any new themes and constructs that may emerge.[100, 127, 128] Content relevance and content coverage are the cornerstones of content validity.[83, 102] Confirmation of which items to include in which groups of items is also instrumental in the establishment of relevant condition-specific constructs. Furthermore, item reduction based on feedback from the patients is critical in to order confirm that item content considered directly irrelevant by the particular patient group is discarded. Finally, in order to ensure valid responses to items, the questions must be worded such that they are easily understood by all potential respondents, regardless of age, socio-demographic background, or other personal factors, and appropriate response categories must be established. This can be attained within focus groups and through field-testing in follow-up single interviews.[100, 102, 118, 129]

4.6.6 *Construct validity*

The last step in creating a valid questionnaire for measurement is to establish the psychometric properties of the instrument. A scale can be defined as the operationalization of magnitudes to construct a variable: “When a variable has been constructed, magnitudes of the properties in entities, which are restricted to persons in this volume, can be measured” (Andrich p. 9)[130] These entities are the items derived from qualitative processes, such as those described above. However, it cannot be assumed that items numerically quantify anything of importance to the persons being measured, without an assessment of the dimensionality of the scale/measure; that is, the degree to which the sum-score actually reflects the level of a person’s ability. Denny Borsboom questions whether the scores are “no more than relatively arbitrary summations of item responses” (Borsboom p. 2).[131]

Scale validation is an immense topic in measurement theory, and there are myriad ways of interpreting, describing, and establishing the validity of measures, depending of course on the objective of the measurement. Samuel Messick contends that the concept of construct validity engulfs all aspects of criterion, concurrent, and in fact all aspects of validity: "The essence of unified validity is that the appropriateness, meaningfulness, and usefulness of score-based inferences are inseparable and that the unifying force behind this integration is the trustworthiness of empirically grounded score interpretation, that is, construct validity."[132] Denny Borsboom goes on to say that validity is not at all complex; the instrument is valid if it measures what it purports to measure: "… a test is valid for measuring an attribute if and only if a) the attribute exists, and b) variations in the attribute *causally* produce variations in the outcomes of the measurement procedure." [Italics added] (p. 150)[131] He writes further:

> Somewhere in the chain of events that occur between item administration and item response, the measured attribute must play *a causal role in determining what value the measurements outcomes will take; otherwise, the test cannot be valid for measuring the attribute.* Importantly, this implies that the problem of validity cannot be solved by psychometric techniques or models alone. On the contrary, it must be addressed by *substantive theory*. Validity is the one problem in testing that psychology cannot contract out to methodology [emphasis added]. (Borsboom, p. 151)[131]

Substantive theory might for example be biomechanical or physical corroboration of PROs used to address musculoskeletal pathologies in case-specific populations.

4.7 Classical Test Theory versus Item Response Theory

In questionnaire development, there are essentially two schools of thought: Traditional methods, known as Classical Test Theory (CTT), and modern test methods known as latent-trait theory or item-response theory (IRT).[133, 134] Conventionally, when CTT methods are used to assess dimensionality, methods such as exploratory factor analysis, correlation, and Cronbachs alpha are employed.[135] Modern test theorists maintain that these methods are insufficient for establishing dimensionality and reliability in data with a categorical response structure.[104, 133, 136-141] However, once the dimensionality of the variable can be established, confirmatory CTT techniques are warranted and commonly used, for example, in conjunction with assessment of interactions between items, and between person factors and items.[142] (See also section 4.5.15 on sources of misfit).

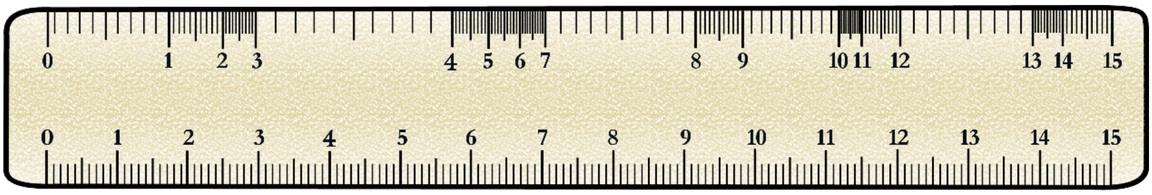
4.7.1 Validating scales with Classical Test Theory and the total score

When questionnaires are validated using CTT, the item-response scores are summed into a total score, which then is used for comparisons and calculations in parametric statistical tests, such as T-tests, Analysis of Variance, and Cronbach's alpha. Parametric techniques assume parametric data structure, which means continuous interval level data, normal distribution of data, relatively homogenous variance in the groups being compared (homogeneity), and equal variance of the residuals (homoscedasticity). At the most basic level, this means that the entities of measurement consist of numeric values that can be added, subtracted, multiplied, and divided as equally weighted units and that the properties represented by these numbers are equal in type and magnitude.[130] Thus, the summary or total score of these numeric entities represents the amount of whatever is being measured. When trying to capture non-physical latent traits, this will always be "more" or "less" of a construct or attribute, such as happiness or pain.[104, 130, 143, 144] As an example, one can consider a situation where ten patients complete a ten-item activity questionnaire. As in Figure 4, the items are polytomous with five response categories, which can be scored from zero to four (i.e., 0, 1, 2, 3, and 4). This means that for ten items the maximal score for a person can be forty. If, say, two persons have a score of twenty-six, this would imply that the persons are equally affected in terms of the latent trait (i.e., they have the same activity levels). However, this assumes that all the items exhibit the same quantity of the underlying construct being measured. One person may have answered three on six items and two on the remaining items. The other person might have responded with a score of three on six other items, four on one item, and two on the last two items. Both combinations add up to twenty-six; however, if the questionnaire consists of items concerning activities such as walking on level ground, stair climbing, and running, then the degree of difficulty associated with the different tasks must of course vary. One person may have scored higher on the most demanding activities, yet both persons appear equally active. In this case, the total score can be misleading because it is based solely on the number of confirmed items and not which items are endorsed. A total score in CTT does not take into consideration which items are more or less difficult or which persons have more or less ability.

Another weakness of CTT is that techniques such as exploratory factor analysis are sometimes used to assess dimensionality for the purpose of item reduction. For example, items that do not load on the first principle component (e.g., eigenvalue less than one)[145, 146] may indicate that the item does not belong to the dimension, and thus might be discarded regardless of content.[108, 147-149] This *data-driven* item reduction method can be problematic in that there must have been a reason for the item being present in the item pool in the first place, and correspondingly, there should be a solid qualitative reason for removal of the item. Good *theory-driven* item generation and item reduction should also include qualitative assessment of the content of all items going in and out of an instrument.[100, 127, 128]

Yet another issue with CTT is that the ordinal item-response structure does not fulfill the assumption of continuous interval data, which in itself warrants the use of other analytic models.[150] The scale must be stable in order to yield valid and repeatable measurement, regardless of which person is being measured, and which part of the scale is being used (the easier or the harder end of the scale or the easier or more difficult items). This means simply that the scale must be *invariant* relative to that which is being measured. Fundamentally, this requires equidistant measurement points along the entire scale.[151, 152] The ruler in Figure 6 illustrates the difference between an ordinal and an interval ruler (scale). Measuring objects with the ordinal edge of the ruler using the CTT paradigm obviously leads to mixed results, in that, the measurements will differ depending on which part of the ruler is applied.

Figure 6. (Illustration from John Brodersen)[153]



Ordinal

Interval

Ordinal versus interval scale

4.7.2 Validating scales with Item-Response Theory

As CTT methods are not equipped to handle categorical/ordinal data, a solution is to use item-response theory (IRT).[103, 104, 152, 154] Whereas, CTT emphasizes only item parameters (e.g., the summary score of items), the focus in IRT models ”is on item and person parameters, which are non-linear transformations of raw scores, and on variances of these estimates”(Andrich, 1988).[130, 155] Thus, in IRT models, both the item and the person scores are manifested as a single value on the same latent variable. Intuitively, this makes sense, also in terms of the fact that it is the person’s ability that is the object of measurement, and not just the difficulty of the test.[155]

4.7.3 Fundamental measurement and Questionnaires

In the physical sciences, fundamental measurement entails a so-called “2-way frame of reference” (Andrich p. 17).[130] For example, to measure the weight of an object, a force must be applied. The measured mass of the object (the output) is an expression of the interaction between the object and the force (an agent) acting on it. Likewise, for measurement to take place using latent variables, a similar 2-way frame of reference must be established.[130, 152] The target population must be clearly identified, that is, patients with a specific pathological condition to be measured (e.g., ACL deficiency). The patients correspond to the objects to be measured. Then, the relevant scale(s) used to measure the objects must be constructed (e.g., Symptoms, Range of Motion, or Activity). This is analogous to the force when measuring a mass.

4.7.4 The Guttman Scale and Unidimensionality

People can be characterized by multiple properties; however, in order to construct a latent variable for measurement, the variable must be identified and mapped on a single real number line. This is known as a *unidimensional* construct (Andrich p. 9).[130] Unidimensionality implies that comparisons in differences of degree (and not just kind) can be made. Unidimensionality is the basis of IRT and can be explained in terms of Guttman scaling. A Guttman scale is considered the ideal in measurement theory.[104, 156] If a scale exhibits a Guttman pattern, then the scale will be unidimensional (NOTE: This is an ideal that does not occur in reality; however, the closer, the better.). A Guttman pattern is illustrated in Figure 7. The table shows ten hypothetical persons with ACL deficiency who might be asked to complete a questionnaire on the occurrence of pain when participating in different activities. For simplicity, the response options are scored dichotomously: “0” for no pain, and “1” for pain during the activity. The persons are represented by letters (rows), and the items addressing different activities are represented by numbers (columns). The pattern observed shows an example of a perfect Guttman structure in a 2-way frame of reference. Person A experienced pain in only one item and is the least affected person. Item J is the least pain-provoking item, with only one person affirming the item. This pattern is rather convenient, for the persons and items are all lined up across from each other. However, which patients were most (and least) affected was unknown before applying the questionnaire, and which activity was most and least pain provoking for the patients was unknown. Therefore, in reality, the data would not line up as neatly as is the case in Figure 7. In Figure 8, the scores do not follow any pattern – or do they? As mentioned, *a priori*, it was not known which patient would affirm most items or which item would be affirmed by most patients. However, if the persons and items are reordered from highest to lowest according to the number of items affirmed, and the number of persons who affirmed the items, the pattern in Figure 8 is transformed to the pattern in Figure 9. In Figure 9, it becomes apparent that person I (blue) has affirmed all items and was most affected, person H affirmed only one item and thus was least affected.

Figure 7.

Persons	Items 1	2	3	4	5	6	7	8	9	10
A	1	0	0	0	0	0	0	0	0	0
B	1	1	0	0	0	0	0	0	0	0
C	1	1	1	0	0	0	0	0	0	0
D	1	1	1	1	0	0	0	0	0	0
E	1	1	1	1	1	0	0	0	0	0
F	1	1	1	1	1	1	0	0	0	0
G	1	1	1	1	1	1	1	0	0	0
H	1	1	1	1	1	1	1	1	0	0
I	1	1	1	1	1	1	1	1	1	0
J	1	1	1	1	1	1	1	1	1	1

A Guttman pattern (Brodersen 2006)[153]

Figure 8.

Persons	Items 1	2	3	4	5	6	7	8	9	10
A	1	1	1	1	1	1	1	0	0	1
B	1	1	1	1	1	1	1	1	1	0
C	0	1	0	1	0	0	0	0	0	0
D	1	1	1	1	0	1	0	0	0	0
E	1	1	0	0	1	0	0	0	0	0
F	0	1	1	1	1	1	1	0	0	0
G	1	1	1	1	1	1	0	0	0	1
H	0	1	0	0	0	0	0	0	0	0
I	1	1	1	1	1	1	1	1	1	1
J	0	1	0	0	1	1	0	0	0	0

A more realistic pattern (Brodersen 2006)[153]

Thus, item two in Figure 9 (red), which was affirmed by all persons, is the most pain-provoking item. The yellow responses are those, which deviate from the expected response, as compared to the expected Guttman scale as in Figure 7. It is apparent that some patients have responded in an unexpected manner to certain items when considering the level of difficulty of the item relative to

Figure 9.

Persons	Items: 2	5	4	6	1	3	10	9	7	8
H	1	0	0	0	0	0	0	0	0	0
C	1	0	1	0	0	0	0	0	0	0
J	1	1	0	1	0	0	0	0	0	0
E	1	1	0	1	1	0	0	0	0	0
D	1	0	1	1	1	1	0	0	0	0
F	1	1	1	1	0	1	0	0	1	0
G	1	1	1	1	1	1	1	0	0	0
A	1	1	1	1	1	1	1	0	1	0
B	1	1	1	1	1	1	0	1	1	1
I	1	1	1	1	1	1	1	1	1	1

A probabilistic Guttman pattern (Brodersen 2006)[153]

all the other items, and considering the person's ability relative to all the other persons completing the questionnaire. For example, person D did not affirm item five, despite the fact that item five provoked pain in seven other persons and was the second most pain-provoking item. Conversely, person D was provoked by item three, which is clearly less pain provoking than item five. This pattern is reflective of what actually happens in real life. Sometimes observed responses are not as expected. There is a discrepancy between the observed and the expected response. IRT models allow this type of probabilistic imperfect response pattern as seen in the yellow-green zone of Figure 9. Another way to visualize this probabilistic relationship can be seen in Figure 10. The likelihood of affirming the item, (score of 1), decreases as the likelihood of not affirming the item increases (score of 0). For the pain scale, this means that as the zero increases, the probability of being affected (having pain) gets smaller.[153]

Figure 10.

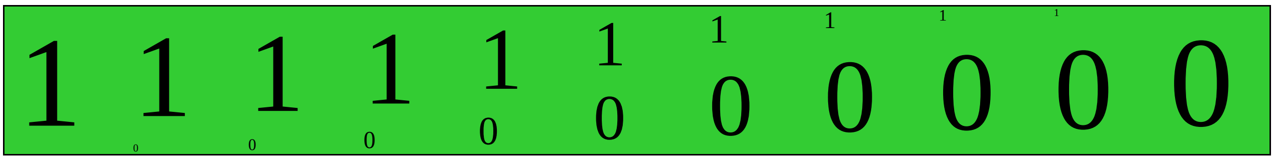


Figure 10 shows the probability of one response being replaced by another. (Brodersen 2006)[153]

4.7.5 The Rasch model

The Rasch model is a probabilistic item-response function, [152] where the dichotomous model is simplest to explain in practical terms.

The dichotomous Rasch model is:

$$p(\beta) = \frac{e^{(\beta - \delta)}}{1 + e^{(\beta - \delta)}} \qquad (1)$$

As can be seen in formula (1), the Rasch model is a logistic function, which states simply that the probability "p" of a person with the ability "β" to affirm an item with a level of difficulty "δ", is a function of the natural log of the difference between these two parameters.[130, 152, 157]

This means that when the parameter estimate of the item difficulty (δ) is equal to the parameter estimate of the person's ability (β), there will be a 50/50 chance of affirming the item, because β – δ will then be zero, and e^0 is equal to one. Thus, by substituting $e^{(\beta - \delta)}$ with e^0 in formula (1), the probability becomes ½. When the item parameter (δ) is greater than the person ability parameter (β), the likelihood of affirming goes from 0.5 towards zero (the probability decreases). Conversely, if β is greater than δ, the probability increases from 0.5 towards one. As the Rasch model calculates the probability of a given response, it does not make distributional assumptions. The importance of this becomes apparent when considering the purpose of questionnaires. Items in a questionnaire are meant to measure the ability of the person responding to the questions, such that the set of items constitutes the scale (agent) used to quantify the person's (object) ability in a 2-way frame of reference.

Possibly the best analogy to explain the concept of the Rasch model is to consider high jumpers of different abilities attempting to jump over a bar set at different heights.[158] The probability that a jumper will clear the bar depends on the ability of the jumper and the height of the bar. The height at which the jumper clears the bar on every other attempt, fifty-percent likelihood, is that particular jumper's level of ability. The height of the bar is of course the level of difficulty of the task (item). Note that in this context, the bar height is assumed to be a unidimensional construct; the higher the bar, the more difficult the objective.

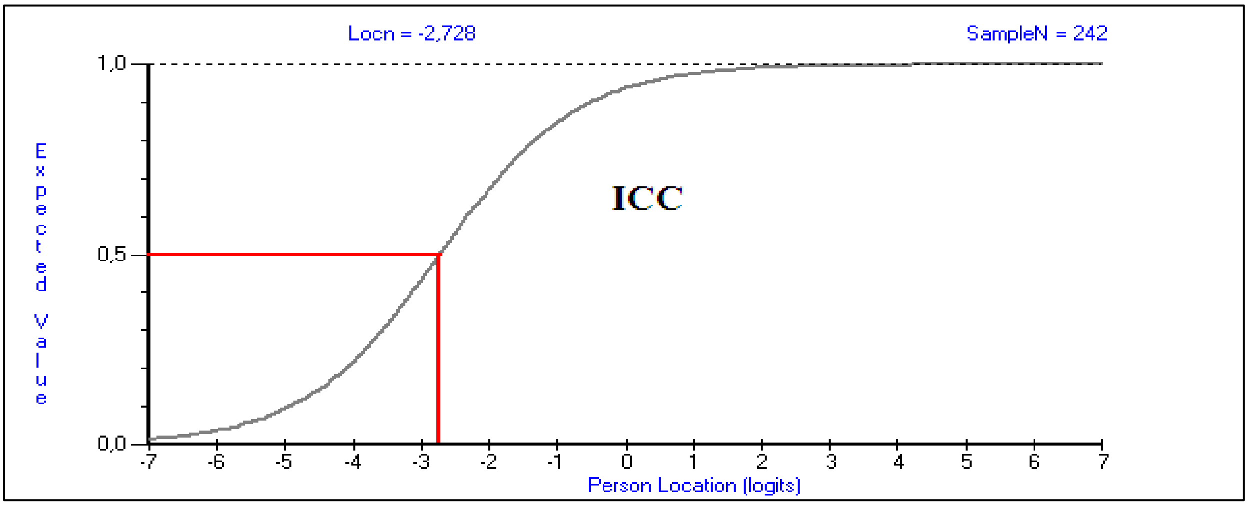
4.7.6 Item characteristic curve (ICC)

This probability of "clearing the bar" can be rendered as an *item characteristic curve* (ICC) [130, 159] (not to be confused with intra-class correlation coefficients), which is a graphical expression of the Rasch model in equation (1). Thus, the ICC predicts that as a person's ability increases on the latent variable (x-axis), so will the probability that the person will affirm the item (y-axis). Figure 11 exhibits an example of an ICC. The point of inflection of the curve as it is projected onto the latent scale (x-axis) is known as the *item threshold.* This is the point at which a person has a fifty percent likelihood of affirming or not affirming the item (red line). The item threshold is considered the item's level of difficulty, as each item will have a different location along the latent variable. The Rasch model calculates the ICC as the expected value of an item based on the way all persons have responded to all items and the way in which all items have been responded to by all persons. Note that the ICC is the ideal curve, if the data were to fit a Guttman structure.[130, 159] The item in Figure 11 has a threshold of -2.728 on the latent scale. Hence, persons with this ability will have a fifty percent likelihood of affirming or not affirming the item. The result can go either way. Persons with a higher ability than -2.728 will have an increased likelihood to affirm the item, and persons under -2.728 will have a decreased likelihood to affirm the item.

4.7.7 Model misfit

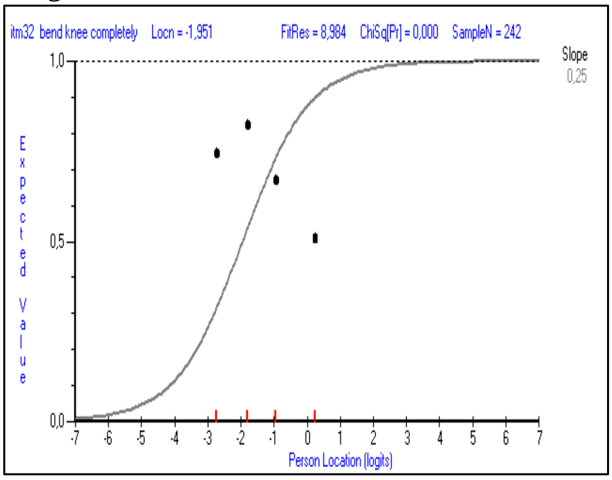
The values of the observed data are plotted and compared with the expected values as generated by the model. Various approaches are used to assess the degree of fit to the Rasch model, although they all employ a likelihood ratio test, which produces a Chi-square statistic.[158, 160-162]

Figure 11.



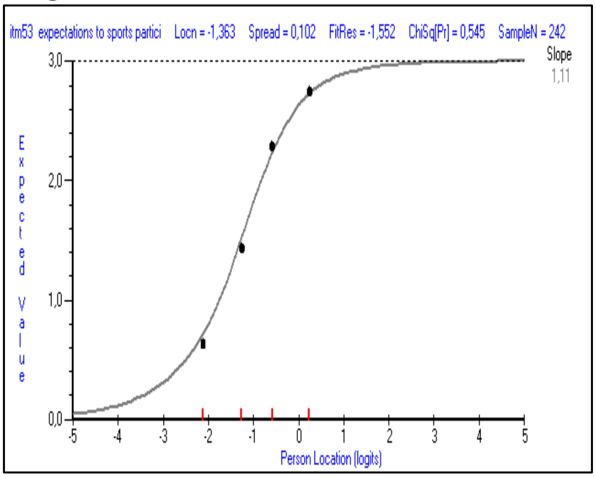
The Item Characteristic Curve: The item threshold (red line) is the point of inflection.

Figure 12A



Misfit to model

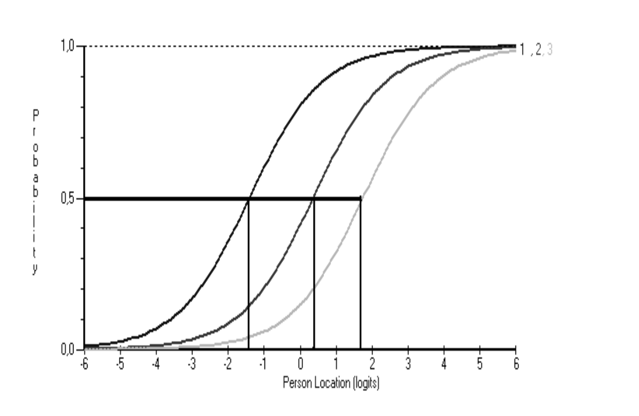
Figure 12B



Good fit to the model

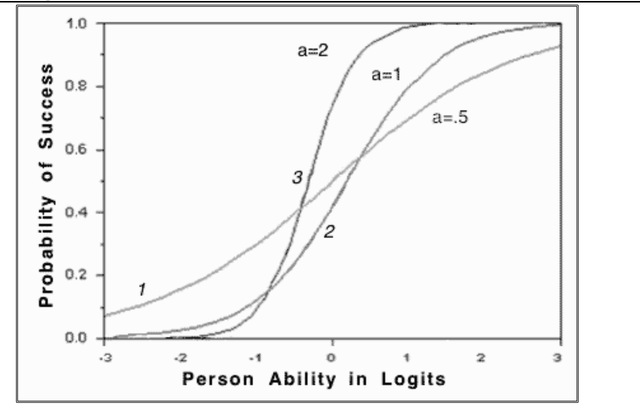
Figure 12A shows an example of observed data with significant lack of fit to the expected model. Conversely, Figure 12B shows a "well-fitting" item where the observed data for all persons nicely converge on the expected ICC. The items in Figures 12A and 12B are, in fact, examples taken from the analyses carried out in paper three of this study. Interestingly, 12A is one of the items that did not function as a polytomous partial credit item in the analysis of KOOS,[2] as shown in Figure 4. In the present study, this same item was applied to patients pre- and post-ACL reconstruction using a dichotomous response structure: "Can you bend your knee completely?": "Yes"/"No". As can be seen in Figure 12A, the item showed severe lack of fit (fit residual = 8.984 [normative range ± 2.5][163] with a chi-square probability of $p<0.000005$), and as can be visualized clearly in Figure 12A, the observed data points diverge substantially from the theoretically derived ICC curve. This means that the item does not work for patients with ACL deficiency in either polytomous or dichotomous forms. Conversely, the item in Figure 12B exhibits adequate fit (fit residual = -1.552, chi-square probability = 0.545) and the observed data points can be seen to visually converge on the ICC. Another aspect worth mentioning, in terms of the ICC, is that in an item set within a Rasch model, all item curves rendered by a Rasch model have the same level of discrimination (and thus slope).[130, 133, 164] If not, then the curves will interact, which could indicate multidimensionality or other anomalies, such as *non-uniform Differential Item Functioning* (see next section).[133] Figure 13A shows three hypothetical items rendered by a Rasch model. Other IRT models purposely model this interaction, such as the 2-parameter logistic model (2-PLM) [165, 166] (see Figure 13B). The only concern with this model is that it allows for a reversal of item difficulty levels for different person ability levels. Item one is easiest at minus one logit with a probability of .30 of affirming the item. As the level goes up to plus two logits, the item is now the most difficult item with a probability of just .70. Items 2 and particularly three are completely reversed relative to item one. It is difficult to imagine when this would actually be the case in real life in the context of ACL deficiency.

Figure 13A.



Rasch IRT model (3 items – same slopes)

Figure 13B.



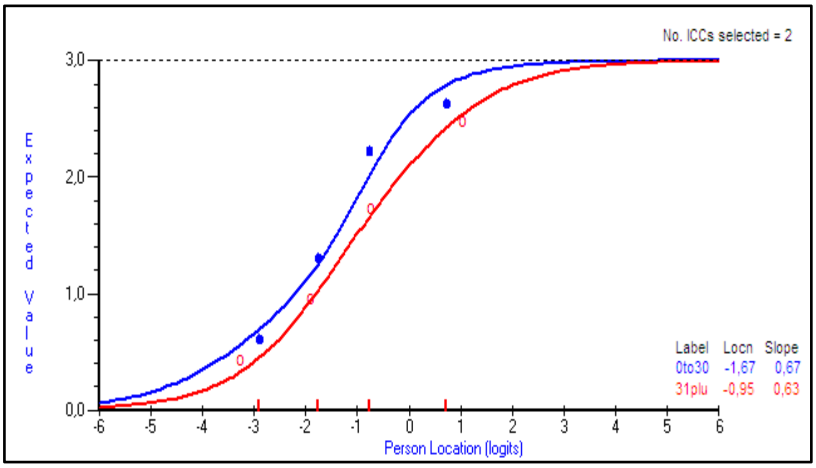
2-PLM IRT model (3 items – different slopes)

4.7.8 Sources of misfit

Fit of the observed data to the theoretically expected ICCs is paramount to establish unidimensionality.[104, 133, 167] If even a single item shows significant "misfit" as in Figure 12A, this can undermine the dimensionality of the entire scale.[168] Sources of misfit can include *multidimensionality,* interactions between subgroups of persons, also called *Differential Item Functioning* (DIF), and interactions among the responses to the items themselves, known as *Local Response Dependency* (LD).[142, 169, 170]

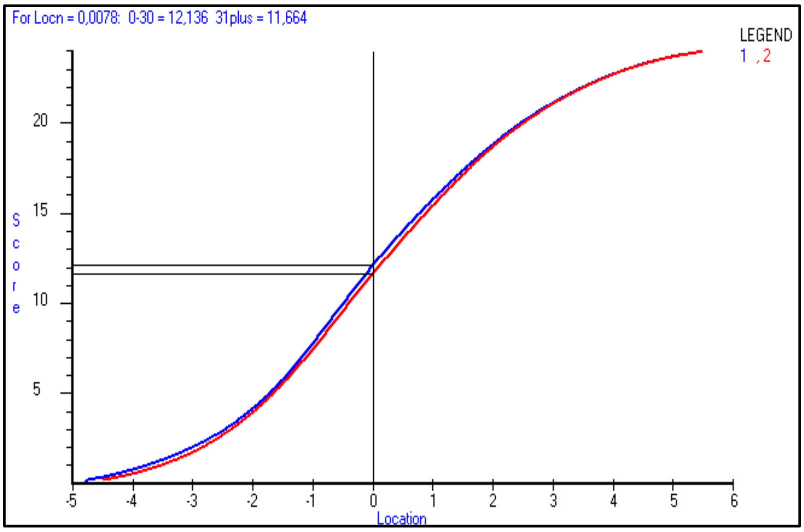
Multidimensionality indicates that a subset of items measures a different latent construct than the other items in the scale. Interactions between item-responses and person factors, such as gender or age, create a type of item bias known as differential item functioning (DIF), which leads to spurious results if not addressed.[168] There are two types of DIF, *non-uniform* and *uniform* DIF[142]. Uniform DIF is present when the ICCs for a covariate, such as age, deviate in a uniform manner across the spectrum of the latent variable (Figure 14.). In other words, the responses are systematically different along the entire range of the latent variable. For example, younger patients may respond differently to an item than older patients, as is the case in Figure 14, which shows an item concerning difficulty when crawling on hands and knees. The blue curve shows that persons thirty years old and under are not as affected (they have less difficulty on the latent scale) as those over thirty. This type of bias can cause misfit, but moreover, it implies that a correction of values should be implemented in order to compare test scores, for example from before and after a treatment intervention.[168] Uniform DIF can lead to misinterpretation of score results, but can, and must be identified, and resolved.[162, 168, 171, 172] When uniform DIF is found, a solution is to ascertain the degree to which the DIF affects the test-score for the group of items and adjust for this difference. This method of compensating for uniform DIF is referred to as DIF *test-equating.*[168] Figure 15 shows how the DIF in Figure 14 is reflected in the test score for the whole dimension (the latent variable). It shows that for comparison of these patients, it is necessary to heighten the test scores of the over-thirty year-old subjects by maximally 0.37 points in the bottom and middle region of the scale, that is, the range corresponding to ± one logit on the latent ADL variable, and corresponding to between eight and fourteen on the raw-score scale. The actual DIF-equating scores, used to generate the curves in Figure 15, are seen to right of the graph.

Figure 14.



Uniform DIF by age-group: 0-30 scores are higher than 31plus.

Figure 15.



DIF-equating. The 31plus patients (red) are slightly lower on the test score.

DIF equating scores:

Score	AGEGRP 31+	AGEGRP ≤30
1	1.00	1.16
2	2.00	2.19
3	3.00	3.19
4	4.00	4.19
5	5.00	5.21
6	6.00	6.23
7	7.00	7.27
8	8.00	8.30
9	9.00	9.33
10	10.00	10.35
11	11.00	11.36
12	**12.00**	**12.37 Max**
13	13.00	13.36
14	14.00	14.34
15	15.00	15.32
16	16.00	16.29
17	17.00	17.26
18	18.00	18.22
19	19.00	19.17
20	20.00	20.13
21	21.00	21.09
22	22.00	22.05
23	23.00	23.00

Non-uniform DIF is characterized by interacting ICCs between subgroups, in fact, in the same way as in the example of the 2-PLM in Figure 13B. Truly excessive non-uniform DIF that cannot be resolved may require removal of the item, as DIF in particular effects the overall model fit.[168, 171]

Interestingly, the search for DIF can also induce *artificial DIF*.[173] Artificial DIF is an artifact, which can surface due to simultaneous estimations of DIF in the presence of substantial DIF in one item. This underscores the fact that misfit of single items influences the entire item set. In addition, artificial DIF can surface in the presence of moderate DIF for a single item if the number of items is small. Different methods are suggested to ascertain the difference between real and artificial DIF, which of course is crucial to ensure appropriate removal or retention of items.[173]

Local Response Dependency can also affect model fit and is a phenomenon that until recently had not really been thoroughly addressed. LD indicates that a response in one item depends on the response to another item. In practical terms, it involves some degree of redundancy between items. If you can walk a hundred yards, then you can also walk ten yards. This does not mean that the lesser item needs to be removed. It can be included in a *composite item*,[174] in that retention of items is desirable in order to retain as much relevant item content as possible.[162, 171, 174]

4.7.9 Different Rasch models

As mentioned above, the dichotomous Rasch model is the simplest way to explain the mechanisms of the model. However, various Rasch models exist, and in particular, special cases of the Rasch model have been formulated to allow for polytomous response data (for example the Partial Credit Model (PCM),[103] the Rating Scale Model (RSM),[104] and Graphical Loglinier Rasch Models (GLLRM)).[162] The PCM is a modification of the dichotomous model and allows for the probability of multiple response options to be mapped out along the latent variable. The item in Figure 4 is an example of a partial credit structure. The RSM is a special case of the PCM and assumes equidistance between item thresholds. For example, the distance between the vertical black lines in Figure 13A (and for all items in an instrument) is assumed to be equal.[104] GLLRM excels at identifying DIF and LD and is more sensitive to a broader spectrum of violations to the Rasch model.[162, 171, 175, 176]

4.7.10 Reliability, Responsiveness, and Known-Groups Validity

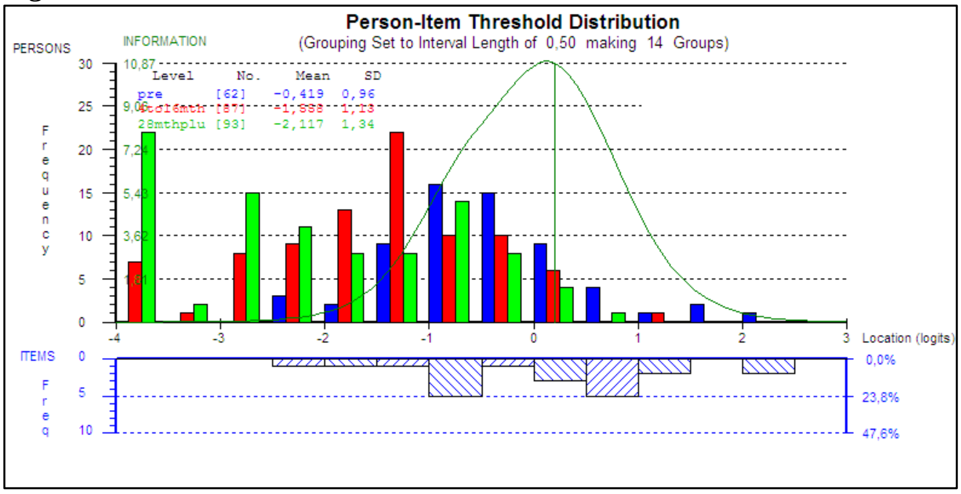
Test reliability is also an essential part of the validation process and can be problematic, because any statement concerning the stability, reproducibility, and internal consistency of a test relates equally as much to the population being tested as it does to the test itself.[177, 178] A summated score must accurately reflect the underlying trait being measured. If the trait is stationary, the score must convey this, and is thus reliable.[179] Conversely, the score must also be *responsive* to change in the underlying trait, if change for example due to treatment truly occurs. As Borsboom states, variations in the attribute being measured must have a causal effect on the values of the outcome measure.[131]

Reliability in CTT is defined by the “true score”, the observed score, and the error score.[178] Many methods are used to calculate reliability; however, baseline techniques used as a reference for others are the Kuder-Richardson Formula 20 (KR-20), for dichotomously scored data, and Chronbach’s alpha (gives a lower bound) for polytomous items.[155, 179] The drawback to these tests, within the framework of CTT, is that they are sample dependent. The reliability indices can be increased by increasing the number of items.[178] A practical example of this was seen in Table 3 in which the two WOMAC domains of Pain and Symptoms, which consist of few items, exhibited low alpha coefficients compared with the 17-item ADL domain. This was despite the fact that the ADL domain exhibited greatest misfit to the Rasch model. In Rasch models, reliability is assessed using the *Person Separation Index* (PSI). The PSI is calculated in virtually the same manner as alpha, except that it is generated from the data after the Rasch factor has been extracted, that is, on unidimensional data. Table 3 shows how the PSI and alpha are virtually the same when the data fit the Rasch model, as can be seen with the two non-WOMAC domains. This supports the implication that unidimensional scales possess internal consistency and are thus reliable.[155, 179]

Responsiveness can be assessed using different methods such as *Receiver Operating Characteristic* (ROC) curves to determine the performance of diagnostic classification tests. ROC curves are applicable when there is a single variable (e.g., ACL deficiency) with two categories by which persons are classified, such as ACL deficient: Yes/No.[180] The ROC Curve procedure is essentially the same idea as described in section 4.1.4 regarding diagnostic rates. Yet another variation of this theme is *Known-groups validity* assessment, which involves comparison of group means in either a within-subject repeated-measures design or between-subject comparison of different groups. The instrument should be able to measure differences between the groups in order to validate the intervention, but also to validate the measure itself. For example, it is assumed that patients will benefit from reconstruction of the ACL. Therefore, there should be a difference in the mean values of the summary scores between preoperative and postoperative patients. Figure 16 shows an example of this concept using results from the Rasch analyses in the present study. The graph shows the frequency of person scores relative to the item thresholds on a latent Symptoms trait (Sensation of Slackness – see papers two and three). The severity of the scale increases from left to right. In other words, the blue columns represent the patients who are most affected in terms of the latent trait (this is the preoperative group) and the green columns are the least affected persons (these are the patients, who are at least twenty-eight months post-op). The pattern indicates that the severity of the problems decreases across the groups from preoperative to postoperative decreases, which are the expected results in terms of the known-groups scenario. The fact that groups two and three have a statistically significant reduction in the level of symptoms relative to group one warrants the comparison of these groups using ROC curve analysis. For example, Group 3 can be used as a reference relative to Group 1.

However, true proof of benefit requires an external base of evidence to substantiate that the patients actually have improved after ACL reconstruction, and such a *gold standard* does not in fact exist. In order to truly confirm causal relationships and demonstrate external criterion validity, some substantive reference base, which should mirror the latent trait, and yet is independent of it, is needed. As previously mentioned in the section on validity, this might be biomechanical or biomedical indices known to reflect the condition of ACL deficiency.

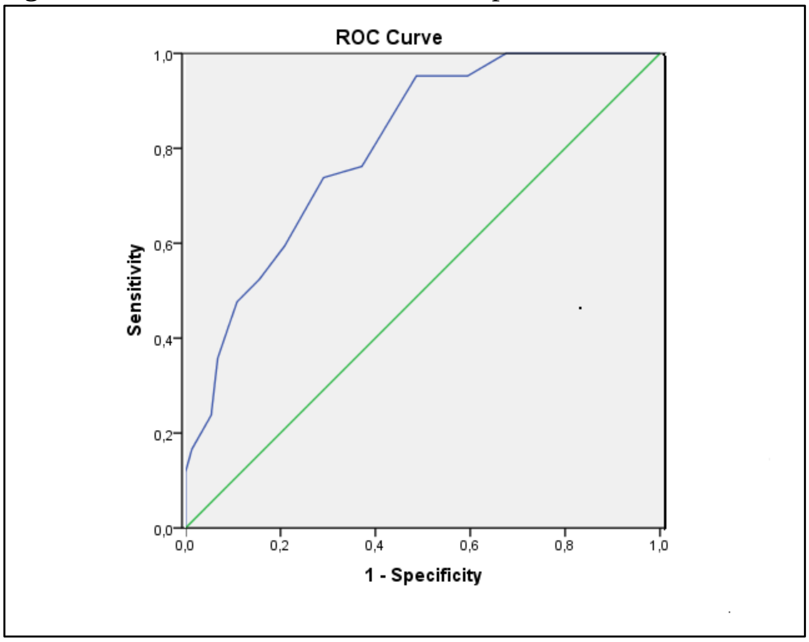
Figure 16.



Example of known-groups difference. The severity of the trait diminishes from right to left. Thus the green group is least affected (≥ 28 months post operative).

A ROC curve generated from the same Slackness scale as seen in Figure 17, comparing Group 1 with Group 3, shows respectable results, in that the area under the ROC curve is 0.805. The drawback to this analysis is that Group 3 is not a gold standard, as there are certainly patients who are not "completely" ACL sufficient.

Figure 17 shows a ROC curve of Groups 1 and 3.



Area Under the Curve Test Result Variable (s): Slackness				
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval: Lower Bound	Asymptotic 95% Confidence Interval: Upper Bound
0.805	0.034	0.000	0.737	0.872
ROC analysis performed with SPSS, Version 18.				

A final note on the Rasch model in terms of reliability and construct validity is the fact that when an item set fits a Rasch model, the scale will possess what is known as *statistical sufficiency*.[181, 182] This means that the summary score will yield all relevant information about the person, and it is impossible to extract more intrinsic information than is contained in the total score. The dichotomous and partial-credit Rasch models are the only IRT models known to satisfy the requirements of sufficiency.[177, 181, 182]

4.8 Rasch analysis in Physical Therapy

Rasch IRT has been used to evaluate the psychometric properties of some PROs used in the field of Physical Therapy. A Medline search combining “Rasch analysis” and “Physical Therapy” shows an increase in studies involving Rasch analysis over the past several years. The Abilhand Measure of Manual Ability is a “Rasch-built” PRO for rheumatoid arthritis, which dates back to 1998.[183] The same authors have more recently created other instruments using similar methods.[184-189] Campbell et al.[190] published a seminal paper in 1995 on construct validation of a test for infant motor performance using Rasch Rasch analysis, and the study was proclaimed paper of the year in *Physical Therapy*.[191] In terms of knee-specific PRO instruments, the IKDC – Subjective Knee Form has been subjected to a G-IRT Graded Response Model (used for Likert Scales),[192] as well as Rasch analysis using the partial credit model.[193] The Lysholm Scale has recently undergone a modification and validation using Rasch modeling,[194] and the Oxford Knee Score,[195] the KQoL-26, [196] the OAKHQOL,[197] and particularly the WOMAC scores [106, 198-200] have been assessed using the Rasch model. Notwithstanding, no condition-specific PRO for ACL deficiency has yet been constructed using the Rasch model.

4.9 Development and Validation of PROs Using Rasch Analysis – A Summary

The advantage of using Rasch IRT to construct and validate PROs is that it provides construct validation. The construct is generated from theoretical considerations about the latent variable based on empirical and clinical experiences with the condition of interest. The instrument is assembled (items generated) using the information and qualitative characteristics of the construct(s) derived from the target patient groups and experts. The specific target group to be measured is confronted with the measurement scale and the output scores are acquired. An attempt is made to fit an appropriate Rasch model to the data. If there is adequate fit, the scale will exhibit unidimensional invariant measurement for the selected group of individuals. The power of Rasch analysis lies in its confirmatory nature. It simply allows us to ascertain the validity of our measure based on the manner in which people have responded and not by qualitative assumptions of how we believe they ought to have responded. These qualitative assumptions, which optimally are based on solid empirical observations, are the nucleus of constructing a scale to be tested. In formal terms, if the observed response converges on the expected response, as specified by the Rasch model, then the output score is the sufficient statistic. Thus, it yields all necessary information about that person, and the score can be used for comparison across treatment and over time.[160] Only sum scores derived with the Rasch model can be used in this way.

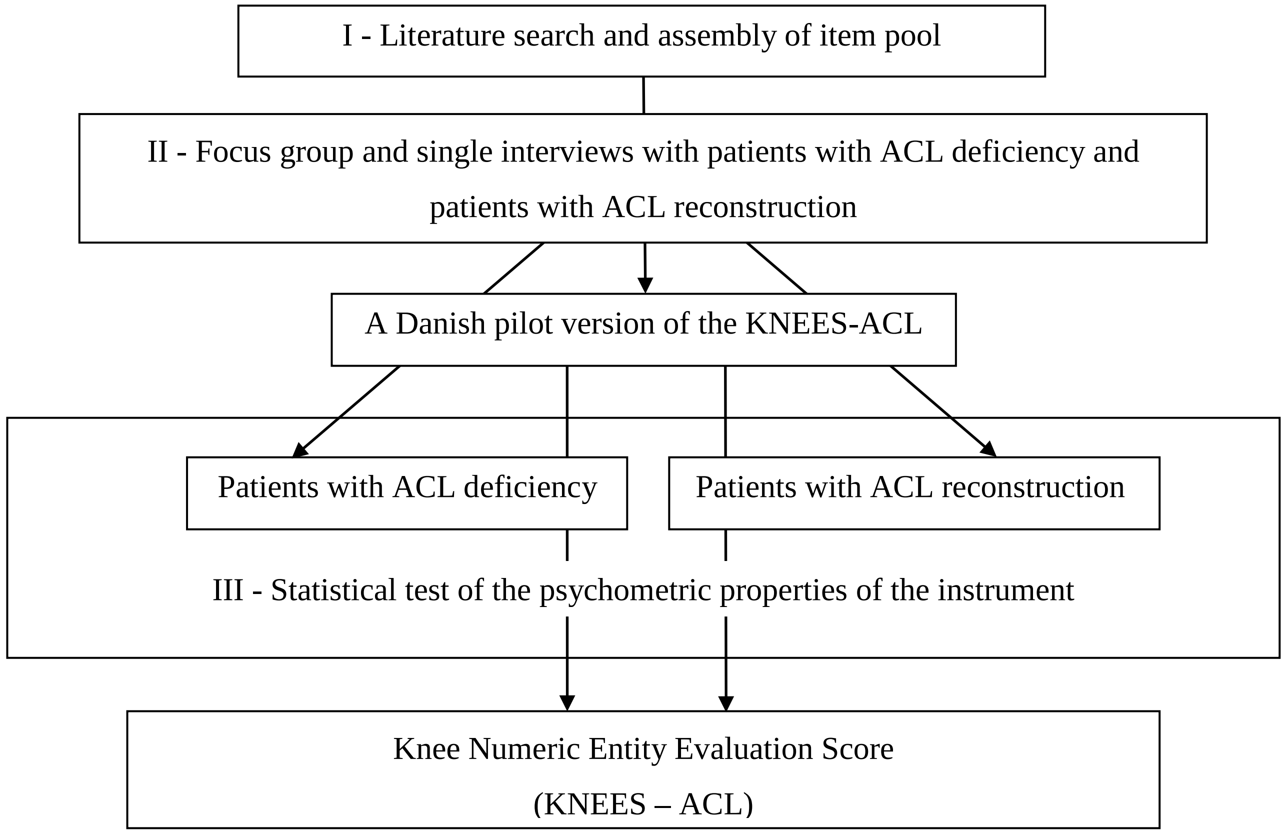
4.10 The Objective of this PhD Study

The overall purpose of this study was to create a PRO questionnaire, which could be used for pretest-posttest studies of treatment for ACL deficiency. This required identifying item content for patients with knee disease, confirming the content relevance and coverage of the items in groups of patients with ACL deficiency and ACL reconstruction, and testing the psychometric properties of this content on a cohort of patients with ACL deficiency and ACL reconstruction. The aims of the three papers were:

1) To review studies where PRO instruments were used to assess outcome in patients with knee disease in order to identify possibly relevant items and constructs for patients with ACL deficiency and ACL reconstruction.
2) To assess the content validity of the identified items from the review and construct a pilot questionnaire for psychometric testing and validation
3) To statistically assess the psychometric properties of the constructed PRO on patients with ACL deficiency and patients with ACL reconstruction.

4.11 The steps of the PhD study

The Roman numerals in the flow chart correspond to the steps of the study described in each of the papers.



5. Article 1 (accepted for publication)

Ensuring Face Validity in Patient-Related Outcome Scores – a matter of content

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Key words: Face validity, Content validity, PRO, Knee, ICF

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Abstract

Patient reported outcome (PRO) questionnaires are increasingly used to measure treatment effect in patients with knee pathology. PRO’s commonly used to assess outcome in patients with knee conditions can be generic, knee-specific, or condition-specific. Most PRO´s have been created on the basis of clinician-based consensus and are not patient-centered. Items (questions plus their response options) in PROs can be generated by clinicians or through patient interviews. Items created by clinicians possess face validity. The objective of this study was to find all existing PRO items with potentially relevant content for patients with knee pathology. An exhaustive literature search was conducted for PRO questionnaires in English, German, and Scandinavian languages used to assess outcome in patients with knee pathology. The items from the collected PROs were assessed for content redundancy and item reduction was carried out to isolate items of unique content. These items were grouped into one of the components of the ICF classification system. Thirty-one PRO’s used for assessment of patients with knee problems were identified, yielding a total of 539 items. Approximately 70 percent of these items consisted of redundant content matter and were reduced to a pool of 157 items of unique content. The identified items can be used to build condition-specific PRO questionnaires for patients with different types of knee pathology.

Introduction

Knee disease imparts substantial economic, physical, and psychosocial consequences on society. The socioeconomic impact of knee osteoarthritis (OA) alone is just under a third of a percent of the gross national product in Western countries [1]. This corresponds annually to nearly half a billion Euros in Denmark, a country of 5.4 million inhabitants. In Western countries, OA affects 10 percent of the general population and roughly thirty percent of persons aged seventy [1, 2]. Rupture of the anterior cruciate ligament significantly increases the risk of knee OA [3, 4] and is present in nearly a quarter of patients with knee OA [5].

Recommendations for treatment of knee disease are increasingly based on trials where patient reported outcome (PRO) questionnaires are used as primary outcome. Frobell and colleagues recently used a well known PRO questionnaire to conclude that patients with ACL rupture are subjected to surgical over treatment [6], despite evidence that the PRO measure employed in the study was found to be insufficient for application on these patients [7, 8]. Such conclusions can obviously influence recommendations for clinical treatment guidelines and thus clinical decision-making. Therefore, it is essential to confirm that the outcome instrument used for specific disease conditions adequately measures the effect of treatment in that group, for meaningful interpretation of results. This is not always the case when PROs are used, as treatment outcome for specific conditions are often measured using instruments designed for broader or completely other purposes [7-11].

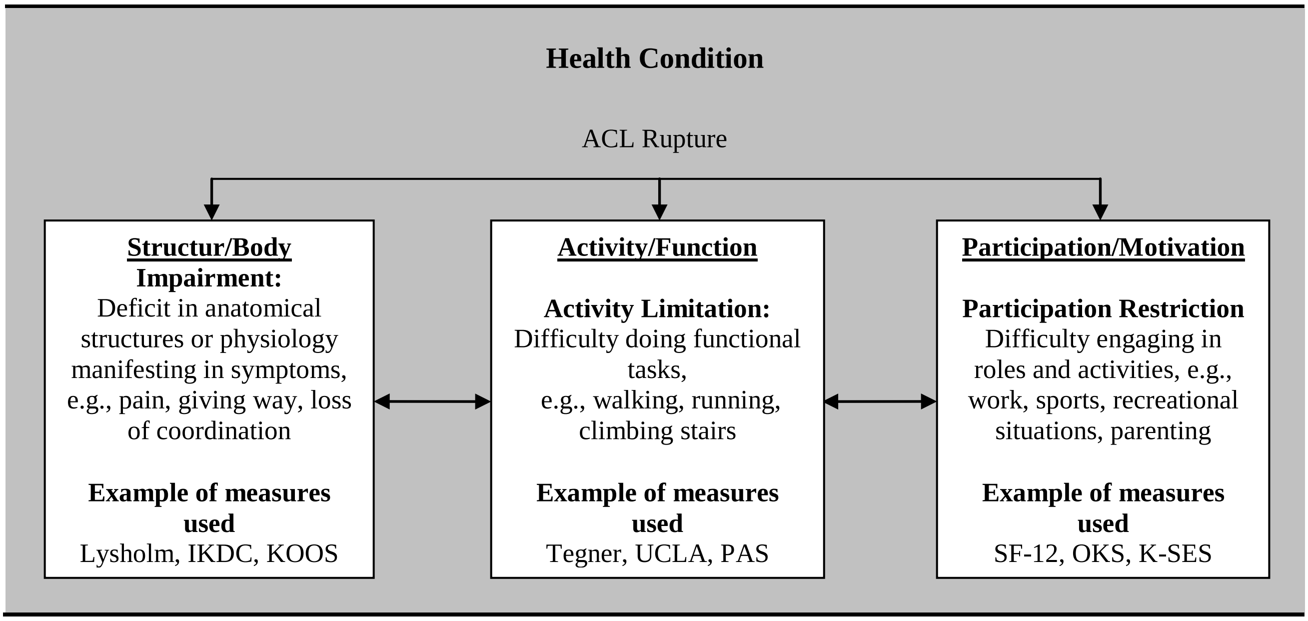
What are PROs?

A PRO is “any report coming directly from subjects without interpretation of the physician or others about how they function overall or feel in relation to a condition and its therapy” [12]. PRO data are collected via standardised questionnaires designed to measure underlying constructs not directly measurable, such as pain (or other symptoms), or the ability to carry out functional tasks. Individual items (questions plus their response categories) are grouped into one or more domains, depending on the concept they represent. A domain can be used as a measurement construct or scale only if it can be shown that the addition of the raw scores from each item is mathematically justifiable [7, 10, 13-15]. The importance of PROs in health care assessment is increasingly being recognised, as PROs address the patient’s own perception of function and treatment effect. Conversely, clinical and para-clinical outcomes seek to quantify pathology from the perspective of the clinician [16, 17]. The American Food and Drug Administration (FDA) strongly recommends the use of PROs stating “physical examination and performance testing is not sufficient to measure what may be most important from the patients perspective” [18].

Development of PROs

The first step in developing PRO questionnaires is to choose a theoretical framework to ensure the integrity and content relevance of the constructs to be measured [17, 19, 20]. Conventional classification concepts in health related PROs, are Impairment (symptoms), Activity limitations (functioning), Participation restrictions, and Health related quality of life (HRQoL). The concepts of impairment, activity limitations, and participation have been explicitly defined in the International Classification of Functioning, Disability, and Health (ICF) (WHO, 2001) and are broadly used to classify patients in terms of health status. The ICF can be instrumental in establishing a common conceptual reference [21-24]. Impairment is defined as the loss or abnormality of psychological, physiological, or anatomical structure or function, and largely equates to symptoms and signs [17, 22-26]. Impairment relates to dysfunction at the bodily level manifesting in such problems as restricted mobility and pain, but also in depression and anxiety. Impairment is conceived as some deviation from the norm in an individual’s biomedical status. Activity limitations are any restriction or lack of ability to perform activities within some normative range [17, 21]. This might include problems with dressing, walking, or personal care. Activity limitations are often referred to as disability or decreased functional status [17, 21, 26, 27]. Instruments that assess the impact or treatment of disease at this level typically target the construct of activity. This is essential when the objective of a study is to assess activities of daily living, for example. Participation is defined as a person’s involvement in life situations. The construct of participation is closely related to activity, but differs in that it emphasizes the degree to which a person is able to and actually does take part in areas of life, regardless of their level of impairment or the degree to which their ability to perform activities is limited [17, 21, 26, 27]. A bilateral amputee sprinter would be considered highly impaired, yet at an exceptionally high participation level. Impairment, activity, and participation are well-suited constructs for determining and planning interventions, and particularly important in studies of interventions intended to increase patients' participation in life [17, 21, 26-28]. Constructs targeting lifestyle, psychosocial, and general satisfaction are somewhat problematic in the ICF model. Alternative models are likely more appropriate to deal with existential aspects of HRQoL [29]. Figure 1 shows the structural model of the ICF system as applied to instruments for outcome assessment of patients with ACL deficiency. The arrows indicate a dynamic interaction between the components of the model. Items and constructs can be placed within one or another component depending on the perspective of the author of the instrument. This can seem arbitrary. However, it is important to keep in mind that the ICF is intended as a classification tool which can be useful for conceptualizing and constructing PROs. The ICF is not a measure in itself. It is analogous to a tool box, where the ruler in this context would be the PRO questionnaire itself.

Figure 1. The ICF model as applied to ACL rupture



Specific as opposed to generic instruments

PROs can be generic, anatomically specific, or condition specific. Generic PROs are developed for overall assessment of Health Status regardless of underlying pathology and diagnostic criteria. Instruments such as the Medical Outcome Study - Short Form (SF-36) and the Sickness Impact Profile are examples of generic PROs. Anatomically specific PROs are constructed for patients with pathology associated with a specific organ or anatomic region, such as the knee or hip, without regards to type of pathology. Knee-specific instruments such as the International Knee

Documentation Committee Knee score (IKDC), the Lysholm Score, and the Knee Injury and Osteoarthritis Outcome Score (KOOS) are examples of anatomically specific PROs. Instruments addressing specific pathologies in specific organs are said to be condition-specific, for example the Western Ontario Meniscal Evaluation Tool (WOMET) for meniscus injuries. The need for condition-specific PROs is increasingly emphasized [30-32]. The main weakness with generic instruments is that they are not designed to target areas of concern in particular patient populations and thus most likely enquire about issues that are irrelevant for specific patient groups [33, 34]. Asking patients to answer non-relevant questions can alienate respondents and increase the potential for missing data [29, 33]. Therefore, condition-specific instruments are preferred as they provide information that is more detailed and are more sensitive to disease-specific and treatment-specific effects [32, 35].

Face and content validity

Item content should be drawn from the most appropriate source in order to confirm that items in PRO instruments measure concepts that are relevant for the targeted patient group [15, 17, 21, 36]. Items are typically derived from two sources; pre-existing PROs and individual clinical experts or consensus groups; focus group and individual interviews with patients [14, 17, 28]. While items measuring symptoms are best generated from the perspective of the patient, with possible input from the clinician, items used to measure participation, psychosocial attributes, and HRQoL can really only be derived from the patient [17]. Items obtained from pre-existing instruments through literature reviews will possess face validity [37]. Mosier states that the instrument ”is considered to be valid, if the sample of items appears to the subject matter experts to represent adequately the total universe of appropriate test questions“ [37, 38]. Item content relevancy and coverage (content validity) is confirmed by confronting the particular patient group with the items in question. Tanner and colleagues selected eleven knee-specific questionnaires to assess which items in the instruments were most relevant for different knee pathologies based on consensus interviews with orthopedic specialists [31]. The authors constructed a composite 111-item pilot questionnaire to assess condition-specific item-content relevancy through semi-structured focus group interviews with three separate diagnostic groups of knee patients: ACL-deficient, meniscus tears, and knee OA [31]. Others have used similar methods for the purpose of item generation [39-42]. Thus, for the purpose of creating new PROs, review of existing instruments can be particularly relevant in the initial stages of item generation.

Aim

The objective of the present study was to find all PRO questionnaires with knee-specific content, to identify items with unique content contained within them, to classify these items according to the ICF model.

Methods

A literature search was conducted in the Medline, CINHAL, EMBASE, and PEDRO databases to find existing PROs used to assess knee pathology. The search was designed to capture articles which identified questionnaires used to assess outcome for patients with knee ligament and/or knee cartilage injuries, and/or knee OA. Questionnaires written in English, German, and Scandinavian languages were included. Hierarchically, the search term “questionnaire” included all categories of patient related outcomes (e.g., PRO, POEM, etc.). Thus, the terms: ”knee”, “knee joint”, “articular ligaments”, “articular cartilage”, and “knee injury” were combined with the dependent response term “questionnaire”. The original search was conducted in April 2009. The search was progressively updated in Medline and the reference lists of the included papers were further scrutinized to search for knee-specific PROs.

Titles generated from the initial search were screened to identify abstracts in which questionnaires were used to assess treatment effects relating to knee pathology. Unique instruments were noted. Identified abstracts were scrutinized to determine the specific application of the PRO for knee patients. Identified measures were excluded if they were:

: Not a PRO; the instrument was not a questionnaire, but contained only objective, clinician-based measures of outcome

: Condition non-specific; the instrument was designed for other or more general pathologies such as inflammatory disease (e.g., rheumatory arthritis), extra-articular injuries (e.g., tibiofibular joint), bony fractures, tumours, acute trauma, emergency room conditions, or for evaluation of acute-care post-operative status

: Anatomically non-specific; the instrument was designed for other anatomic regions or was solely generic

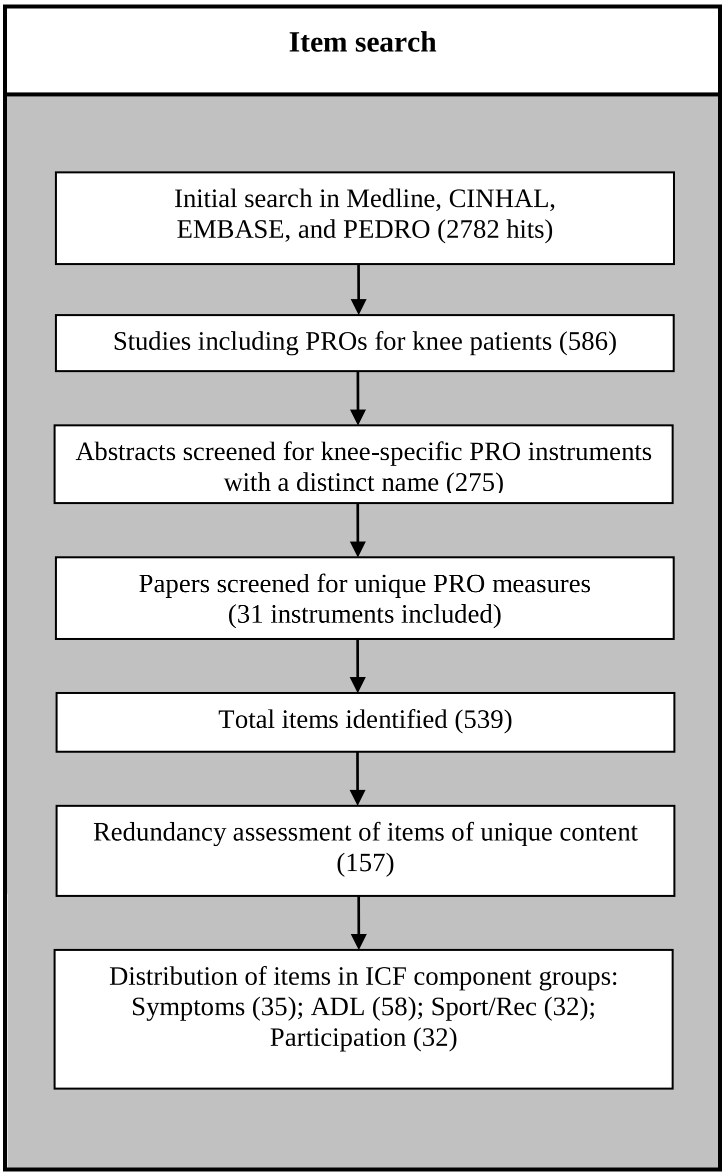
Assessment of item content redundancy and item reduction

After knee-specific PRO instruments were identified, all individual constructs, such as pain, function, activity level, as well as the items comprising these domains, were distinguished. Qualitative assessment of the meaningful content of each item was conducted, as the main purpose of this study was to extract only items of unique content from PROs used to assess knee patients. Item-content redundancy was assessed in the following way: All the collected items from the different PROs were extracted from the host instrument and placed into a single grouping and the main topic or theme of each item was then ascertained. These items were stripped of their grammatical structure to extract the meaningful content of the item. For example, an item involving walking ability:"Are you able to walk on rough ground, inclines, or negotiate curves?" became "walking ability in uneven terrain." The result was a single group of truncated items consisting only of item content matter. The wording and structure of the response scales for the items was not considered, as only the content of the item attribute was of concern. Finally, the truncated items were classified according to the most appropriate ICF component (Table 2).

Results

The search and screening pathways are shown schematically in figure 2. The original search yielded 2782 articles. From these, 586 studies were identified where PRO questionnaires were mentioned in conjunction with knee pathology. Screening of article titles resulted in 275 abstracts, which in turn yielded 81 measures with unique names. Thirty-one of these instruments were judged to have met the inclusion criteria of being a knee-specific PRO.

Figure 2. The search pathway for PROs used to assess knee pathology.



The final 31 instruments included 87 separate sub-domains, such as pain or other symptoms, where the majority of these domains across the instruments were redundant. Table 1 shows the 31 PRO instruments in alphabetical order. The 31 instruments contained 539 items, which after qualitative assessment of item topic redundancy was reduced to 157 items of discrete item content. The final 157 list of non-redundant items as related to the ICF classification system are shown in Table 2.

As can be seen in Table 2, thirty five items were classified into the Impairment (Symptoms) component of the ICF, 58 items in the Activity of Daily Living (Daily Function) component, 32 items in Sport and Recreational Activity (Sport Function), and 32 items belonged to the Participation (Psychosocial) ICF component. Seventeen of the 35 items, which were classified in the Symptoms domain, consisted of item content where pain with or without movement of the knee was the main topic. The other item topics were symptoms relating mostly to mechanical sensations, such as grinding or clicking during movement. In addition, items concerning variations of impinged motion and the sensation of mechanical instability and numbness were represented. In the Function in Daily Activities domain, the 58 item topics were quite evenly distributed throughout topics of walking at different levels of difficulty, daily mobility, such as getting in and out of cars and bed, work abilities, and a broad range of other functional topics during daily life. The Sports and Recreational Activity items consisted of 32 items dealing with high-level activity demands in different functional contexts, such as type of sports, type of movement, or intensity level of competition. The Participation domain consisted of 31 items with an array of psychosocial topics, which could influence the level and ability to participate in normal life activities, from emotional distress at work to social isolation.

Table 1. PRO instruments used to assess knee outcome

	PRO instrument	**Ref.**
1	**Activity Rating Score (ARS)**	**41**
2	**British Orthopedic Association Score (BOAS)**	**43**
3	**Cincinnati Knee Rating System(CKRS)**	**44**
4	**Crosby/Insall**	**45**
5	**Hospital for Special Surgery Score (HSS)**	**46**
6	**Hughston Clinic knee self-assessment questionnaire**	**47**
7	**International Knee Documentation Committee (IKDC)**	**48**
8	**Knee injury and Osteoarthritis Outcome Score (KOOS)**	**49**
9	**Knee self-efficacy scale (K-SES)**	**50**
10	**Knee Outcome Survey (KOS)**	**51**
11	**Knee Society Score (KSS)**	**52**
12	**KOOS – PS**	**53**
13	**Kujala**	**54**
14	**Lequesne index**	**55**
15	**Lower Extremity Functional Scale (LEFS)**	**56**
16	**Lysholm**	**57**
17	**McGill Pain Questionnaire**	**58**
18	**Mohtadi (ACL-QOL)**	**59**
19	**Musculoskeletal Function Assessment Questionnaire (XSMFA)**	**60**
20	**Orthopadische Arbeitsgruppe Knie (OAK)**	**61**
21	**Oxford Knee Score (OKS)**	**62**
22	**PFPS Pain Severity Scale (PSS)**	**63**
23	**Physical Activity Scale (PAS)**	**64**
24	**SF-12**	**65**
25	**Shelbourne**	**66**
26	**Stanford Health Assessment Questionnaire (HAQ)**	**67**
27	**Tegner Activity Scale**	**68**
28	**Total Knee Function Questionnaire (TKFQ)**	**69**
29	**UCLA Activity Scale**	**70**
30	**Western Ontario and McMaster Universities Osteoarthritis Index function scale (WOMAC)**	**71**
31	**WOMET**	**30**

Table 2. Items with unique content as related to the ICF

Impairment (Symptoms)	Activity (Function in ADL)	Activity (Function in Sport/Rec)	Participation (Psycho-social)
1. Pain when turning/twisting knee	**36. Walking - independent outdoors**	**94. Jogging 3-4 X pr week**	**126. Feeling relaxed and tranquil**
2. Pain when walking on flat surface	**37. Walking – flat surface**	**95. Straight running in sport**	**127. Feel depressed or sad**
3. Pain when walking in uneven surface	**38. Walking - uneven surface (e.g. woods, hills)**	**96. Run with change of direction**	**128. Being reminded of knee injury**
4. Pain when walking up stairs	**39. Limited walking distance**	**97. Run with sudden stopping**	**129. Anxiety over contact sport**
5. Pain when walking down stairs	**40. Walking with assistive device**	**98. Running with turning/pivoting**	**130. General safety worries**
6. Pain when jumping/hopping	**41. Walking down stairs**	**99. Running with turning/pivoting on injured knee**	**131. Worries about lifestyle and family activities**
7. Pain when running	**42. Walking up stairs**	**100. Running in woods**	**132. Self confidence due to knee injury**
8. Pain when getting up from sitting, lying, or crawling.	**43. Walking down stairs with hand rail**	**101. Full competition running**	**133. Insecurity over re-injury**
9. Pain after running	**44. Walking up stairs with hand rail**	**102. Jumping/hop**	**134. Emotional distress in ADL or at work**
10. Limping	**45. Standing still**	**103. Full competition jumping and landing**	**135. Energy level**
11. Pain when kneeling	**46. Sitting in squatting position**	**104. Hop on injured knee**	**136. Fear of injury worsening due to sport/activity**
12. Pain when crouching	**47. Lying in bed**	**105. Side to side hop from one leg to the other leg**	**137. Fear of knee giving way during sport**
13. Pain when straightening knee	**48. Sitting with bended knee**	**106. Competitive sports**	**138. Fear of external factors (slippery floors etc.)**
14. Pain when bending knee	**49. Putting on stockings**	**107. Recreational soccer**	**139. Apprehension during sport due to knee injury**
15. Pain at night	**50. Taking off stockings**	**108. Amateur level soccer**	**140. Social isolation**
16. Pain when sitting	**51. Washing hair**	**109. Division III soccer or lower**	**141. Ability to go all out during sport**
17. Pain when lying	**52. Standing up from sitting**	**110. Elite division I - II soccer**	**142. Level of participation in sport of first choice**
18. Pain when standing	**53. Getting into car**	**111. Elite contact sports (handball, basketball, hockey, athletics, tennis and squash**	**143. Level of participation in sport of second choice**
19. Clicking in knee	**54. Getting out of car**	**112. Alpine skiing**	**144. Level of participation in fitness and physical training**
20. Grinding in knee	**55. Getting into bed**	**113. Nordic skiing**	**145. Level of pleasure in life**
21. Crunching in knee	**56. Getting out of bed**	**114. Swimming**	**146. Shyness because of injury**
22. Other sounds from knee	**57. Assistance getting in/out of bed**	**115. Non-contact sports**	**147. Acceptance of limitations due to injury**
23. Limited range of motion in knee	**58. Getting in/out of shower/bathtub**	**116. Recreational tennis/squash**	**148. Changes in expectations to sport**
24. Stiffness in knee in the morning	**59. Getting on/off toilet**	**117. Horseback riding**	**149. Fulfillment of competition needs**
25. Stiffness in knee later in the day	**60. Transfer in bed**	**118. Recreational cycling**	**150. Changes in lifestyle**
26. Locking of knee	**61. Moving into crouched position**	**119. Elite cycling**	**151. Being reminded of injury**
27. Catching of knee	**62. Walking or crawling on knees**	**120. Long distance cycling**	**152. Magnitude of problem**
28. Something slipping in knee	**63. Bending down to floor**	**121. Hard physical training**	**153. Focus on injury**
29. Strength reduction of knee	**64. Pivoting on knee**	**122. Stretching**	**154. Satisfaction with knee**
30. Loss of knee control	**65. Twisting on knee**	**123. Strength exercises for lower extremities**	**155. Trusting the knee**
31. Giving way	**66. Bicycling**	**124. Slightly limited deep knee bends**	**156. Comparison of activity level before/after injury**
32. Thigh is thinner than the other	**67. Going out dancing**	**125. Unlimited deep knee bends**	**157. Participation in sport with/without symptoms**
33. Knee swelling	**68. Running after small children**		
34. Impinged knee movement	**69. Running to catch bus/train**		
35. Numbness in/around knee	**70. Jumping from a pier to a boat**		
	71. Bending forwards/backwards		
	72. Turning or pivoting		
	73. Light activities		
	74. Carrying heavy objects		
	75. Unable to work – sick leave		
	76. Light work		
	77. Moderate work		
	78. Part time work		
	79. Full time work		
	80. Change of occupation		
	81. Heavy industrial labor		
	82. Hobbies or recreational activities		
	83. Light home activities		
	84. Heavy home activities		
	85. Dusting and watering flowers/plants		
	86. Vacuuming and mowing grass		
	87. Heavy housework		
	88. Light housework		
	89. Gardening		
	90. Moving a table – distance		
	91. Shopping		
	92. Carrying groceries		
	93. Moving around in a rocking boat		

Discussion

We assembled an item pool stemming from all questionnaires in English, German, and Scandinavian languages that target patients with knee ligament, meniscus, and cartilage injury. These items were classified according to the ICF classification system.

Tanner et al. [31] collected 111 items selected from questionnaires recommended by only five surgeons, and Tanners items were restricted to those found in the English language. We performed an analysis of item content redundancy by isolating the meaningful content. It is unclear how Tanner dealt with content redundancy. Thus, their coverage of item content was not comprehensive and may have included redundant items.

Our items can be used in the development PRO measures for patients with knee pathology. The items are knee-specific, which means, in principle, they can be used to construct knee scores for different knee pathologies. However, in this case, it is essential to confront each diagnostic group with the content of each item through focus group - and individual cognitive interviews to confirm comprehensiveness and content validity, and to explore whether other items or constructs can emerge. Only four previously developed knee-specific PROs have included the process of patient confrontation, and just two of these were condition-specific [32]. It is also possible that certain items could be used within a “core” instrument with content covering multiple diagnostic groups of knee pathology, for example, patients with meniscus, cartilage, or ligament injuries, or combinations of these. Other items would be condition-specific for individual diagnostic groups.

The separation of items into a core and condition-specific groups has not previously been proposed for knee PROs. The items in SF-36 were extracted from the original long-form MOS 116 item set, a core instrument for assessment of general health and well-being [72]. However, the items and domains of the MOS instruments (i.e., SF-20, SF-36, and SF-12) were never intended to be condition-specific. Regardless of the path used to construct the questionnaire, once the content has been derived and the PRO measure assembled, appropriate methods to confirm the dimensionality and other measurement properties of the instrument must be employed. This lack of confirmation is a fundamental flaw in earlier knee PRO development, although this has been done for other conditions [4].

We used a novel approach to isolate the meaningful content of items by stripping the items of their grammatical structure and discarding the response options. In this way, we could eliminate cultural, linguistic, and grammatical contexts, since our search included instruments from different cultures and languages. This made it possible to easily identify items that coincided in content regardless of the original language. The truncated items were grouped into one of the ICF components once the item content was isolated, allowing a standardized conceptual reference platform from which the items can be combined to explore the development of new measures. This approach is supported by the findings of Wang and colleagues [32]. They concluded, in a recent critical review of knee PROs that condition-specific instruments are preferred, stating, “Because no standardized knee instrument exists, clinicians and researchers must assess an instruments utility based on their specific disease and patient population of interest.” The fact that we found at least 157 items with distinct content defining different attributes of knee dysfunction supports the importance of confirming the content relevance of each item in the specific patient group. There are multiple reasons why items should be condition-specific for distinct diagnostic groups. The activity or task may be too easy or difficult for the patient group being tested, which results in a ceiling or a floor effect. This happens, for example, when young cruciate ligament injured athletes are asked to complete questions designed to measure function in patients with OA [7]. If response scores to particular items lie at the top or the bottom of the spectrum of response options, then the item cannot yield valid information about the particular condition. This means the item cannot differentiate between patients or measure change over time [7, 14]. Also, an item might perform differently for patients with similar, but not the same pathologies, because functional difficulties can vary considerably depending on which anatomical structures (ligament, muscle/tendon, neural, cartilage, bone, etc.) are affected. Moreover, there may be cultural, gender, or age-dependent differences in the way certain items are perceived by patients. Condition-specificity has not previously been addressed adequately, except in one case [32].

We may not have found all PROs relevantly used to assess patients with knee pathology. The WOMET was missed in the original search because the Medical Subject Headings (MeSH) term “knee” does not encompass the hyphenated term “knee-specific”. Tanner (2007) mentioned the WOMET, but also used the term “knee-specific” [31]. However, with the inclusion of 31 questionnaires in five languages containing 539 items, we maintain that the probability of item content saturation is high. The fact that approximately 70 percent of the original item pool was redundant supports this argument.

Another problem when searching for items is that the concepts of the measurement domains from which they originate is so heterogeneously interpreted and understood. Even PROs purporting to measure outcome in the same patient groups are made up of a multitude of different domains, sub-domains, constructs, scores, and scales, and there is no consensus as to which domains items belong. This is reflected in the way items are grouped within instruments and in the way in which measurement constructs are operationalised. For example, Marx and colleagues, the creators of the Activity Rating Scale (ARS) [41], discuss the "arbitrariness" of ranking different types of sports activities in terms of level of difficulty. Is tennis more or less difficult than football? Can they be compared? This issue is particularly relevant when scores from items that represent different constructs such as activities or symptoms are added together to yield a sum score. Marx and associates mention the Tegner Activity Score as having Gutman scaling properties. Gutman structure is a basic requirement a scale must fulfil to yield valid measurement as an interval scale. It assumes that an item-response score quantitatively subsumes itself and any item below it on the scale and no items above it. However, this must be mathematically confirmed through testing using appropriate methods such as Item Response Theory (IRT) models (e.g., Rasch analysis). Neither the Tegner Score nor the ARS have been subjected to this type of construct validation. In fact, very few PROs have been assessed using IRT. Most PRO instruments are validated using Classical Test Theory (CTT), such as correlation or factor analyses. It is increasingly recognized that IRT, particularly Rasch analysis, is the most appropriate method to validate PROs [7]. The only knee-specific PROs assessed with Rasch analysis are the OKS [73], the Lysholm Score [74], and the KOOS [7]. The KOOS was found to be insufficient for use on patients who had received an ACL reconstruction [7].

As a result of this study, we present a collection of items that possess face validity for patients with knee pathology. The items can be used to construct content relevant condition-specific PROs.

Conflict of interest statement

No conflicts of interest to declare. All authors contributed substantially to the study and writing of the manuscript. Each of the authors has read and concurs with the content of the final manuscript.

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6. Discussion of article 1

6.1 Major Findings

The literature search revealed thirty-one knee-specific PROs with 539 items addressing knee-related dysfunction. Approximately seventy percent of the items were redundant in terms of item content, and the items were reduced on a qualitative basis to 157 item themes of unique content. These items were grouped by item content into the ICF categories of Symptoms (Impairment), Perceived Activity Level (Functional Limitations), and Participation (Psychosocial Consequences).

6.2 Assessment of Methods

The literature search identified thirty-one PROs with five hundred thirty-nine items in four languages that fulfilled the inclusion criteria. Well over four hundred of these items were not in Danish, and thus the 2-panel translation originally planned was not feasible. Therefore, it was decided to remove the sentence structure and context of all the items and truncate them into just the meaningful content of the item. This allowed easy evaluation of content redundancy. This method is recommended for searches, where large numbers of items are generated.

Most often, the objective of systematic reviews is to conduct cumulative statistical analyses of treatment efficacy and/or evaluate the validity of the end-point measures used in the included papers. In such cases, PRISMA,[201] COSMIN,[202] or similar guidelines can be followed. In the present study, the procedure used (if any) to validate the included instruments was not of concern, and thus, neither PRISMA, nor other guidelines were applied. The objective was simply to identify PRO item content, which could be used to assess knee function in patients with ACL deficiency and ACL reconstruction. An advantage of this method is that existing knee PROs have been developed within the context of the ICF model, thus allowing a common theoretical platform. The ICF model was chosen as a theoretical frame because most all PROs used for assessment of musculoskeletal pathologies are rooted in the ICF. The design was similar to the study by Tanner et al., in that the item pool was generated from existing questionnaires.[125]

6.3 Feasibility of the Comprehensive Literature Search

The literature search strategy in Medline, CINHAL, EMBASE, and PEDRO involved different combinations of the terms ”Knee injury”, ”ligament”, ”cartilage”, ”osteoarthritis” and “function”, “outcome”, “patient-related outcome”, “questionnaire”, “scores”, and “scales”. The language restrictions were English, German, and Scandinavian. The complete Medline search strategy is reported in Appendix I (page 118). The abstracts identified through the search were assessed for relevant PRO instruments. The instruments were considered relevant if they were used to report patient-reported outcome in knee pathology. Patient-reported outcome was defined as any symptoms, bodily impairment, functional activity limitations, participation, and psychosocial consequences with relation to knee pathology. In order to focus the search on intra-articular traumatic knee injury, exclusion criteria were anatomic non condition-specific and generic PROs, and PROs used to assess treatment outcome in completely heterogeneous conditions relative to ACL and intra-articular cartilage lesions, such as fractures, inflammatory or other systemic diseases, and emergency room and intensive care settings. Thus, the items in the item pool stem from instruments deemed relevant by the clinicians, who had developed or applied the instrument to patients with knee disease; and therefore, the criteria established for face validity, as defined by Mosier [120], were fulfilled.

6.4 Justification of Conclusion

The 157 items of unique content as identified in this study possess face validity for patients with knee pathology because they have been extracted from PRO instruments used by clinical experts for this purpose. Because the items have been removed from the context of their original instruments, there can be no preconceived bias towards use of one or another PRO.

Item reduction from the gross item pool of 539 items to 157 items of unique content was carried out by assessment of the core content theme of each item. Content redundancy was determined by inspection of the meaningful topic of the item statement within the sentence structure and by comparing the content across instruments on an item-by-item basis. The items were stripped of their grammatical structure and syntax, which enabled avoiding the translation of each PRO to Danish. Two German PROs, the XSMFA[203] and the OAK,[204] were included. A bilingual expert in German and Danish was used to extract the meaningful content of the items. All other PROs consisted of English or Scandinavian worded versions, which considerably eased content interpretation. Also, the response options were removed from the items, which precluded any difficulties with ambiguous response themes. Determination of when items are redundant in terms of content may not always be straightforward.

6.5 Contribution to Current Knowledge

The method of determining content redundancy by truncating item statements and translating the overall basic meaning of the item into the target language (Danish, in this case) is novel. The method is useful, in that, the number of included instruments, domains, and items cannot feasibly warrant translation of all the included patient-related instruments. The item pool can be used as a core set of items to generate various PROs for ligament and cartilage conditions of the knee.

7. Article 2 (in review)

Symptoms, function, and psychosocial consequences in patients with anterior cruciate ligament deficiency: Development of a condition-specific questionnaire

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ABSTRACT

Study Design: Qualitative study using focus groups and single interviews to construct a patient-related outcome (PRO) questionnaire with content confirmed to be relevant for patients pre- and post ACL-reconstruction.

Objectives: To construct a condition-specific PRO appropriate for use in longitudinal assessment of patients pre- and post ACL-reconstruction.

Background: PRO scores are increasingly used to assess treatment effects in patients with anterior cruciate ligament (ACL) deficiency. Valid measures of specific conditions depend on relevant item content. While items in PROs can be generated from the perspective of clinicians and patients, item relevance and comprehensiveness can only be confirmed by the patient.

Methods: Focus group and single interviews were conducted with patients scheduled for ACL-reconstruction and patients post ACL-reconstruction. Item sources included focus groups and single interviews, and a pool of 157 items derived from a systematic literature search of knee-specific questionnaires. The ICF was used as a conceptual model for the constructs of symptoms, function, and psychosocial consequences.

Results: Content saturation was achieved after 3 focus groups and 7 single interviews. Thirty-eight of the 157 items from the literature search were directly endorsed and five modified items were endorsed. Twelve new items emerged. The result was a 55-item pilot questionnaire consisting of 6 conceptual domains, two of which consisted of new item content.

Conclusion: We have constructed condition-specific PRO for use in longitudinal assessment of ACL deficiency. The questionnaire possesses face and content validity. The psychometric properties and construct validity must now be confirmed using appropriate statistical models.
xxxxxxx xxxxxx xxxxx xxxx;xx:xxx-xxx.

Key words: *acl, content validity, condition-specific, icf, pro*

INTRODUCTION

Current measurement tools used to assess outcome in patients with anterior cruciate ligament (ACL) deficiency fail to find differences in treatment effect when used to compare the efficacy of different interventions.(1) When just 50%-70% of ACL deficient athletes regain full pre-operative levels of activity,(1;2) the necessity for better results and valid methods to measure these results is obvious. Rupture of the ACL is the second most common knee ligament injury in Western civilisation.(3) It significantly affects knee function and increases the risk of knee osteoarthritis (OA).(4;5) Nearly one quarter of all patients with knee OA have an ACL rupture in that knee, (6) and ACL-reconstruction is one of the most commonly performed knee surgical procedures in modern society.

Increasingly, the validity of outcome measures commonly used in clinical trials is being challenged.(1;7;8) The need for improved outcome measures has been emphasised, particularly when patient-related outcome (PRO) questionnaires are used as endpoints.(1) Confirmation that questionnaires in fact measure what they intend to measure is essential for meaningful interpretation of treatment results. PRO questionnaires used to assess outcome in patients with ACL deficiency have historically not been rigorously validated.(9-12) This notwithstanding, PROs now play a major role in clinical outcome and treatment efficacy assessment.(11) Snyder-Mackler and Risberg point out in a recent editorial the need for quality longitudinal studies of large cohorts to ascertain which patients need ACL surgery.(13) But such studies require rigorously developed and validated outcome measures, particularly when patient-reported measures are used as clinical endpoints. The use of unsubstantiated PROs as primary endpoints in clinical trials is unwarranted. The validity of results stemming from these trials is questionable. This subject has recently been the object of rather considerable debate.(11;14;15)

In order to conduct longitudinal within-group studies or between-group comparisons of the effect of different treatment modalities, the PRO must be specifically relevant for the targeted patient group.(16) The following definition of a PRO underlines the importance of this point. A PRO can be characterized as “any report coming directly from subjects without interpretation of the physician or others about how they function overall or feel in relation to a condition and its therapy.”(17) Thus, the objective of the PRO is to measure latent constructs (latent variables) not directly measurable by the clinician, such as symptoms, or a patient’s perceived ability to carry out functional tasks.(18;19) Constructing PROs that actually measure attributes of clinical importance requires rigorous qualitative and quantitative research methods.(14;17;20-23) Establishing meaningful constructs involves generating questions that address truly relevant concepts for the targeted patient groups.(16)

Constructing PROs

In questionnaire development and psychometric assessment, questions are referred to as items. Items consist of a topic (the item theme or statement) and a number of response options for that topic. Reponses can be dichotomous (e.g., agree/disagree or yes/no), or polytomous (e.g., none/a little/a lot) depending on what response structure is deemed appropriate by the target group. There are essentially two sources for deriving item themes (item content) in questionnaires: The clinician (the “clinical expert”) and the patient (the “condition expert”). Items generated from the clinician are said to possess “face validity”, implying that the measurement instrument is ”considered to be valid if the sample of items appears to the subject matter experts to represent adequately the total universe of appropriate test questions“.(24;25) Hence, face validity addresses the condition from the perspective of the subject-matter experts. Whether the content of the subject matter is relevant and comprehensive for patients with a specific condition can only be confirmed by the patient group itself. (21;26) Content relevance and content coverage are the foundation of content validity.(16)

A disadvantage of many generic health status instruments is that they include items not applicable to specific health conditions.(27) Problems of non-applicability are avoided and face and content validity maximized by deriving item content from relevant sources, thus ensuring the instrument specifically addresses the condition of interest.(25;28;29) Regardless of whether items originate from experts or from patient interviews, feedback from the targeted patient-group is mandatory in order to confirm content validity.(21;25;29;30)

Aim

The purpose of this study was:

1. to construct a PRO questionnaire specifically for patients with ACL-deficient knees and patients post ACL-reconstruction for use in pre-post longitudinal clinical studies, and;
2. to generate the content of the questionnaire using existing knee-specific PROs, and if necessary, develop new items specifically relevant for patients with ACL deficiency.

METHODS

A systematic literature search was performed earlier in order to identify questionnaires with relevant items for ACL outcome assessment. The scope of the search was broadened to include questionnaires used to assess outcome in patients with intra-articular knee cartilage and ligament injury. This was to maximize the capture of possibly relevant item content for ACL deficiency. Thirty-one questionnaires were included in the review (Appendix 1). These instruments contained in total 539 items, which were reduced to 157 items of unique content (Appendix 2). A complete description of the methods and results of the search is presented in Comins et al (in review).(31)

Following the assembly of the item pool generated from the literature search, group interviews were conducted with patients at three different stages of surgical treatment for ACL-deficiency. The first group was 2-3 weeks prior to scheduled ACL-reconstruction, the second group consisted of patients, who were approximately 6-months post ACL-reconstruction, and the third group were patients, who were at least two years post reconstruction. Patients in the pre-operative group were identified from the ACL-reconstruction waiting list at Bispebjerg Hospital. Patients in the two postoperative groups were found in the postoperative ACL-reconstruction database at Bispebjerg. For each group, invitations were sent to a convenience sample of the first 10 persons who met the inclusion criteria, as between 4 and 8 patients were desirable for interviews.(32) The objectives of the patient sampling were to include as diverse a spread of patients in terms of age, gender, race, and social background as possible. Native Danish language proficiency was mandatory. Inclusion criteria for the pre-operative focus group (group 1) were clinically and/or para-clinically confirmed ACL rupture and scheduled surgery within a three-week timeframe. The inclusion criterion for the two postoperative groups was isolated ACL-reconstruction approximately 6 months prior to the interview (group 2) and at least two years prior to the interview (group 3). Exclusion was concomitant injuries to other structures of the knee (e.g., other ligaments, cartilage injury greater than grade 1, meniscus repair requiring postoperative bracing), and serious postoperative complications such as arthrofibrosis or infection.

The focus group interviews were *semi-structured* and lasted roughly two hours. They consisted of two parts. The first part involved a more *open-ended* discussion of topics within the realms of *Symptoms*, *Activity Limitations*, and *Psychosocial Consequences* as related to ACL deficiency or postoperative issues. The conceptualization of symptoms, activity limitations, and psychosocial consequences was based on the WHO ICF model of classification of impairment and function in which the constructs of Impairment (symptoms), Activity Limitations (functional deficits), and Participation Restrictions were viewed as outcomes of interactions between health conditions (diseases and disorders) and contextual factors (personal and environmental).(33;34) The 157 items generated from the literature search had prior to the group interview been grouped into the ICF domains. These domains were used by the group moderator to guide discussion. When specific items (or item topics) from the literature search were mentioned during the open-ended discussion, the item was noted and ticked off on the list.

The second part of the group interview began with a summarization and discussion of items mentioned in the open discussion to confirm their relevance. Then participants were confronted with the items from the literature search which had not surfaced in the open-ended discussion and asked to discuss the relevance of all the items. Thus, all items were individually probed in order to confirm which items could be endorsed. One person at least had to endorse an item topic for it to be considered relevant. The item was then included in a cursory questionnaire and presented to the participants of subsequent interviews. Special care was taken to avoid professional jargon and ambiguous wording when generating item statements in the cursory questionnaires.(16;35) In the latter focus groups, the participants were asked in the second part of the interview to complete the cursory questionnaire and comment on the wording, instructions, and ease of completion. Thus, respondents were asked to complete a questionnaire, which included changes resulting from the previous interview.

Cognitive Interviewing techniques were used on an item-by-item basis to address content relevance, content coverage, and understandability.(36;37) *Verbal probing* was used to address comprehensiveness and response category preferences.(16;38-40) Probing phrases included “Try to put in words how you feel,” or “Explain what problems you have, for example, in your daily life”. These interviewing techniques were used to illicit as descriptive *verbatim* responses as possible. The group interviews were audio-recorded and attended by all authors. Only one author at any given time was group moderator. J.B. was primary moderator assisted by J.C. in the second and third interviews. M.K. was passive as moderator but controlled the audio-recorder. All authors took notes for later content analysis. The audio-recordings were independently audited by the authors after each interview. Thematic analyses to determine the nature and content of the endorsed items were conducted. These themes were explored and discussed in detail in subsequent interviews. Verbatim comments from the participants were used to define new themes and constructs.(32;36;41) Also, item response option categories to address the intensity or magnitude of the constructs were probed. Finally, the analyses of the results were compared and discussed. If there was discordance between the authors, the audio-recordings were re-audited until consensus was reached. The focus groups were repeated until no further themes emerged. An overview of the focus group respondents is presented in Table 1.

TABLE 1. Description of respondents in focus groups

Group 1	Group 2	Group 3
Two men aged 24 and 25. Two women aged 28 and 43. Interviewed 2-3 weeks before ACL-reconstruction.	Seven men aged 23, 24, 27, 35, 38, and 40. One woman aged 47. Interviewed 22-27 weeks after ACL-reconstruction.	Two men aged 30 and 48. Three women aged 27, 29, and 53. Interviewed 101-181 weeks after ACL-reconstruction.

After the group interviews were concluded, single interviews were carried out with individual patients, who also were pre- and post- ACL-reconstruction. The interviews were conducted using *think-aloud* and verbal probing techniques to further test item *understandibility*, response category structure, recall period, and questionnaire layout.(36;39;40) Respondents were asked to read the entire questionnaire aloud and complete the questions while "thinking out loud." If the respondent had difficulties comprehending or answering items or critical comments on any aspect of the questionnaire, the interviewer probed the nature of the problem. The single interviews were also audio-recorded and independently assessed by the authors. Solution strategies were discussed by the authors after auditing the audio and items were modified and tested in subsequent interviews. Interviewing was stopped when no new information or problems emerged. The single interview respondents are described in Table 2. The first single interview was attended by all authors and moderated by J.B., the remaining were carried out by J.C. alone.

TABLE 2. Respondents of single interviews

Age and sex	Time span to/from operation
15 year old man	3 weeks pre-op
25 year old woman	5 weeks pre-op
22 year old man	6 weeks post-op
35 year old woman	22 weeks post-op
62 year old woman	56 weeks post-op
26 year old woman	4 weeks post-op
31 year old woman	9 weeks post-op

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RESULTS

Forty-two items from the assembled item pool were endorsed by participants in the first group. Thirty-eight items were directly endorsed and five items were modifications of the themes from the item pool. Clearly, the most important issues for the preoperative patients were symptoms and functional limitations, particularly in ADL and recreational tasks. Existential aspects such as job security, social isolation, and worries about lifestyle and family activities were also endorsed. Other existential aspects such as romantic and sexual dysfunction due to knee problems were probed and found irrelevant. The concept of “giving way” was endorsed by the first group. However, when it was rigorously probed in subsequent interviews, the participants could not agree on the meaning. Therefore, the item content was later “un”-endorsed. The term giving way was found to be too abstract and ambiguous. Through in-depth discussion and probing, giving way emerged to reflect the sensation of “lack of control,” or not being able to “trust” or “depend” on the knee during movement. These themes were thus used to drive the formulation of new items, which fall under the theme of “looseness” in the final version of the questionnaire (Table 3). The item “horseback riding” was endorsed by the first group. However, as one of the participants of the group was an elite equestrian, which clearly influenced the group, the item was found irrelevant in all subsequent interviews and discarded. Range of Motion items such as bending or straightening the knee fully, and stiffness were not strongly endorsed but enough to be included in the cursory questions for further assessment in subsequent interviews. Specific sports activities were not endorsed, as they were not relevant for all patients. No new item topics emerged from the first focus group.

The participants in the second group interview generated new concepts. The verbatim terms in Danish for the constructs were *slaphed* and *løshed*, which in English might be translated to slackness and looseness. One verbatim statement translated from Danish was analogous to: “It’s such a drag walking around with a knee that feels so slack all the time." The other participants concurred and went on to describe the feeling as a sensation of "fuzziness" or "mushiness" in the knee while performing knee exercises. The sensation coincided with "shakiness" when exercising, or balancing on the injured leg. "The knee feels mechanically stabile, but you just aren't sure it will hold up" is another verbatim statement. The group also agreed that the sensation was most pronounced early in the postoperative rehabilitation regimen, and had diminished over time with balance and strength training. Six items with similar themes were endorsed by subsequent participants to form the construct "Slackness," as can be seen in Table 3. In addition, a group of five items dealing with "lack of knee control" and "trusting the knee" were grouped together to form the construct of "Looseness" (Table 3). Several subjects in Group 2 maintained that stiffness and pain were important, and bending down to pick something up off the floor was clearly preferred to "squatting" because of the discomfort of full weight-bearing knee flexion.

The third focus group recognized and endorsed the slackness and looseness constructs as well as the other items and constructs endorsed in Group 2. There was greater focus on longer-term considerations such as timing of return to "all-out" activity and how much the reconstructed knee could be "depended upon" or "trusted.". Focus group 3 was instrumental in resolving issues of item readability, choice of wording, negatively versus positively posed questions, and so on. One issue of discussion was whether to refer to the ACL deficient knee as "the bad knee", "the injured knee", or "the sick knee" (a term used colloquially in Danish). Verbal probing revealed that "injured" and "healthy" knee were generally endorsed by patients pre- and postoperatively. Response categories for functional activities were rigorously addressed in focus groups 2 and 3. For example, for items such as "difficulty bicycling" and "difficulty dancing", some respondents in the second group endorsed four categories; "none at all", "yes, a little", "yes, somewhat, "yes, a lot". However, these were found inadequate for those patients who had not attempted these activities due to injury or who did not participate in these activities on a habitual basis. Thus, the response category of *non-applicable* was added to these and other items with similar response issues. The response categories were endorsed by the third group. No new item topics emerged in the third group and thus the focus group interviews were terminated.

Fifty-four items were deemed relevant by the end of the third group interview and a draft questionnaire containing these items created for further content validation in single interviews. The single interviews revealed that respondents endorsed all items in terms of content coverage and relevance, as well as layout and "understandability" of the pilot questionnaire. However, there were issues to resolve. One problem that surfaced was the concept of "avoidance of sport".

Originally the construct consisted of several discrete items “avoidance of sport due to pain” (the response options were yes/no), and “avoidance of sport due to swelling”, and several other topics. However, some patients in the single interviews reported that they only avoided certain sports. Through cognitive probing in the interviews and discussion in the author group, the strategy chosen was first to create a single item (item 40 in Table 3) consisting of “avoidance of all sport”, “avoidance of some sports”, and “no avoidance of sport at all”. The respondent is instructed to mark one of these responses. Then, the next five questions ask if the patient has avoided sport for different reasons as expressed in the focus groups 2 and 3, for instance due to pain, swelling, and so on. The response options of yes/no were employed. This item content and response structure was subsequently endorsed by the remaining single respondents. As the topics were sports-related, we elected to place the items in the Sports/Rec domain (Table 3). At the conclusion of the single interviews, we had 55 items in all.

In the group interviews, items addressing the concepts of “instability”, “laxity”, and “giving way” were closely related to “lack of control”, “not trusting the knee”, “sense of tiredness”, and the new themes of “looseness” and “slackness”. These items were endorsed for content relevance. The single interview respondents were probed to test specifically which items they thought should be grouped together, as this would constitute a domain or construct. This resulted in the division of the Symptoms domain into three separate domains; “Symptoms” (13 items), “Looseness” (5 items), and “Slackness” (6 items). Three other constructs were proposed and endorsed covering activity, “ADL” (10 items), “Sport/Rec” (16 items), and “Psychosocial” (5 items). The distribution of items into the separate domains was determined by probing and feedback from respondents in the focus group and single interviews.

Of the 157 items from the original item pool (Appendix 2), thirty-eight items were directly endorsed by the patients and integrated into the instrument, and 5 items were in some way modified. Twelve items were of original content. An example of item modification was the response options of items “Bend knee fully” and “Straighten knee fully” in the Symptoms domain were changed from polytomous to the dichotomous response options of yes/no based on focus group and single interview feed-back. Thus, the final version of the PRO encompasses fifty-five items distributed across 6 domains. Table 3 shows the items grouped into domains.

TABLE 3. The 55 items distributed in 6 domains.

ADL	Psychosocial	Looseness	Slackness	Symptoms	Sport/Rec
1. Have had difficulty walking on level ground 2. Have had difficulty walking on uneven ground 3. Have had difficulty walking down stairs 4. Have had difficulty bending down on knee to pick something up off the floor 5. Have had difficulty sitting in a chair with knee bent 6. Have had difficulty bicycling 7. Have been unable to crawl on all fours 8. Have had difficulty squatting 9. Have been unable to dance 10. Have had difficulty running	11. A mental strain not knowing when the knee would be okay* 12. A daily mental strain to make ends meet because of knee problems 13. A mental strain to make ends meet at work because of knee problems 14. A mental strain to make ends meet in family life because of knee problems 15. A mental strain not being able to participate in hobbies because of knee problems†	16. Have felt the injured knee was unstable due to lack of strength in muscles* 17. Have felt the injured knee was loose when moving around* 18. Have felt that I should monitor the injured knee when moving around* 19. Have felt that I lacked control over the injured knee when moving around* 20. Have felt that I could not trust the injured knee when moving around*	21. Have had a slack feeling in my injured knee when moving around* 22. Have spared the injured knee* 23. Have overloaded the "healthy" knee* 24. Felt shakiness in injured knee during knee exercise* 25. A sense of fatiguing more quickly in the injured leg compared to the other leg during knee exercise* 26. Difficulty balancing on injured knee during knee exercise*	27. Have had pain when twisting on the injured knee 28. Have had knee pain when walking up stairs 29. Have had knee pain when walking in uneven terrain 30. Have had knee pain after a long walk 31. Have had knee pain when sitting in a chair with bent knees 32. Have been able to bend my injured knee completely† 33. Have been able to extend my injured knee completely† 34. Have had stiffness in the knee in the evening 35. Have had stiffness in the knee in the morning 36. Have had swelling of the knee 37. Have had a feeling of lost knee control when moving† 38. Have had knee pain when jumping 39. Have had knee pain after knee exercises	40. No avoidance of sports, avoidance of some sports, or avoidance of all sports† 41. Avoidance due to restriction from MD/PT* 42. Avoidance due to pain 43. Avoidance due to swelling 44. Avoidance due to worries of new knee injury 45. Avoidance due to worries of worsening knee injury 46. Have been more cautious when playing sports 47. Have been limited when playing sports 48. Have had difficulty "going all out" when playing sports 49. Have had difficulty changing direction when running 50. Have had difficulty with sudden stops when running 51. Have had difficulty with jumping 52. Have had difficulty landing when jumping 53. Have had to reduce expectations to sport 54. Feel isolated from the people I used to do sports with before injury 55. Feel that competitive needs no longer met

Note: *Items that were generated in the focus groups are marked with an asterisk. †Items that were modified in the interviews are marked with a dagger.

Discussion

We confronted our focus group respondents with 157 items of unique content derived from preexisting PROs. Just 38 of these items were found relevant (and 5 modified items) and included in the final draft questionnaire. This might indicate that much of the item content commonly used to assess ACL patients is irrelevant, which would raise questions as to the validity of results stemming from studies in which such items have been used. However, our items originated from PROs used to assess an extended range of knee pathologies and thus were not condition-specific for ACL injury. We chose to include questionnaires commonly used to assess more general knee problems. This was done primarily because we could not find PROs specifically constructed and validated for assessment of patients with ACL deficiency. The fact that 12 new item topics emerged in the patient interviews, which were not identified, in the general literature indicates that content coverage had not previously been achieved. This also adds to the question of validity of results from previous surveys irrespective of whether the original item pool stemmed from condition-specific or anatomically specific PROs.

All 55- items and 6 domains consist of item and domain content endorsed by patients with ACL deficiency. Twelve of the items emerged in patient interviews. The items that did not were derived from existing PROs. This combination of clinician and patient item content source ensures high face and content validity. We believe the process illustrates the methodology needed to create condition-specific PROs that actually address the most clinically relevant aspects for the targeted patient group.

The interviews were semi-structured in the sense that the discussion topics were conceptually contained within the theoretical foundation of the ICF, and guided by the cognitive interviewing and verbal probing methods as mentioned above. However, the patients were encouraged to discuss freely the sensations relating to the topics. This allowed the emergence of new themes beyond those obtained through the literature search. Only four previously developed knee-specific PROs have included the process of patient confrontation, just two of these were condition-specific, and none were ACL-specific (42). Also, the fact that the items and constructs of our PRO are anchored within the framework of the ICF model places emphasis specifically on the constructs of physical impairment and functional deficit, also allowing the components of participation, motivation, and emotional aspects to be addressed. Item content addressing these constructs are appropriate for most orthopaedic conditions such as knee injuries. For more life-threatening conditions, such as cancer, item content rooted in other paradigms, for example the “Needs-based Model”, are likely more applicable.(20;21;26)

The items and conceptual constructs that have been assembled in this questionnaire are based on 3 focus group and 7 single interviews of patients with an ACL rupture. This means that the content validation of this instrument depends on interpretation of information stemming from just twenty-three persons. Can we generalize our results based on these samples? We believe so for the following reasons: Although the respondents were convenience sampled, we feel we achieved an adequate spread in terms of age, gender, and socio-economic background. We continued interviewing until no new themes emerged (data saturation). The methods we used to determine content relevance are straightforward. If themes from the items of the literature search emerged in the discussion within the scope of the cognitive interview, then the item was endorsed. If not, the items were individually probed and either endorsed or not. Our approach towards determining relevance was to include any theme that could be endorsed by at least one person. This resulted in certain items being included that may have been discounted by respondents in subsequent interviews (e.g., horseback riding), and thus removed. In this sense, items were more readily included than excluded. For instance, the statements from one participant in favor of including horseback riding are outweighed by arguments from all other subsequent participants opposed to including the item. This combined with other clinically theoretical and contextual considerations determined removal. The group moderator was highly experienced in cognitive interview techniques, and the verbatim statements were independently assessed and compared, so we are confident that our analyses are trustworthy.(43-45)

Although the respondents belonged to a condition-specific patient group (ACL rupture), they invariably had varying degrees of concomitant damage to other knee structures at the time of injury. Some subjects had previous meniscus damage or small meniscal lesions at the time of surgery. For the pre-operative group, we confirmed by post-op medical chart audit that the patients had no major concomitant injuries to structures of the knee at the time of surgery. This was also confirmed for participants in the postoperative groups. In that sense, the sampling strategy was the same across all involved respondents. Most importantly, the patients in the pre-operative group were per-operatively confirmed to have an isolated ACL rupture at the time of the interview. Patients in the postoperative groups were also confirmed to have had isolated ACL-rupture at surgery, as this was a prerequisite for invitation to the interviews.

We sampled homogenous groups of patients (pre- and postoperative sampling groups) for the focus group interviews. This was done to center discussion on problems and experiences common for patients at each stage of treatment instead of focusing on differences between the stages. Had we mixed patients from the different stages (e.g., pre and post), or conducted interviews with patients and clinicians together, then the discussion would invariably have been more focused on between-group instead of within-group experiences and consequences. This pre-post sampling method conceptually supports the notion that the groups represent a spectrum of treatment, from pre-operative impairment to postoperative health, a point that is paramount for this study, in that the questionnaire is designed for use in pre-post longitudinal studies.

Another point of emphasis is the concept of generating items for questionnaires based on verbatim statements from the target patients. We believe this is crucial in order to ensure that patients with that particular condition will understand and be able to “relate to” the question being posed.

Also a weakness with this study is that we have not differentiated between the surgical techniques used for reconstruction in our samples. Hamstring (Semi-T/Gracilis) and Bone-Patella-Tendon-Bone graft techniques are both standard procedures at our department. There are clearly short-term postoperative differences in terms of symptoms for these patients, for example due to graft site morbidity. We argue, however, that at six months post-surgery, the time of the first postoperative group, these differences should be negligible, unless the patient had experienced postoperative complications, in which case he/she was precluded from being invited to participate.

A point of discussion is how specific items were designated to certain domains. For example bicycling was placed in the ADL domain instead of Sport/Rec, which in this case is due to Danish cultural norms. Bicycling is a primary form of transportation in Denmark. The majority Danes depend on a bicycle in daily life, clearly not the case in other cultures. This notwithstanding, cross-cultural differences are not a straightforward issue. We specifically asked our participants where they believed items belonged. Thus, items were placed in domains the patients felt were appropriate. Based on group discussion and probing, particularly in the single interviews, we came to these conclusions. However, the response option of “not applicable” was added to certain items to allow the possibility of a neutral answer, in case the activity or task had for whatever reason not been attempted.

The domains are conceptually rooted in the ICF model encompassing Impairment (symptoms), Activity (function), and Participation (psychosocial themes). The two new domains of Slackness and Looseness were clearly related to bodily functions and thus symptom-related. However, the items of these two domains were a challenge to place into the one or the other domain, as the domains are conceptually quite close. We used the single interviews to test the item-domain relationship by writing the names of the items on small slips of paper and the names of the domains on two separate large pieces of paper. The participants were then asked to physically place each item on the piece of paper with the domain they thought was conceptually most appropriate. There was not always agreement between respondents, so the items were distributed to the domain the majority of respondents had chosen.

CONCLUSION

We have constructed a questionnaire specifically for patients with ACL deficiency and ACL-reconstruction. The instrument possesses face- and content validity. The final stage of validation is to confirm the psychometric properties of the six suggested constructs on a larger cohort of the same type of patients as our respondents. This construct validation will be carried out using Rasch analysis.(11;16;28;46-53) Although the Rasch model has been used to assess dimensionality of knee-specific PROs,(54;55) it has not been used to construct scores targeting patients with ACL rupture. Other issues to be resolved using Rasch analysis are differential item functioning (DIF), particularly with respect to group factor (pre-op vs. post-op). DIF means that an item does not function the same way in two or more different groups, for instance diagnostic group, gender, or social status.(32;41;56)

This PRO exists only in Danish. Once the questionnaire has been shown to satisfy the requirements of fundamental measurement in Danish patients, it will be translated to English using appropriate 2-panel methods,(29) and cross-cultural validation will be carried out also using the Rasch model.(41;56) The English translation of the truncated items are shown in Table 3. It is important to note that these items cannot yet be used, for although the primary author is a native English speaker and fully bilingual, the translation from Danish to English is informal at best. A perfunctory English version of the entire questionnaire can be seen in Appendix 3, and Appendix 4 shows the Danish version to be used for field-testing in Denmark.

Key Points

Findings In this study, we describe the construction of a condition-specific PRO questionnaire that consists of item and domain content confirmed to be relevant for patients scheduled for and subsequent to ACL-reconstruction.

Implication The next step is to assess the psychometric properties using Rasch analysis in to order to test the hypothesis that construct validity depends on relevant and comprehensive item content. If construct validity can be established, the PRO can be used for measurement of patient-related outcomes in pretest-posttest longitudinal studies.

Caution The PRO generated in this study cannot be used on the target patient group until the psychometric properties of the items and constructs are confirmed.

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8. Discussion of article 2

8.1 Major Findings

Of the 157 items of unique content from the literature search of non condition-specific PROs, fifty-two items from the initial item pool were endorsed by the first focus group. The most important issues confirmed in the patient interviews were symptoms, functional limitations (particularly in ADL and recreational tasks), and existential aspects such as job security, social isolation, and worries about lifestyle and family activities. Other existential themes such as romantic or sexual dysfunction due to knee problems were found irrelevant. Several new item topics emerged in the second focus group interview. These were endorsed by subsequent respondents. “Slackness” and “Looseness” were verbatim terms that were closely related to other symptoms and activity items, which were grouped around the verbatim items to form separate constructs. In all, fifty-five items spanning six suggested-constructs were found to cover the spectrum of outcome for the target patient group. These items and constructs were used to assemble a pilot questionnaire for field-testing and psychometric validation.

8.2 Assessment of Methods

Through an extensive literature search, an item pool consisting of items which possessed face validity was generated. Focus group interviews in the target patient groups were used to assess which items from the pool could be endorsed. Endorsement was based on the mention of the topic in open discussion, as well as verbal probing, and then direct confirmation of all items. Certain items such as “giving way” were endorsed, but further probing in subsequent interviews disqualified these items as being too obscure and ambiguous. Items themes that were new were based on verbatim descriptions of the particular topic. These items and themes were subsequently probed, also in single debriefing interviews until the item groupings were stable. By the end of the third focus group interview, no new topics emerged, and no topics were deemed irrelevant by the respondents. Fifty-four items were distributed across six conceptual domains, which the respondents also endorsed as relevant. Single debriefing interview confirmed the content relevance of the instrument, and one more item was generated. The method of using item content from instruments previously created for patients with knee problems is a viable means of generating possibly relevant item content. Cognitive interviewing techniques on an item-by-item basis to address content relevance, content coverage, and comprehension are highly effective in conjunction with verbal probing. Item content generated based on verbatim expressions seems to be an effective tool.

8.3 Justification of Conclusion

The resulting 55-item PRO questionnaire consists of item and domain content endorsed by clinicians and by patients with ACL deficiency. This combination of content sources is constructive and necessary as a basis for the creation of PROs that measure constructs most important to the target group. The major strength of this study is that face validity and content validity of a condition-specific instrument are ensured by combining qualitative techniques. The interviews transitioned from open-ended to semi-structured, although they were never completely open-ended because items from existing instruments and the ICF model were used as a type of interview framework. This allowed for the emergence of new themes beyond those obtained through the literature search, thus satisfying the aspect of content validity known as content coverage, or comprehensiveness. In general, patient confrontation is sparsely used in the development of knee-specific and condition-specific PROs, particularly concerning ACL-specific instruments.[205] Also, the fact that the items and constructs are anchored within the framework of the ICF model places emphasis specifically on the constructs of physical impairment and functional deficit, and allows the components of participation, motivation, and emotional aspects to be included.

8.4 Contribution to Current Knowledge

Of the original 157 items, 43 items were endorsed by the respondents and twelve new items emerged. Thus, 55 items confirmed to be relevant and comprehensive for patients with ACL deficiency and patients with ACL reconstructions are presented. The twelve new items consist of content based on verbatim expressions in patient interviews. Six domains addressing constructs of ADL, Psychosocial consequences, Looseness, Slackness, Symptoms, and Sport/recreational activities have been assembled. The constructs possess face and content validity for Danish patients with ACL deficiency and ACL reconstructed knees. These domains require psychometric assessment through pilot testing to confirm construct validity.

9. Article 3 (in review)

Measuring Symptoms, Function, and Psychosocial Consequences of Anterior Cruciate Ligament Deficiency: Development and Validation of a Condition-specific Questionnaire

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Abstract

Background: Rupture of the anterior cruciate ligament (ACL) causes some patients to experience knee instability during functional tasks. Treatment strategies are mainly based on consensus and not necessarily scientifically well-founded studies. Conventional criteria for ACL-reconstruction are being countermined on the basis of patient-reported outcome (PRO) questionnaires. However, valid interpretation of results based on PROs requires rigorous confirmation of the psychometric properties of the PRO. Moreover, PRO questionnaires are increasingly used as primary endpoints in clinical trials. Rasch analysis is considered to be the most stringent method to validate questionnaires. No questionnaire for assessment of patient-related outcome in ACL deficiency has been generated and validated using Rasch analysis.

Aims: The objective of this study was to use Rasch analysis to investigate the psychometric properties of a newly developed 55-item PRO questionnaire for use in patients before and after ACL-reconstruction.

Method: Through a literature search and focus group interviews with patients pre- and post ACL-reconstruction, a 55-item pilot questionnaire was generated. The psychometric properties of the questionnaire were assessed using Rasch models. Unidimensionality, local response dependency (LD), and differential item functioning (DIF) was scrutinized in 242 patients with confirmed isolated ACL-rupture. These patients were pre- and post ACL-reconstruction.

Results: Fourteen of the 55 items were removed due to statistical lack of fit and face validity departure. LD and DIF were identified and accounted for. Seven unidimensional constructs consisting of 41 items measuring different aspects of impairment, functional limitations, and psychosocial consequences were confirmed.

Conclusion: The knee numeric-entity evaluation score (KNEES-ACL) is the first Rasch-validated condition-specific PRO constructed for assessment of patients with ACL-deficiency.

Background

Anterior cruciate ligament (ACL) rupture is the most prevalent knee ligament injury in western civilisation[20, 22, 23] and is known to increase the risk of knee OA.[16, 34] Treatment of anterior cruciate ligament deficiency (ACLD) consists of conservative rehabilitation or surgical reconstruction of the ligament with subsequent rehabilitation.[38] Approximately 25% of patients with ACLD are so-called *copers* who achieve asymptomatic pre-injury levels of activity without surgical intervention.[1, 15, 21, 40] *Non-copers* experience mechanical knee instability during sometimes even low-demand functional tasks such as walking, increasing the risk of meniscus and other intra-articular knee lesions. Consensus is that ACL-reconstruction mechanically stabilizes the knee and diminishes this risk.[28] Thus, approximately 75% of patients with ACLD should be candidates for reconstruction. However, this criterion was recently undermined when delayed surgical treatment was compared to early ACL-reconstruction using a modified version of the Knee-injury and Osteoarthritis Outcome Score (KOOS) as the primary endpoint.[11] The study found no significant between-group difference in summary scores between the groups 2 years after inclusion, and thus it was concluded that ACL-reconstruction is no more efficacious than conservative treatment. However, the psychometric properties of KOOS, a widely used patient-related outcome (PRO) questionnaire, have been shown to be insufficient to measure outcome in patients post ACL-reconstruction,[11, 12, 30] and in fact, the measurement characteristics of many questionnaires can be questioned.[52]

When used to measure outcome in clinical trials, questionnaires must exhibit just as adequate metric properties as physical measures, if the results are to be considered meaningful and valid. PROs measure perceptions, attitudes, and attributes that are not directly observable, so-called latent traits. Therefore, the demands on PROs to yield valid measurement are stringent, as PROs must be confirmed to be robust. The advantage of PROs is that they address the patient's own perception of function and level of treatment success.[14, 35] The U.S. Food and Drug Administration (FDA) recommends the use of PROs to reflect "how much pain patients feel, how depressed they are, how well they sleep at night, or whether they have enough energy to walk up a flight of stairs."[42] While the use and influence of PRO's has substantially increased in recent years,[48] the validity of PRO instruments as viable outcome measures for use in patients with ACLD has been questioned.[29, 52] Clearly, when a person's own perception is to be used as a primary endpoint to measure outcome, the metric properties of the measure must be established.

Psychometric properties

PRO questionnaires have traditionally been validated within the framework of Classical Test Theory (CTT). This involves methods such as exploratory factor analysis and Cronbach's alpha.[47] However, CTT methods are insufficient to establish validity of PROs,[7, 8, 12, 30] partly because these methods assume parametric data structure and normal distribution. Item responses from questionnaires are by definition categorical entities, and are thus inappropriate for CTT analysis.[32, 33, 50] Moreover, CTT does not address fundamental assumptions of construct validity, such as *unidimensionality*, *additivity*, *specific objectivity*, and *invariance of measurement*.[7, 51] Item responses in PROs are assigned numerical values, which are then summed. *Summary scores* must be unidimensional in order to quantify score changes.[3, 12] This applies to single-scale instruments and individual scales within multidimensional instruments.[6] It is now accepted that *item-response theory* (IRT) is the most appropriate method to establish measurement properties of PROs.[46, 49] Analyses using the Rasch models of IRT explore the degree to which items response scores in a questionnaire can be summarized into a statistically sufficient index providing *objective measurement*. [37152152152152151150150150150150] Such indices are independent of arbitrary choices made during the design of the questionnaire, and any study in which the scale is used[45, 46]. Items sets and individual items that fit a Rasch model will satisfy the basic criteria of fundamental measurement, thus allowing invariant comparisons.[46] The Rasch models are the most stringent of IRT models. A thorough comparison of IRT and CTT methods can be found in Table 2 of Turk, et al.[47]

Item generation

Although Rasch analysis is a powerful tool for construct validation and item reduction, it does not address the root qualitative processes of item generation. Item content must reflect meaningful constructs for the target group to yield meaningful measurement.[6, 13]*Meaningfulness* and *understandibility* of items for the targeted population is a primary requirement for item quality. A disadvantage of generic health status instruments is that they include items that do not apply to specific health conditions.[6] *Condition-specific* PROs with content derived from relevant sources will ensure that the instrument specifically addresses the condition of interest, and thus problems of non-applicability can be avoided, and face and content validity maximized.[7, 41, 44] Relevant sources include clinical experts and the patients themselves. Data collection and sampling methods include literature review, focus group interviews, and individual cognitive debriefing interviews.[31] Regardless of whether the item content originates from experts or from patient interviews, endorsement of all items from the patient group is essential in order to ensure content validity.[41, 44] Thus, once face and content validity of the condition-specific PRO are established, the dimensionality of the metric constructs must be confirmed. Rasch analysis has not been used to construct and validate condition-specific PROs for patients with ACLD or patients post ACL-reconstruction. Unidimensionality must be confirmed on pre- and post-operative patient groups for the PRO to be appropriate for pretest-posttest longitudinal studies.

The *a priori* hypothesis was that by deriving item content from existing PROs and the targeted patient group(s), and then through qualitative confirmation of content relevance and coverage of the items; that a condition-specific PRO could be generated, which exhibited adequate psychometric properties as confirmed by Rasch analysis.

Objective

The objective of this study was to use Rasch analysis to assess the psychometric properties of a newly created condition-specific PRO for use on patients with ACL deficiency and patients with ACL reconstructed knees.

Methods

Development of item pool

We derived the content of the PRO from the following relevant sources a) literature review, b) patients awaiting ACL-reconstruction, and c) patients who had received an ACL-reconstruction. The systematic literature search was conducted to identify all PROs used to assess self-reported outcome in patients with knee disease.[13] The search yielded 31 PROs with 539 items in total. Of these, 157 items of distinct content emerged.

Focus group and single interviews were then conducted to confirm the content relevancy and to assess content coverage of the items from the literature search. Participants invited to the interviews were patients at three different time-phases of treatment: Group 1 - patients scheduled for ACL-reconstruction; Group 2 - patients who had undergone isolated ACL-reconstruction approximately 6 months prior to the interview; and Group 3 - patients who had undergone isolated ACL-reconstruction at least two years prior to the interview. Forty-three of the 157 items from the item pool were endorsed by the respondents of the focus groups, and twelve new item themes were generated. This resulted in a 55-item pilot questionnaire with items distributed across six domains. Table 1 shows the items and domains of the provisional questionnaire. The domains were *activity of daily living* (ADL) (10 items), *psychosocial aspects* (5 items), *looseness* (5 items), *slackness* (6 items), *symptoms* (13 items), and *sport- and recreational activities* (Sport/Rec) (16 items). Looseness and slackness are verbatim terms that emerged in the second focus group interview to describe sub groups of items in the symptoms or physical impairment category. The qualitative process and creation of the instrument is described in a previous study.[10]

TABLE 1. The 55 items distributed across the 6 theoretically derived domains.

ADL	Psychosocial	Looseness	Slackness	Symptoms	Sport/Rec
1. Have had difficulty walking on level ground	11. A mental strain not knowing when the knee would be okay	16. Have felt the injured knee was unstable due to lack of strength in muscles	21. Have had a slack feeling in my injured knee when moving around	27. Have had pain when twisting on the injured knee	40. No avoidance of sports, avoidance of some sports, or avoidance of all sports
2. Have had difficulty walking on uneven ground	12. A daily mental strain to make ends meet because of knee problems	17. Have felt the injured knee was loose when moving around	22. Have spared the injured knee	28. Have had knee pain when walking up stairs	41. Avoidance due to restriction from MD or PT
3. Have had difficulty walking down stairs	13. A mental strain to make ends meet at work because of knee problems	18. Have felt that I should have constant focus on the injured knee when moving around	23. Have overloaded the "healthy" knee	29. Have had knee pain when walking in uneven terrain	42. Avoidance due to pain
4. Have had difficulty bending down on knee to pick something up off the floor	14. A mental strain to make ends meet in family life because of knee problems	19. Have felt that I lacked control over the injured knee when moving around	24. Felt shakiness in injured knee during knee exercise	30. Have had knee pain after a long walk	43. Avoidance due to swelling
5. Have had difficulty sitting in a chair with knee bent	15. A mental strain not being able to participate in hobbies because of knee problems	20. Have felt that I could not trust the injured knee when moving around	25. A sense of fatiguing more quickly in the injured leg compared to the other leg during knee exercise	31. Have had knee pain when sitting in a chair with bent knees	44. Avoidance due to worries of new knee injury
6. Have had difficulty bicycling			26. Difficulty balancing on injured knee during knee exercise	32. Have been able to bend my injured knee completely	45. Avoidance due to worries of worsening knee injury
7. Have been unable to crawl on all fours				33. Have been able to extend my injured knee completely	46. Have been more cautious when playing sports
8. Have had difficulty squatting				34. Have had stiffness in the knee in the evening	47. Have been limited when playing sports
9. Have been unable to dance				35. Have had stiffness in the knee in the morning	48. Have had difficulty “going all out” when playing sports
10. Have had difficulty running				36. Have had swelling of the knee	49. Have had difficulty changing direction when running
				37. Have had a feeling of lost knee control when moving	50. Have had difficulty with sudden stops when running
				38. Have had knee pain when jumping	51. Have had difficulty with jumping
				39. Have had knee pain after knee exercises	52. Have had difficulty landing when jumping
					53. Have had to reduce expectations to sport
					54. Feel isolated from the people I used to do sports with before injury
					55. Feel that competitive needs no longer met

Pilot-testing

The provisional questionnaire was completed by 242 patients identified from the ACL-registry database at Bispebjerg Hospital. The respondents consisted of patients from approximately the same category groups (or stages of treatment) as the patients in the qualitative interviews:

Group 1 consisted of 62 patients scheduled for ACL surgery tested within 3 weeks of their scheduled surgery. All respondents in this group were post-operatively confirmed to have an isolated ACL rupture.

Group 2 consisted of 87 patients who were between 4 and 16 months post isolated-ACL-reconstruction. These patients were included if they had an uncomplicated postoperative course of treatment and were finished with, or finishing the scheduled rehabilitation regimen.

Group 3 consisted of 93 patients who were at least 28 months post isolated- ACL-reconstruction. These patients avoided contact with clinical hospital system (due to the ACL-reconstruction) since conclusion of the post-operative rehabilitation regimen and surgical follow-up. Thus these patients should theoretically be stable in terms of the condition of injury and post operative effects of surgery. Table 2 shows the gender, age, response percentages, and frequency distribution of the respondents in the three groups.

Table 2. Demographics of respondents who completed the provisional questionnaire

Group	n	Gender (Freq. and %)		Agegroup (Freq. and %)		Questionnaires sent (Response %)	Excluded after inclusion
		Males	**Females**	**0-30 yrs**	**31 yrs ≤**		
Preop	62	33(53.2%)	29 (46.8%)	43 (69.4%)	19 (30.6%)	137 (57.7% responded)*	17 (12.4 %)†
4-16 months postop	87	57(65.5%)	30 (34.5%)	51 (58.6%)	36 (41.4%)	150 (58.0% responded)	0
≥28 months postop	93	47 (50.5%)	46 (49.5%)	34 (36.6%)	59 (63.4%)	167 (55.7% responded)	1 due to re-injury
Total	**242**	**137**	**105**	**128**	**114**	**454**	**18**

*Note: 79 persons in the preoperative group responded to the questionnaire, of which 17† were excluded due to concomitant knee injuries.

The primary inclusion criteria for all groups were isolated ACL rupture confirmed at surgery, and primary ACL-reconstruction using autologous bone-patella-tendon-bone (BPTB) or semitendinosis-gracilis (STG) graft, as both procedures are standard at Bispebjerg Hospital. Exclusion criteria were concomitant injuries found per operatively requiring interventions that required amendments to the post-operative rehabilitation regimen (e.g., weight bearing restrictions, chondral lesions exceeding grade 1, meniscal repair with fixed bracing to restrict knee range of motion, or post-operative infection).

Statistical analysis of dimensionality

Misfit of an item or subgroup of items to the Rasch model and violation of unidimensionalty indicates that the item belongs to a separate theoretical dimension than was projected. The goal is to retain as many content-valid items as possible, for valid measurement; yet also weed out information that belongs to other dimensions. Other than multidimensionality, two important sources of misfit include differential item functioning (DIF) [5, 8, 18, 43] and local response dependency (LD).[9]

DIF is an item bias where responses to items are uniformly different[*] due to *exogenous* person factors such as gender, culture, or age group. DIF items can be split into so-called virtual items to calculate the magnitude of difference in raw sum-score for the groups. The score in the one subgroup relative to the other can then be adjusted after data collection. The procedure is known as DIF-equating.[8]

Local response dependency (LD) is another anomaly associated with violations of unidimensionalty. LD arises when a response on one item depends on the response of another item. For example, the SF-36 physical function dimension contains the item *walking one block* (PF9), and the item *walking several blocks* (PF8). Affirmation of PF9 is conditionally dependent on PF8. Thus, the information in PF9 is in some degree redundant. Fundamental measurement requires that items measure separate aspects of the same underlying construct – the items must be conditionally independent. [9, 25] LD is particularly common in generic health scales, even when items appear to be valid.[27] Locally dependent items can be combined into so-called *super items* or *composite items* by adding item interaction terms to the model, which allows them to be treated as summed item scores in a Rasch model.[26]

In this study, overall model fit and assessment of DIF was evaluated using Andersen's conditional

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[*] For uniform DIF. Non-uniform DIF is more difficult deal with as this indicates problems across levels as well as the covariate.

likelihood ratio test (CLR-χ^2).[2] Individual item fit to the Rasch model was assessed by conditional infits and outfits,[24] and by comparison of observed and expected correlations between scores for separate items and the summated *rest-scores* over all other items.[24, 27] Criterion validity and dependence on exogenous covariates was assessed by calculation of the degree of association between the total scores and the latent variables using Goodman & Kruskal's γ coefficient, as all variables are ordinal in response structure.[17] Exogenous covariates for overall DIF analysis were group (pre-op, 4-16 months post-op, and minimum 28 months post-op), age-group (0-30 years and 31 plus years), and gender. LD was identified using graphical loglinier Rasch models (GLLRM) [19, 27]. The Benjamini-Hochberg procedure was used to account for multiple testing.[4] All analyses were conducted first using the software program RUMM 2030 (http://rummlab.com.au). Further confirmatory analyses were carried out using DIGRAM (Department of Biostatistics, Institute of Public Health, University of Copenhagen, Denmark).

Results:

As expected, the combined set of 55 items did not fit a Rasch model. Subsequent analysis of the separate theoretically derived domains revealed 6 unidimensional constructs. The overall fit statistics for each domain are presented in Table 3. Individual item fit for all items is reported in Table 4. Specific results for each separate domain are described in the following sections.

Table 3 shows the overall fit statistics for the Rasch domains. The conditional likelihood chi-square, degrees of freedom, and the probabilities are presented.

Domain	**CLR χ^2**	**df**	***P***
ADL	26.8	41	0.957
Psychosocial	*11.9*	18	0.853
Looseness	10.9	24	0.990
Slackness	50.0	50	0.475
Symptoms (pain)	20.7	19	0.355
Sports behavior	36.5	33	0.309
Sports physical	6.0*	12	0.915

* Fit statistic calculated in RUMM 2030, which employs a weighted maximum likelihood test (MLR χ^2).

ADL overall fit statistics

Eight ADL items exhibited good overall fit (χ^2 = 26.8, df = 41, *P* = 0.957). There was marginal DIF by age-group (χ^2 = 57.3, df = 35, *P* = 0.01). Item 5 *sitting in a chair with knee bent* exhibited misfit to the Rasch model, and item 9 *dancing* exhibited DIF. These items were assessed for face validity and consequently removed.

ADL individual item fit statistics

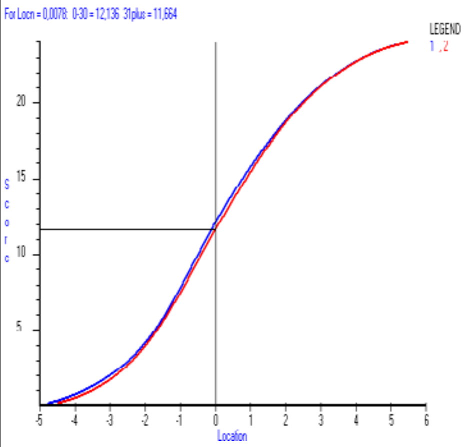
Individual item fit statistics for all items in all domains are presented in Table 4 as conditional infit and outfit statistics and observed and expected γ coefficients measuring associations between items, and *rest-scores* without items.[27] There was marginal misfit of items 7 *crawling on all fours*, 8 *squatting*, and 10 *running* (*p* = 0.03432), (*p* = 0.06206), and (*p* = 0.01990). The analysis revealed LD between 6 pairs of items, 1 and 2 *walking on level ground* and *walking on uneven ground* (lr = 47.51, df = 9, *p* = 0.0000), 3 and 6 *walking down stairs* and bi*cycling* (lr = 21.73, df = 9, *p* = 0.0098), and items 4 and 8 *bending down to pick something up off floor* and *squatting* (lr = 47.54, df = 9, *p* = 0.0000). These were combined into 3 composite partial credit items. The analysis revealed DIF of item 7 by age-group (lr = 9.98, df = 3, *p* = 0.0187), and the item was split into virtual items to calculate the magnitude of raw score adjustment. This corresponded to a maximum raw score difference of 0.37 at the midrange of the latent trait. Figure 1a shows DIF-equating for the ADL domain in a graphical rendering.

Table 4: Fit statistics of all individual items.

Scale	Item	Item statement	Outfit observed	SD	*P*	Infit observed	SD	*P*	Item rest-score observed	Gamma expected	SD	*P*
	1	Walk on level ground	0.826	0.559	0.911	0.967	0.174	0.849	0.804	0.822	0.043	0.680
	2	Walk on uneven ground	0.915	0.188	0.650	0.916	0.148	0.571	0.750	0.744	0.048	0.899
	3	Walk down stairs	0.831	0.169	0.314	0.835	0.125	0.185	0.777	0.701	0.050	0.131
ADL	4	Bend down on knee	1.350	0.261	0.179	0.952	0.123	0.698	0.815	0.801	0.032	0.659
	6	Bicycling	0.608	0.813	0.629	0.777	0.199	0.261	0.897	0.790	0.054	0.046
	7	Crawl on all fours	1.234	0.110	0.034	1.023	0.105	0.826	0.679	0.682	0.041	0.944
	8	Squatting	1.546	0.293	0.062	1.086	0.114	0.448	0.760	0.781	0.032	0.510
	10	Running	1.292	0.125	0.019	1.177	0.109	0.104	0.632	0.686	0.041	0.189
	11	A strain not knowing when knee will be OK	1.187	0.107	0.079	1.150	0.109	0.167	0.789	0.819	0.031	0.318
	12	A daily strain to make ends meet	0.618	0.199	0.055	0.711	0.132	0.028	0.905	0.849	0.030	0.059
Psychosocial	13	A strain to make ends meet at work	0.897	0.159	0.518	0.986	0.143	0.920	0.819	0.774	0.041	0.266
	14	A strain to make ends meet in family life	0.805	0.358	0.584	0.919	0.181	0.655	0.810	0.782	0.058	0.631
	15	A strain not being able to participate in hobbies	1.337	0.158	0.033	1.185	0.118	0.118	0.742	0.780	0.035	0.286
	16	Felt knee unstable due to muscle weakness	1.064	0.089	0.469	1.116	0.101	0.249	0.664	0.697	0.045	0.454
Looseness	17	Felt the knee was loose	0.916	0.119	0.572	0.935	0.110	0.554	0.829	0.809	0.033	0.543
	18	Constant focus on knee	0.912	0.096	0.361	0.927	0.101	0.466	0.759	0.726	0.039	0.393
	20	Could not trust knee	0.961	0.099	0.827	0.962	0.103	0.710	0.809	0.809	0.031	0.991
	19	Lacked control of knee	1.046	0.123	0.058	0.828	0.114	0.130	0.644	0.519	0.062	0.043
	21	Slack feeling in knee	0.910	0.156	0.768	1.045	0.131	0.729	0.629	0.630	0.056	0.973
	22	Spared the knee	0.919	0.165	0.584	0.968	0.124	0.794	0.645	0.633	0.058	0.839
Slackness	23	Overloaded "healthy" knee	1.354	0.109	0.456	0.928	0.106	0.497	0.665	0.616	0.051	0.339
	24	Shakiness in knee during exercise	1.036	0.149	0.017	1.252	0.114	0.027	0.466	0.590	0.056	0.025
	25	Fatiguing more quickly	1.018	0.112	0.747	1.022	0.110	0.843	0.566	0.607	0.056	0.460
	26	Balance on knee during exercise	0.767	0.114	0.876	0.976	0.117	0.835	0.590	0.575	0.056	0.777
	27	Pain when twisting on knee	1.153	0.115	0.182	1.232	0.120	0.052	0.721	0.760	0.038	0.299
	28	Pain walking up stairs	1.077	0.204	0.707	0.936	0.136	0.639	0.747	0.750	0.049	0.951
	29	Pain walking uneven terrain	0.896	0.194	0.594	0.765	0.128	0.066	0.806	0.742	0.052	0.215
Symptoms	30	Pain after long walk	0.859	0.115	0.221	0.842	0.122	0.193	0.769	0.715	0.046	0.239
	31	Pain sitting in chair with knee bent	1.402	0.152	0.008	1.346	0.129	0.007	0.569	0.679	0.058	0.056
	38	Pain when jumping	0.922	0.117	0.504	0.942	0.121	0.632	0.776	0.755	0.041	0.601
	39	Pain after exercise	0.879	0.134	0.364	0.911	0.137	0.516	0.802	0.759	0.046	0.346
	46	More cautious playing sports	1.190	0.122	0.120	1.162	0.123	0.187	0.747	0.776	0.035	0.401
	47	Limited in playing sports	1.313	0.191	0.100	1.196	0.131	0.135	0.800	0.829	0.029	0.310
Sport Behavior	48	Not able to “go all out” in sports	1.046	0.119	0.701	1.031	0.117	0.788	0.775	0.780	0.033	0.883
	53	Reduced expectations to sport	0.734	0.116	0.021	0.754	0.108	0.022	0.804	0.714	0.039	0.023
	54	Isolated from sports comrades	1.030	0.148	0.842	0.996	0.109	0.971	0.722	0.702	0.040	0.619
	55	Competitive needs no longer met	1.107	0.143	0.542	1.080	0.115	0.487	0.710	0.724	0.038	0.705
	49	*Changing direction when running	1.271	0.164	0.953	†	†	†	†	†	†	†
Sport Physical	50	*Sudden stops when running	0.791	0.159	0.793	†	†	†	†	†	†	†
	51	*Jumping	-1.247	0.160	0.305	†	†	†	†	†	†	†
	52	*Landing from jumping	1.270	0.302	0.795	†	†	†	†	†	†	†

Note: The significance of the fit statistics is assessed by the Benjamini-Hochberg procedurecontrolling the false discovery rate (FDR).[177] *Due to numerical convergence problems with substantial LD, fit statistics for these items were calculated solely using RUMM2030. †These test statistics are not available in RUMM2030.

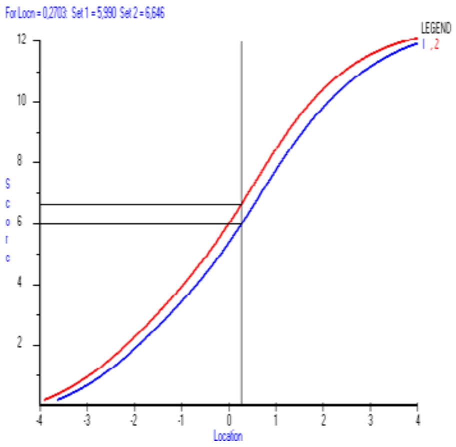
Figure 1a. DIF-equating curves for ADL by Age-group



DIF sources: Age	
0-30 yr	≥31yr
1.00	1.16
2.00	2.19
3.01	3.19
4.02	4.19
5.00	5.21
6.00	6.23
7.00	7.27
8.00	8.30
9.00	9.33
10.00	10.35
11.00	11.36
12.00	**12.37**
13.00	13.36
14.00	14.34
15.00	15.32
16.00	16.29
17.00	17.26
18.00	18.22
19.00	19.17
20.00	20.13
21.00	21.09
22.00	22.05

The curves show the difference in raw scores between 0-30 yr olds (1) and 31 plus (2). The scores for Group 2 need to be adjusted slightly upwards (0.37), at the middle of the latent scale, for accurate comparison. To the right are the score coordinates plotted in the curves.

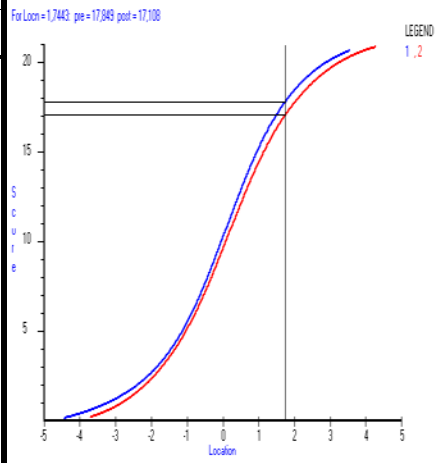
Figure 1b. DIF-equating curves for looseness by group variable



DIF sources: Group	
Gr 1+2	Gr 3
1.00	1.32
2.00	2.44
3.01	3.47
4.02	4.50
5.00	5.54
6.00	6.58
7.00	7.62
8.00	8.70
9.00	9.83
10.00	**10.97**
11.00	11.00

The raw score for postop Group 3 needs to be adjusted approximately 1 point downwards for accurate comparison to preoperative scores. To the right are the score coordinates plotted in the curves.

Figure 1c. DIF-equating curves of the slackness domain by group



DIF sources: Group	
Gr 1	Gr 2+3
1.00	0.57
2.00	1.61
3.01	2.67
4.02	3.70
1.00	0.57
2.00	1.61
3.01	2.67
4.02	3.70
5.01	4.66
6.03	5.64
7.03	6.58
8.04	7.52
9.01	8.43
10.03	9.39
11.00	10.32
12.03	11.29
13.02	12.25
14.01	13.22
15.01	14.21
16.03	15.23
17.02	16.25
18.02	**17.29**
19.00	18.36
20.00	19.51

The raw scores for the postop groups need to be adjusted 0.73 points upward at the top end of the scalefor comparison with preop scores.

Psychosocial overall fit statistics

In the domain of psychosocial difficulties, the analyses supported overall and individual item fit to the Rasch model (χ^2 = 11.9, df = 18, *P* = 0.853).

Psychosocial individual fit

All items fit the Rasch model. GLLRM revealed LD between items 12 and13 *daily mental strain to make ends meet* and *a mental strain to make ends meet at work* (lr = 22.00, df = 9, *p* = 0.0089). These were combined into a composite item. Item 15 *participate in hobbies* showed under-discrimination; although, this was not significant when accounting for LD.

Looseness overall fit

Four looseness items fit a Rasch model and thus fulfilled the requirements of a unidimensional construct (χ^2 = 10.9, df = 24, *P* = 0.990).

Looseness individual fit

Item 19 *lack control of knee when moving around* was found to belong to the slackness construct and was merged with those items. There was LD between items 16and18 *felt unstable due to lack of strength* and *constant focus on injured knee when moving around* (lr = 33.85, df = 9, *P* = 0.0001), and item 20 *could not trust the injured knee* had DIF relative to the exogenous factor of treatment group (lr = 15.19, df = 6, *P* = 0.0189). DIF equating revealed that raw scores for group 3 must be adjusted downwards between a half and a whole point relative to groups 1 and 2, highest at the upper end of the scale (same process as shown in Figure 1b).

Slackness overall fit

Seven items in the slackness dimension fit the Rasch model (χ^2 = 50.0, df = 50, *P* = 0.475). These were the original 6 items plus item 19 from the looseness domain.

Slackness individual fit

There was LD between items 19 and 21 *lack knee control when moving around* and *slack feeling in injured knee* (lr = 33.33, df = 9, *P* = 0.0001), 22 and 23 *spared injured knee* and *overloaded "healthy"* *knee* (lr = 23.88, df = 9, *P* = 0.0045), and 24 and 25 *shakiness in injured knee* and *sense of fatigue in injured knee* (lr = 23.25, df = 9, *P* = 0.0057). Also, there was DIF relative to group in items 22 (lr = 20.83, df = 6, *P* = 0.0020) and 25 (lr = 22.38, df = 6, *P* = 0.0010). The long-term post-op raw scores must be adjusted upward by approximately one point in the range of 17 to 21 for comparison over time (Figure 1c.). Item 26 *balancing on injured knee during knee exercise* was a regular partial credit item.

Tests of multidimensionality for Looseness and Slackness

Confirmatory tests of multidimensionality were performed on the combined dimensions of Looseness and Slackness, as they were closely related in the qualitative interview phase. The combined analysis rejected a joint model (χ^2 = 99.8, df = 75, *P* = 0.030).

Symptoms (pain) overall fit

The 13 items of the symptoms domain did not fit a Rasch model (χ^2 = 302.3, df = 39, *P* = 0.0000). There was misfit of the subgroup of items relating to stiffness and loss of range of motion (items 32, 33, 34, 35, and 36) (χ^2 = 146.9, df = 18, *P* = 0.0000). These items were removed due to low face validity and statistical misfit. Conversely, all pain items 27, 28, 29, 30, 31, 38, and 39 fit a Rasch model (χ^2 = 20.7, df = 19, *P* = 0.355).

Symptoms individual fit

There was marginal misfit of item 31 *pain when sitting in a chair with bent knees* which exhibited low discrimination (*P*= 0.0082). This item was retained due to overall fit despite low face validity. Item 37 *feeling loss of knee control when moving around* was excluded due to misfit (*P*= 0.0000) and heterogeneous face validity relative to the other items, but also due to content redundancy with item 19.

Sport and recreation overall fit

Initial analysis of the combined Sport/Rec items rejected a Rasch model (χ^2 = 697.7, df = 45, *P* = 0.0000). All items concerning avoidance of sport in the sport and recreation domain (items 40, 41, 42, 43, 44, and 45) did not fit a Rasch model (χ^2 = 46.0, df = 18, *P* = 0.0001). These were excluded from further analysis. The remaining items: 46, 47, 48, 49, 50, 51, 52, 53, 54, and 55 exhibited fit (χ^2 = 20.7, df = 19, *P* = 0.355). However, exploratory Rasch analysis revealed a bi-dimensional substructure. Items 46, 47, 48, 53, 54, and 55 showed strong evidence of a single dimension (χ^2 = 18.9, df = 15, *P* = 0.216). Items 49, 50, 51, and 52 did as well (χ^2 = 6.0, df = 12, *P* = 0.915). The four physical sports items, 49-52, were also exploratively assessed in combination with the ADL items to see if a Rasch model would be generated. This would conveniently have yielded an overall physical activity scale. However, GLLRM rejected unidimensionality of the composite item set (*P* = 0.000).

Sport and recreation individual fit

There was LD between items 46 and 47, *more cautious when playing sports,* and *limited when playing sports* (lr = 37.97, df = 9, *P* = 0.0000); 47and48, *difficulty "going all out" when playing sports* (lr = 22.56, df = 9, *P* = 0.0073); 49 and 50, *difficulty changing direction when running* and *difficulty with sudden stops when running* (lr = 64.50, df = 9, *P* = 0.0000); and 51 and 52, *difficulty jumping* and *difficulty landing when jumping*(lr = 96.44, df = 9, *P* = 0.0000). These items were combined into 3 composite items: (46, 47, 48), (49, 50), and (51, 52).

Reliability and targeting

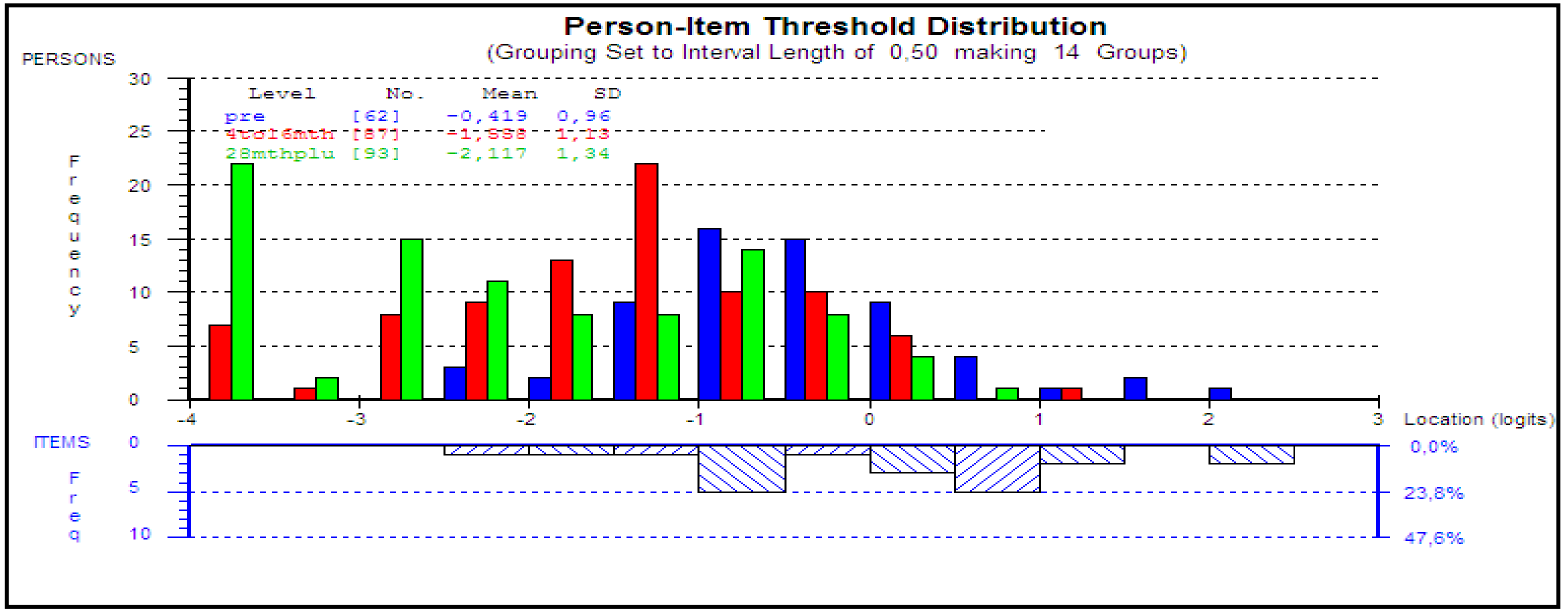
Test-retest reliability depends on the distribution of scores on the latent variable. Since this distribution depends on the interpretation of how much or how little a person feels he or she is affected in terms of the latent variable, reliability has to be assessed in subpopulations defined by outcomes on these variables. We had 3 subgroups, pre-operative, 4-16 months postoperative, and more than 28 months postoperative. We saw a general trend towards better targeting and reliability in the pre-operative group, mostly due to a larger standard error in the post-operative groups. However, despite the redundancy in responses to locally dependent items, reliability was high in all domains, between 0.83 and 0.92, except in the Slackness dimension (between 0.65 and 0.78). Table 5 shows Chronbachs alpha for all for all domains and Figure 2 shows the distribution of persons and items on the ADL latent Slackness variable across the 3 groups. Targeting is best for the blue group (pre-op group1), as the item thresholds in the bottom of the graph can be seen to cover the continuum of the latent variable for the blue group.

Table 5: Relibility indices **(**Chronbachs-α) for all domains, including overall α for groups combined and each group separately.

***ADL**	**α 0-30**	**α ≥31**	**Psycho-social**	**α**	**Loose-ness**	**α**	**Slack-ness**	**α**	**Symp-toms**	**α**	**Sport/ behav**	**α**	**Sport/ phys**	**α**
Overall	.883		Overall	.859	Overall	.866	Overall	.805	Overall	.872	Overall	.916	Overall	.947
Preop	.775	.817	Preop	.808	Preop	.841	Preop	.669	Preop	.701	Preop	.748	Preop	.907
Postop1	.858	.767	Postop1	.839	Postop1	.834	Postop1	.834	Postop1	.737	Postop1	.872	Postop1	.864
Postop2	.764	.801	Postop2	.853	Postop2	.826	Postop2	.780	Postop2	.784	Postop2	.898	Postop2	.958

***Results in the ADL domain are presented for all age by group combinations due to DIF by age-group. Chronbach's alpha calculated using SPSS.

Figure 2. shows the distribution of the person scores on the latent variable relative to the distribution of item thresholds.



The logit scale from -4 to +3 on the x-axis represents the latent variable of Slackness with the severity increasing towards the right. The y-axis shows the frequency of persons (on top) and items (bottom) relative to the latent trait. Groups 2 and 3are towards the least affected end of the scale. Targeting is best for Group 1.

Discussion

This study demonstrates that our patient-related outcome questionnaire consists of seven scales with unidimensional measurement properties that can be applied to patients who are waiting for ACL-reconstruction and patients who have received an ACL-reconstruction. Thus, the summary scores can be used for comparison in preoperative and postoperative settings, and for pretest-posttest comparisons. The items comprising the constructs were derived from a rigorous qualitative process with specific focus on face and content validity. Construct validity was then confirmed using Rasch IRT models.

Traditionally, CCT has been used to validate PRO instruments for patients with ACL deficiency. Mohtadi[36] used t-tests and correlation to validate the ACL-QoL, and KOOS was validated using CTT and generated from items and constructs from previously existing instruments used for other purposes (WOMAC).[38] Ours is the first PRO for ACL deficiency, which consists of constructs specifically confirmed by patients with ACL deficiency to be relevant, and subsequently assessed using Rasch analysis. The methods employed by Mohtadi to develop the ACL-QoL questionnaire are at first glance similar to ours: an initial literature search, item generation through patient contact, and construct validation.[36] However, we used cognitive interviewing to extract the patients' verbatim description of the sensations comprising relevant item themes, whereas Mohtadi's qualitative methods involved a broader survey of patients and clinicians to confirm the relevance of pre-formulated items. Moreover, Mohtadi did not use IRT.

The analyses disclosed item pairs with evidence of local dependence, which can explain why some items are marginally significant and yet there is still overall fit to the Rasch model (i.e., items 6, 12, 19, 24, 31, and 53). Item misfit is often used to dictate item removal. Therefore, with a large enough item-bank, a unidimensional item set can be derived simply by discarding items stepwise based on individual item misfit. This *data-driven* approach can be unwarranted if LD and DIF is the cause of misfit. From a clinical perspective, the objective of LD-analysis is to identify and ensure that no relevant item content is lost due to single item misfit, or even misfit of the item set. In this study, we constructed composite items when there was evidence of local dependence. Technically, this entails adding item interaction terms to the Rasch model.[26] The total score is statistically sufficient, and as with a pure Rasch model, such models have been shown to be essentially valid and objective.[27] Thus, the total score is the same, and the item scores are calculated in precisely the same manner in the questionnaire. This is from a statistical and measurement perspective convenient; however, it is also supported empirically and qualitatively, in that all locally dependent item couples can be confirmed to consist of similar themes. For example in the ADL domain, item 4 *Difficulty* b*ending down on knee to pick something up off the floor* is intuitively linked to item 8 *Difficulty* s*quatting.* This is also the case with items 12 and 13 *Daily mental strain to make ends meet* and *A mental strain to make ends meet at work.* The interesting aspect here is that this statistical outcome is a function of how the patients have actually responded to the items, which is heartening, because it allows quantitative confirmation of what seems clinically obvious. At the opposite end of the spectrum, the matchup between items that are statistically “on-the-edge,” and qualitatively heterogeneous, is striking. Item 31, *Pain when sitting with bended knee*, which exhibits marginal misfit and under-discriminates, thematically resembles item 5, *Difficulty sitting with knee bent.* Item 5 was removed with other misfitting items that seemed to cover a stiffness-related dimension. Our approach is to retain items that may possess any meaning for patients. This is a “when in doubt *don’t* throw it out” strategy. Removal can be justified if the item continues to show misfit in future samples.

DIF is clearly more problematic because it entails a difference in scores across exogenous variables, in other words an interaction between the subjects and the items, and not between the items themselves. We saw DIF in some domains relative group and age group. We have calculated DIF-equating scores so the scores can be adjusted and post-hoc controlled for valid comparisons.

Two new constructs emerged because of focus groups and single interviews with item content based on verbatim expressions Slackness and Looseness. The item themes in these domains were closely related and one item from Looseness (item 19) fit in the Slackness domain. We conducted joint tests of dimensionality for the domains combined, and confirmed that there are two separate dimensions (p= 0.034). However, p-values of this magnitude cannot be considered strong empirical evidence. These two domains are clearly symptom-related and reflect the sensation of functional impairment that patients diagnosed with ACLD feel they have. The objective when generating these items was to capture and base the item content on the verbatim descriptions of the sensations. This seems to have been successful, in that unidimensional Rasch models were achieved. However, these themes and items obviously need to be monitored prospectively, in that both subscales exhibited LD, and Slackness possessed LD and DIF, which can be psychometrically challenging.

Even with good fit to Rasch models and successful strategies to account for LD and DIF, there were some anomalies. Fourteen of the original 55 items were removed from the final Rasch model due to misfit, combined with low face validity. For this reason, all stiffness and range of motion items were removed. Clinically, the stiffness items could indicate problems associated with concomitant cartilage or meniscus injury, which invariably had been experienced by some of our focus group respondents. This would clearly indicate a separate dimension, and thus, these items can possibly be used for other patients. The entire range of items addressing avoidance of sport showed misfit and were excluded. These items warrant another round of explorative qualitative assessment to derive adequate item statements and response options, and thus hopefully a "Sports-avoidance" Rasch scale can be achieved.

The Sport/Rec domain revealed itself to consist of two underlying sub-scales, one addressing physical sports-related tasks, the other consisting of sport behaviour aspects. This structure was revealed with GLLRM methods, which in fact indicated that items 54 and 55 could be included, despite misfit in the original analysis.

A weakness with this study was that we did not have the time to carry out test-retest analyses. The question, of course, is what is actually being measured? Is it the ability of the instrument to capture the stability of the scores, or is it the patient's ability to recall the responses from the previous test. We did assess internal consistency of the scales with Chronbachs alpha and the person separation index, however, future study of test-retest reliability is planned.

In conclusion, this PRO instrument consists of seven unidimensional constructs, which can be used to assess symptoms, activity, and psychosocial consequences in patients with ACLD and the same patients after conservative or surgical treatment. Thus, numeric comparisons can be conducted on summary scores between groups. We have also demonstrated that overall, the subscales are independent of gender, age, and whether the patient was pre- or post reconstruction. This is the first PRO created specifically for patients before and after ACL-reconstruction, which consists of Rasch-IRT confirmed unidimensional constructs.

Conflict of interest statement

No conflicts of interest to declare. All authors contributed substantially to the study and writing of the manuscript. JC, JB, and MK planned the study. JC collected and statistically analyzed the data together with JB. SK performed confirmatory statistical analyses on all data. Each author has read

and concurs with the content of the final manuscript.

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10. Discussion of article 3

10.1 Major Findings

Seven dimensions addressing ADL (8 items), Psychosocial Consequences (5 items), Looseness (4 items), Slackness (7 items), Symptoms (7), Sports Behavior (6 items), and Sports Physical Activity (4 items) exhibited fit to both the PCM Rasch model in RUMM 2030 and the GLLRM in DIGRAM. Thus, all 41 items within these dimensions fit the Rasch model, except item 31 *Pain sitting in chair with knee bent*, which was retained because of overall fit and marginal face- and content relevance. Two items in ADL were removed due to misfit and lack of face validity (items 5 and 9), six items related to stiffness in the symptoms dimension exhibited misfit (items 32 to 37) and were removed; the six Sport avoidance items (40 to 45) showed misfit and must be qualitatively reconsidered. Therefore, of the fourteen items removed from the KNEES-ACL scales, five items could be included in another form in the instrument, most probably in an independent scale.

10.2 Assessment of Methods

Two Rasch approaches were used to assess the scale validity of the item sets. The GLLRM model confirmed the results of the Rasch PCM model and shed extra light on the nature of the items response interdependency (LD) and item-covariate interactions (DIF).

10.3 Justification of Conclusion

Construct validation of the dimensions of the KNEES-ACL is substantiated using the polytomous partial-credit Rasch model and confirmed using the graphical loglinear Rasch model. The methods used to assess the psychometric properties are the most stringent methods available to confirm unidimensionality.

10.4 Contribution to Current Knowledge

Two new scales based on verbatim qualitative interviewing techniques emerged in Danish, which address what patients describe as Looseness and Slackness sensations while participating in functional activities. These scales fit Rasch models in their entirety with no removal of item content. All scales exhibit good internal consistency, targeting, and show clear differences in mean scores between preoperative and postoperative groups. Thus, all scales can be used for invariant assessment of treatment effect between groups, and within-groups with repeated measures. Methods to adjust for LD and DIF are presented.

11. Conclusions of this PhD study

The purpose of this study was to create a condition-specific PRO questionnaire for use in pretest-posttest studies of non-surgical and surgical treatment effect of ACL deficiency. Item content was identified through an extensive literature search of knee-ligament- and cartilage- PROs, whereupon face validity was established. The content relevance of these items was tested in focus groups and individual cognitive interviews of patients pre- and post-ACL reconstruction. Content coverage of the items was found to be insufficient, in that new item content emerged from the interviews. The content relevance of these new items was confirmed in subsequent groups of patients. A pilot PRO was constructed, and finally, the psychometric properties were assessed on a cohort of 242 patients with ACL deficiency and ACL reconstruction. The scales of the KNEES-ACL exhibit face-, content-, and construct-validity. This is the first condition-specific PRO questionnaire that consists of scales, which with certainty can be used for invariant comparison of treatment effect pre- and post- ACL reconstruction. Thus, the KNEES-ACL will potentially allow clinicians to differentiate more reliably between patients who require surgery and those who do not.

12. Implications for research

The results of this study imply that the methods employed for PRO scale construction optimally should follow the sequence used and described in this PhD-project: PROs should be developed starting with a literature search, followed by patient confrontation, and finally psychometric validation using item-response theory. The questionnaire will then possess adequate psychometric properties. Further, the requirements of invariant measurement are met if the Rasch model is used. Without invariant comparison, construct validity cannot be assumed. Earlier methods using CTT can produce arbitrary results, which may just as well reflect the properties of the items rather than the condition of the patient. In summary, utilization of carefully structured qualitative and then quantitative procedures will yield superior results.

Another research implication is the potential to investigate the costs and benefits of surgery, as more accurate methods for determining treatment strategy would have substantial utility. Patients who do not need ACL reconstruction would be more likely to avoid unnecessary surgery, and patients who need surgery would more likely receive timely treatment. Avoidance of unnecessary surgery benefits both the patient and society. Patients avoid pain and loss of income that could result from needless surgical procedures. Moreover, those patients receiving needed surgery promptly can avoid long-term impairments. Society benefits from the cost avoidance of late complications from untreated pathology.

13. Implications for practice

The KNEES-ACL consists of items with high content validity and confirmed psychometric properties. The instrument can be used as an evaluative tool for the establishment and verification of clinical guidelines for efficacious treatment of ACL deficiency. This PRO should be used in preference to existing questionnaires due to its substantiated unidimensional properties.

14. Perspectives

Ideally, we would like to show a correspondence between the subjective responses of the patient and objectively assessed biomechanical deficiency in the knee. The score on each dimension is the response of the patient, and the biomechanical deficiency is captured by kinematic and kinetic analyses. This can be achieved through video-based motion capture, or stereo X-ray techniques. Correlation of the subjective and the objective measurements can yield external criterion validation. The correlation analyses will be carried out most likely using graphical models or structural equation models.

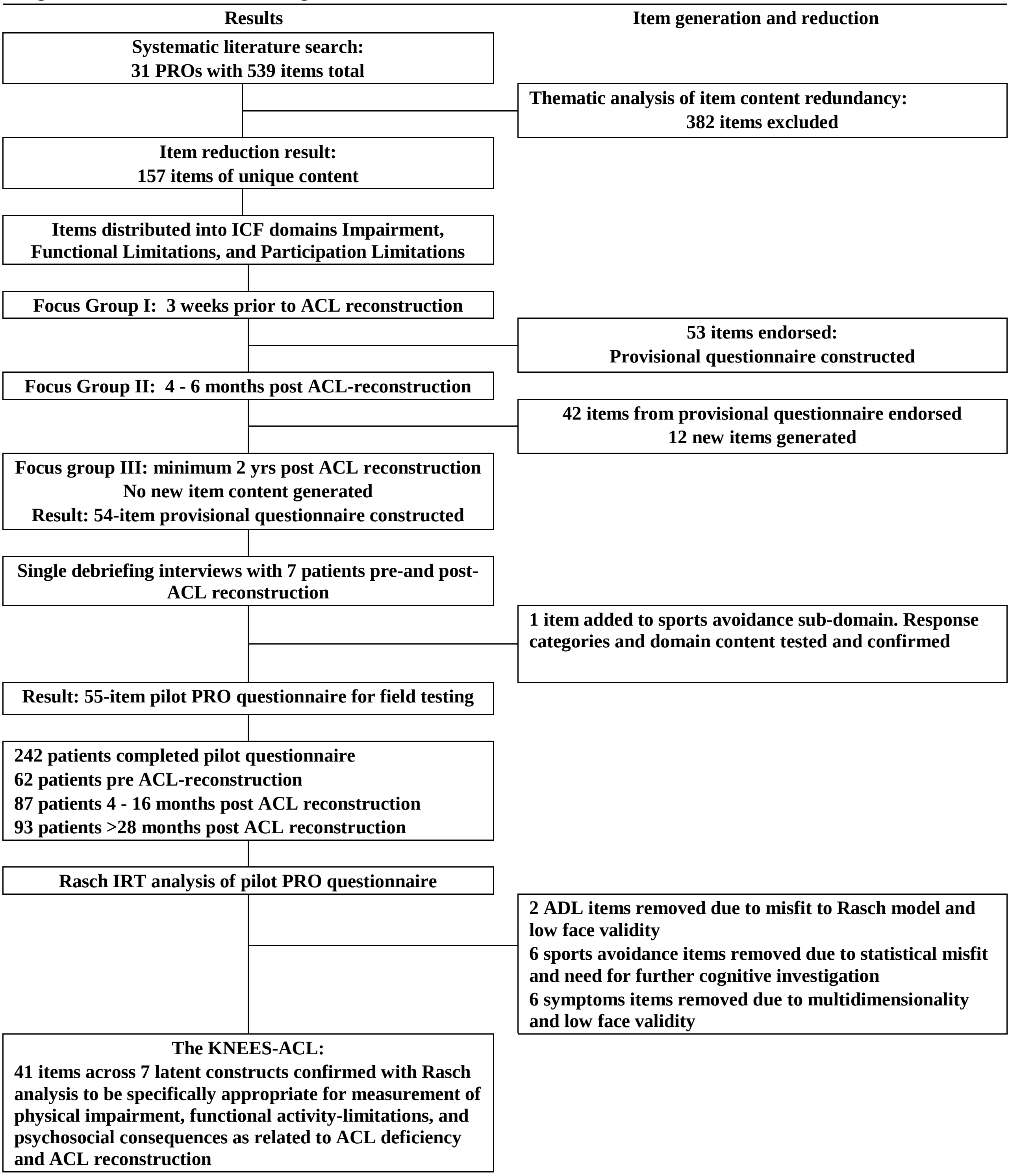
As mentioned in Article 3, the sub-domain of sports avoidance warrants exploration using the above-described qualitative methods on a sub-group of athletes. The sports avoidance items may target this elite group of patients more appropriately. The new scale would not be a part of the KNEES-ACL, but it could be a relevant tool for this patient group. In fact, the initial item pool of 157 items can be used to generate other condition-specific instruments for patients with impairments due to cartilage injury and anterior knee pain.

The pilot versions cannot be used for clinical purposes. Appendices II and III show the English and the Danish versions of the KNEES-ACL. The final KNEES-ACL is not included in this thesis, because the optimal formats still need to be determined; that is, how the appearance and layout will be presented, what the most appropriate clinician/patient interface platforms will be (e.g., digital versus physical formats and design), as well as other practical aspects in terms of instrument application.

Therefore, the English version cannot be considered valid in any way, as it is simply a coarse translation of the Danish version, solely for the purpose of illustration. Because it has not been properly translated to English, it cannot yet be validated on a group of native English speakers. For formal validation, 2-panel translation, qualitative item content analysis, assessment of unidimensionality and invariance must first be carried out in English-speaking patient groups.

15. Trajectory of the study

Figure 1. Flowchart of item generation, reduction, and statistical validation



16. Abbreviations and professional terminology

ACL	Anterior Cruciate Ligament
ACL deficient	A mechanical rupture or lesion of the ACL which causes functional impairments
ADL	Activities of Daily Living
Allograft (ACL)	A transplantation graft procured from the body of a donor
Anterior drawer test	A test to assess the mechanical laxity of the knee in the sagittal plane. The excursion of the tibia relative to the femur.
Autograft	A transplantation graft procured from another region of the body of the person receiving the graft
Condition-specific questionnaire	A condition-specific questionnaire measures a specific condition in a specific population in, as opposed to a generic questionnaire, which measures overall concepts (e.g., health status, anxiety, depression, psychiatric morbidity etc.)
Coper	A person diagnosed with ACL deficiency, who progresses to a level of pre-injury function without signs of impairment
CTT	Classical Test Theory
Differential item functioning, DIF	Differential item functioning is where an item functions differently across subpopulations, such as gender, age, or other exogenous group factors.
False negative test result	An impaired person with a normal test result
False positive test result	A healthy person with an abnormal test result
Focus group interviews	Group interviews where both the issue(s) discussed and the participants in the group are focused.
Generic questionnaire	A generic questionnaire measures overall concepts (e.g., health status, anxiety, depression, psychiatric morbidity etc.) in contrast to condition-specific measures developed to measure a specific condition in a specific population.
GLLRM	Graphical Loglinear Rasch Model
GRF	Ground Reaction Force
IRT	Item Response Theory.
Item	A question with its corresponding response options.
Item truncation	Shorten. Disambiguate. Extract meaningful theme of an item.
KNEES	Knee Numeric Entity Evaluation Score
Latent variable, latent trait	A variable, which is unobservable but is supposed to enter into the structure of a system being studied, such as level of pain.
Non-coper	A person diagnosed with ACL deficiency, who cannot progress to a pre-injury level of function without signs of

	functional impairment
Pilot study	A study, usually on a small scale, carried out prior to the main study, primarily to gain information to improve the efficiency of the main study.
Positive predictive value	The positive predictive value of a test expresses how many persons with a positive result actually have the disease.
Prevalence	The prevalence of e.g. disease is the number of existing persons with the disease in a population at a designated time.
PRO	Patient Related Outcome score. A health-related questionnaire.
Psychometric properties	Psychometrics relates to the measurement of mental abilities and attributes. Psychometric properties are in this context an overall term for the validity and reliability of a psychometric measure.
Sensitivity	The ability of a diagnostic test to identify pathology in patients who present with symptoms that might indicate the presence of pathology
Specificity	The ability of a diagnostic test to rule out pathology in patients who do not present with symptoms
Total score (summary score)	When the numeric responses to items are added together to yield a composite score. Represents the amount of the latent trait the person possesses.
Validity, concurrent	Consists of convergent and divergent validity, for example when a new measure is correlated to an existing measure, the correlation between the measures can converge or diverge.
Validity, construct	The overarching concept of validity. Almost any kind of information about a test can contribute to an understanding of its construct validity. Fundamentally, all validation is construct validation, in the sense that all validity evidence contributes to (or undermines) the empirical foundation or trustworthiness of the score interpretation.
Validity, content	Content validity encompasses content relevance and content coverage. Only questions, response categories, and items that are confirmed to be relevant for the target population will possess content relevance. If all relevant items and response categories addressing an area of interest are included in an instrument, content coverage will be achieved.
Validity, face	If an item appears to be relevant from the perspective of the person applying it, the item has face validity
Validity, known group	Also called extreme groups validity. A test where the measure is given to two groups; one of which has the trait or behaviour, and the other which does not. The former group should score significantly higher (or lower) on the instrument.

Validity, predictive	An example of predictive validity could be a test's ability to predict whether students tested before they were admitted to university would graduate three years later as bachelors. Concurrent validity and predictive validity are unified under the term criterion validity. For further explanation, see those kinds of validity.

17. Appendix I – Medline search strategy

(knee injury OR “knee injury” OR “injuries” OR osteoarthritis, knee OR “osteoarthritis, knee” OR knee joint OR “knee joint” OR joints OR ligaments, articular OR “ligaments, articular” OR ligament OR cartilage OR “cartilage, articular” OR pathology OR physiology OR physiopathology OR sports OR “sports injuries” OR athletic OR “athletic injuries” OR “pain” OR pain AND functional outcome AND function AND “function” AND outcome AND assessment AND questionnaire AND “questionnaire” AND “questionnaires” AND questionnaires AND “Outcome Assessment (Health Care)” AND “self-efficacy” AND self-efficacy AND scores AND “scores” AND score AND “score” AND “rating scale” AND rating scale AND scales AND patient-related outcome AND PRO AND “PRO” AND POEM AND “POEM”AND self-rated)

18. Appendix II - KNEES-ACL Pilot version (English)

How is your knee?

A questionnaire for individuals with cruciate ligament injury

Developed by --------------: Department of Sports Traumatology, Bispebjerg Hospital, and

Research Unit and Department of General Practice, Faculty of Medicine, University of

Thank you in advance for your help!

The purpose of this questionnaire is to find out how people who have had a cruciate ligament rupture or have had cruciate ligament surgery are doing.

Our goal is to improve the treatment of ligament injuries. You can help us by answering this questionnaire.

Your responses will help us to find the best treatment strategies.

It is important that you answer all the questions.

Copenhagen, Denmark

Your Name:	**Personal No.**	**Date:**

Part 1.

Difficulty in daily activities

Have you - **in the past week** – experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot
1. I have had difficulty walking on level ground.	☐	☐	☐	☐
2. I have had difficulty walking on uneven ground (e.g., in the woods).	☐	☐	☐	☐
3. I have had difficulty walking down stairs.	☐	☐	☐	☐
4. I have had difficulty bending down on knee to pick something up off the floor.	☐	☐	☐	☐
5. I have had difficulty sitting in a chair with knee bent.	☐	☐	☐	☐

Have you - **in the past week** – experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot	N/A
6. I have had difficulty bicycling.	☐	☐	☐	☐	☐
7. I have been unable to crawl on all fours.	☐	☐	☐	☐	☐
8. I have had difficulty squatting.	☐	☐	☐	☐	☐
9. I have been unable to dance.	☐	☐	☐	☐	☐
10. I have had difficulty running.	☐	☐	☐	☐	☐

Psychosocial strain

Have you – **in the past week** – experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot	N/A
11. It has been a mental strain not knowing when my knee would be okay again.	☐	☐	☐	☐	☐
12. It has been a mental strain to make ends meet in daily life because of my knee problems.	☐	☐	☐	☐	☐
13. It has been a mental strain to make ends meet at work because of my knee problems.	☐	☐	☐	☐	☐

Have you – **in the past week** – experienced the following due to your knee injury??

	Not at all	A little	A bit	A lot	N/A
14. It has been a mental strain to make ends meet at home because of my knee problems.	☐	☐	☐	☐	☐
15. It has been a mental strain not being able to participate in hobbies because of knee problems.	☐	☐	☐	☐	☐

Looseness

Have you – **in the past week** – experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot
16. I have felt that my injured knee was un-stabile because of muscle weakness.	☐	☐	☐	☐
17. I have felt that my injured knee was loose when moving around.	☐	☐	☐	☐
18. I have felt that I should monitor my injured knee when moving around.	☐	☐	☐	☐

Have you – **in the past week** – experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot
19. I have felt that I lacked control over my injured knee when moving around.	☐	☐	☐	☐
20. I have felt that I couldn’t count on my injured knee when moving around.	☐	☐	☐	☐

Slackness

Have you – **in the past week** – experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot
21. I have had a slack feeling in my injured knee when moving around.	☐	☐	☐	☐
22. I have spared my injured knee.	☐	☐	☐	☐
23. I have overloaded my ”healthy” knee.	☐	☐	☐	☐

Have you – **in the past week** – experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot	N/A
24. I have experienced shakiness in the injured knee during knee exercises.	☐	☐	☐	☐	☐
25. I have fatigued more quickly in the injured knee compared with uninjured knee during knee exercises.	☐	☐	☐	☐	☐
26. I have had difficulty balancing on my injured knee during knee exercises.	☐	☐	☐	☐	☐

Symptomer

Have you – **in the past week** – experienced the following due to your knee injury?

		Not at all	A little	A bit	A lot
27.	I have had knee pain when twisting/pivoting on my injured knee.	☐	☐	☐	☐
28.	I have had pain in my knee when walking up stairs.	☐	☐	☐	☐
29.	I have had pain in my knee when walking in uneven terrain (e.g., in woods).	☐	☐	☐	☐
30.	I have had knee pain after a long walk.	☐	☐	☐	☐
31.	I have had pain in my knee when sitting in a chair with bended knee.	☐	☐	☐	☐

Have you – **in the past week** – experienced the following?

		Yes	No
32.	I have been able to bend my injured knee completely.	☐	☐
33.	I have been able to extend my injured knee completely.	☐	☐

Have you – **in the past week –** experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot
34. I have had stiffness in my knee in the evening.	☐	☐	☐	☐
35. I have had stiffness in my knee in the morning.	☐	☐	☐	☐
36. I have had swelling of my knee.	☐	☐	☐	☐

Have you – **in the past week –** experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot	N/A
37. I have had a feeling of lost knee control when in motion.	☐	☐	☐	☐	☐
38. I have had knee pain when jumping.	☐	☐	☐	☐	☐
39. I have had knee pain after knee exercises.	☐	☐	☐	☐	☐

Sport and Recreational Activities

40.	**In the past week** I have:	Tick just one box here
	… avoided **all** sport	☐
	… avoided **some** forms of sport	☐
	… participated in my normal sport	☐

Have you – **in the past week** – experienced the following due to your knee injury?

		Yes	No
41.	I have avoided playing sports because I was told not to by my doctor or therapist.	☐	☐
42.	I have avoided playing sports due to knee pain.	☐	☐
43.	I have avoided playing sports due to knee swelling.	☐	☐
44.	I have avoided playing sports because I've been worried of getting a new injury.	☐	☐
45.	I have avoided playing sports due to worries of injury getting worse.	☐	☐

Have you – **in the past week** – experienced the following due to your knee injury?

		Not at all	A little	A bit	A lot	N/A
46.	I have been more cautious than usual when playing sports.	☐	☐	☐	☐	☐
47.	I have been limited in my capacity to play sports.	☐	☐	☐	☐	☐

Have you – **in the past week** – experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot	N/A
48. I have had difficulty "going all out" when playing sports.	☐	☐	☐	☐	☐
49. I have had difficulty changing direction when running.	☐	☐	☐	☐	☐
50. I have had difficulty stopping suddenly when running.	☐	☐	☐	☐	☐
51. I have had difficulty jumping.	☐	☐	☐	☐	☐
52. I have had difficulty landing when jumping.	☐	☐	☐	☐	☐

Have you – **in general** – experienced the following due to your knee injury?

	Not at all	A little	A bit	A lot	N/A
53. I have had to reduce my expectations to sports.	☐	☐	☐	☐	☐
54. I feel isolated from the people I used to do sports with before my injury.	☐	☐	☐	☐	☐
55. I feel that my competitive needs are no longer met.	☐	☐	☐	☐	☐

Part II:

1. You are:
   - ☐ Employed
   - ☐ Student
   - ☐ Looking for work
   - ☐ Receiving disability or similar

2. What primary school education do you have?
   (Tick one box)

☐ Elementary school

☐ 10th grade

☐ High school, technical school

☐ Other education

☐ N/A

3. What vocational education do you have?
   (Tick one box)

☐ No træning

☐ Special vocational education

☐ Apprentice, apprenticeship, or other training
(eg. social and health care worker, nursing assistant, technical assistant)

☐ Vocation requiring junior college - associates degree

☐ Vocation requiring undergraduate degree (school teacher, Nurse, Journalist)

☐ Vocation requiring postgraduate degree (Engineer, Biologist, Architect, MD)

☐ Other

☐ N/A

4. **What is your current or most recent professional position?**
(Precise details, e.g., Medical secretary not just secretary; smith apprentice, not just blacksmith; agriculturalist, not just farmer; primary school teacher, not just teacher; nursery manager not only an educator, Office Manager of the Treasury, not just Office Manager)

____

5. Do you, or did you have responsibility for employees in your job?
(How many? Write 0, if none)

|__|__|__|__|

6. Du you live alone?
(Tick just one box)

☐ No ☐ Yes

Thank you for your help!

19. Appendix III - KNEES-ACL Pilot version (Danish)

Hvordan går det med dit knæ?

Spørgeskema til personer med korsbåndsskade

Udarbejdet af xxxxxxx: Idrætskirurgisk Enhed, Bispebjerg Hospital, Afdeling for Almen Medicin, Københavns Universitet og Sahva A/S; xxxxxxxxxx: Forskningsenheden for Almen Medicin, Københavns Universitet; samt xxxxxxx: Idrætskirurgisk Enhed, Bispebjerg Hospital, Københavns Universitet (januar 2011).

På forhånd tak for hjælpen!

Gennem dette spørgeskema håber vi at få at vide, hvordan personer med korsbåndsskade har det før og eventuelt efter en korsbåndsoperation.

Vi vil gerne forbedre behandlingen af korsbåndsskader, og det kan du hjælpe os med ved at besvare skemaet.

Svarene fra dig og andre skal være med til at vise, hvilken behandling virker bedst.

Det er vigtigt, at du svarer på alle spørgsmålene.

Dit Navn:	**Cpr.**	**Dato:**

Del I.

Besvær i dagligdagen

Har du - **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget
1. Jeg har haft besvær med at gå på et jævnt underlag.	☐	☐	☐	☐
2. Jeg har haft besvær med at gå på et ujævnt underlag, f.eks. i skoven.	☐	☐	☐	☐
3. Jeg har haft besvær med at gå ned ad trapper.	☐	☐	☐	☐
4. Jeg har haft besvær med at gå ned i knæ, hvis jeg f.eks. skulle samle noget op fra gulvet.	☐	☐	☐	☐
5. Jeg har haft besvær med at sidde på en stol med knæet bøjet.	☐	☐	☐	☐

Har du - **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget	Ved Ikke
6. Jeg har haft besvær med at cykle.	☐	☐	☐	☐	☐
7. Jeg har haft besvær med at kravle på alle fire.	☐	☐	☐	☐	☐
8. Jeg har haft besvær med at sidde på hug.	☐	☐	☐	☐	☐
9. Jeg har haft besvær med at danse.	☐	☐	☐	☐	☐
10. Jeg har haft besvær med at løbe.	☐	☐	☐	☐	☐

Psykisk belastning

Har du – **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget	Ved ikke
11. Det har været en psykisk belastning, at jeg ikke vidste hvornår knæet kom i orden.	☐	☐	☐	☐	☐
12. Det har været en psykisk belastning, at skulle få hverdagen til at hænge sammen pga. mine knæproblemer.	☐	☐	☐	☐	☐
13. Det har været en psykisk belastning, at skulle få mit arbejdsliv til at fungere pga. mine knæproblemer.	☐	☐	☐	☐	☐

Har du – **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget	Ved ikke
14. Det har været en psykisk belastning, at skulle få familielivet til at hænge sammen pga. mine knæproblemer.	☐	☐	☐	☐	☐
15. Det har været en psykisk belastning, ikke at kunne deltage i mine fritidsaktiviteter.	☐	☐	☐	☐	☐

Løshed

Har du – **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget
16. Jeg har oplevet, at knæet har været ustabilt pga. manglende kræfter i musklerne.	☐	☐	☐	☐
17. Jeg har haft en følelse af, at knæet var løst, når jeg har bevæget mig.	☐	☐	☐	☐
18. Jeg har følt, at jeg skulle kontrollere knæet, når jeg har bevæget mig.	☐	☐	☐	☐

Har du – **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget
19. Jeg har følt, at jeg manglede kontrol over knæet, når jeg har bevæget mig.	☐	☐	☐	☐
20. Jeg har følt, at jeg ikke kunne stole på mit skadede knæ, når jeg har bevæget mig.	☐	☐	☐	☐

Slaphed

Har du – **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget
21. Jeg har haft en følelse af slaphed omkring mit skadede knæ, når jeg har bevæget mig.	☐	☐	☐	☐
22. Jeg har skånet det skadede knæ.	☐	☐	☐	☐
23. Jeg har overbelastet det ”raske” knæ.	☐	☐	☐	☐

Har du – **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget	Ved Ikke
24. I forbindelse med knæøvelserne har benet rystet.	☐	☐	☐	☐	☐
25. I forbindelse med knæøvelserne er jeg blevet hurtigere træt i det skadede ben i forhold til det andet ben.	☐	☐	☐	☐	☐
26. I forbindelse med knæøvelserne har jeg haft svært ved at holde balancen.	☐	☐	☐	☐	☐

Symptomer

Har du – **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

		Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget
27.	Jeg har haft smerter, når jeg har vredet knæleddet.	☐	☐	☐	☐
28.	Jeg har haft smerter, når jeg har gået op ad trapper.	☐	☐	☐	☐
29.	Jeg har haft smerter, når jeg har gået på ujævnt underlag, f.eks. i skoven.	☐	☐	☐	☐
30.	Jeg har haft smerter i knæet efter en lang gåtur.	☐	☐	☐	☐
31.	Jeg har haft smerter i knæet, når jeg har siddet på en stol med bøjet knæ.	☐	☐	☐	☐

Har du – **i den sidste uges tid** – oplevet følgende?

		Ja	Nej
32.	Jeg har kunnet bøje mit skadede knæ helt.	☐	☐
33.	Jeg har kunnet strække mit skadede knæ helt.	☐	☐

Har du – **i den sidste uges tid** – oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget
34. Jeg har haft stivhed af knæet om aftenen.	☐	☐	☐	☐
35. Jeg har haft stivhed af knæet om morgenen.	☐	☐	☐	☐
36. Jeg har haft hævelse af knæet.	☐	☐	☐	☐

Har du **– i den sidste uges tid –** oplevet følgende på grund af din knæskade?

	Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget	Ved ikke
37. Jeg har haft en følelse af, at jeg mister styring med knæet, når jeg har bevæget mig.	☐	☐	☐	☐	☐
38. Jeg har haft smerter i knæet, når jeg har hoppet.	☐	☐	☐	☐	☐
39. Efter knæøvelserne har jeg fået ondt i knæet.	☐	☐	☐	☐	☐

Sports- og fritidsaktiviteter

40.	I den sidste uges tid har jeg:	Sæt kun ét kryds her
	… undgået at dyrke al sport	☐
	… undgået at dyrke nogle former for sport	☐
	… dyrket den sport jeg plejer	☐

Har du – i den sidste uges tid – oplevet følgende på grund af din knæskade?

		Ja	Nej
41.	Jeg har undgået at dyrke sport, fordi jeg har fået at vide af en fysioterapeut eller læge, jeg ikke måtte.	☐	☐
42.	Jeg har undgået at dyrke sport, fordi jeg har haft ondt i knæet.	☐	☐
43.	Jeg har undgået at dyrke sport, fordi knæet har været hævet.	☐	☐
44.	Jeg har undgået at dyrke sport, fordi jeg har været bekymret for at få en ny knæskade.	☐	☐
45.	Jeg har undgået at dyrke sport, fordi jeg har været bekymret for at knæskaden skulle forværres.	☐	☐

Har du – i den sidste uges tid – oplevet følgende på grund af din knæskade?

		Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget	Ved ikke
46.	Jeg har været mere forsigtig end jeg plejer, når jeg har dyrket sport.	☐	☐	☐	☐	☐
47.	Jeg har været begrænset i at dyrke sport.	☐	☐	☐	☐	☐

Har du – i den sidste uges tid – oplevet følgende på grund af din knæskade?

		Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget	Ved Ikke
48.	Det har været vanskeligt at give sig fuldt ud med benene, når jeg har dyrket sport.	☐	☐	☐	☐	☐
49.	Jeg har haft besvær med at skifte retning når jeg løb.	☐	☐	☐	☐	☐
50.	Jeg har haft besvær med at bremse op hurtigt.	☐	☐	☐	☐	☐
51.	Jeg har haft besvær med at hoppe.	☐	☐	☐	☐	☐
52.	Jeg har haft besvær med at lande når jeg hoppede.	☐	☐	☐	☐	☐

Har du – overordnet set – oplevet følgende på grund af din knæskade?

		Nej, slet ikke	Ja, lidt	Ja, noget	Ja, meget	Ved ikke
53.	Jeg har måttet nedsætte mine forventninger i forhold til hvor megen sport jeg har kunnet dyrke.	☐	☐	☐	☐	☐
54.	Jeg føler mig isoleret fra de mennesker, jeg plejede at dyrke sport sammen med inden jeg kom til skade.	☐	☐	☐	☐	☐
55.	Jeg føler, at mit konkurrencebehov ikke længere bliver opfyldt.	☐	☐	☐	☐	☐

Del II:

1. Du er:
   - ☐ I arbejde
   - ☐ Under uddannelse
   - ☐ Arbejdssøgende
   - ☐ På førtidspension eller lignende

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2. Hvilken skoleuddannelse har du?
   (sæt ét kryds ved den seneste)

- ☐ 7.- 9. klasse
- ☐ 10. klasse (folkeskoles udvidede afgangsprøve eller realeksamen)
- ☐ Studentereksamen, hf, højere handelseksamen (hh), højere teknisk eksamen (htx)
- ☐ Anden skoleuddannelse
- ☐ Ved ikke

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3. Hvilken erhvervsuddannelse har du?
   (sæt ét kryds ved den seneste)

- ☐ Ingen erhvervsuddannelse
- ☐ Specialarbejderuddannelse
- ☐ Efg, lærling, elevuddannelse eller anden faglig uddannelse
  (f.eks. social- og sundhedshjælper, sygehjælper, teknisk assistent)
- ☐ Kort videregående uddannelse under 3 år
  (f.eks. markedsøkonom, maskintekniker, økonoma)
- ☐ Mellemlang videregående uddannelse, 3 – 4 år
  (f.eks. folkeskolelærer, sygeplejerske, journalist, bacheloruddannelse)
- ☐ Lang videregående uddannelse, over 4 år (f.eks. ingeniør, biolog, arkitekt)
- ☐ Anden uddannelse
- ☐ Ved ikke

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4. Hvad er din nuværende eller seneste erhvervsmæssige stilling?
(nøjagtig angivelse, f.eks.: Lægesekretær, ikke blot sekretær; smedesvend, ikke blot smed; gårdejer, ikke blot landmand; folkeskolelærer, ikke blot lærer; børnehaveleder, ikke blot pædagog; kontorchef i skattevæsenet, ikke blot kontorchef)

____

5. Har du eller havde du nogle underordnede eller ansatte i den stilling?
(skriv antal, hvis ingen skriv 0)

6. Bor du alene?
(sæt kun ét kryds)

☐ Nej ☐ Ja

Mange tak for hjælpen!

20. Appendix IV – Item pool in Danish

Symptoms

Bevægelse	1. smerter ved at dreje/vride knæet
	2. smerter ved at gå på jævnt underlag
	3. smerter ved at gå på Ujævnt underlag
	4. smerter ved at gå op ad trapper
	5. smerter ved at gå ned ad trapper
	6. smerter i knæet når jeg hopper
	7. smerte ved løb
	8. smerter når du rejser dig (siddende/liggende stilling eller på knæ)
	9. smerter efter jeg har løbet
	10. jeg halter
	11. smerter når du ligger på knæ
	12. smerter i hugsiddende stilling
	13. smerter ved at strække knæet
	14. smerter ved at bøje knæet
U. bevægelse	15. nattesmerter
	16. smerte ved at sidde
	17. smerte ved at ligge
	18. smerte ved at stå
Lyde	19. murren fra knæet
	20. knasen fra knæet
	21. klikkende lyd fra knæet
	22. andre lyde fra knæet
Bevægelighed	23. nedsat bevægelighed af knæet
	24. stivhed af knæet om morgenen
	25. stivhed af knæet på andre tidspunkter
	26. låsning af knæet
Styring/kraft	27. nedsat kraft af knæet
	28. jeg mister styring
	29. knæet svigter/give efter
	30. mit ene lår er tyndere end det andet
Andre	31. hævelse af knæet
	32. noget der kommer i klemme i knæet
	33. noget der smutter i knæet
	34. knæet hager sig fast
Womet item	35. følelsesløshed i/omkring knæet*

Function in Activities of Daily Living

Gang	36.	gå ud alene
	37.	besvær med at gå på jævnt underlag
	38.	besvær med at gå på ujævnt underlag – (e.g., skoven, bakker)
	39.	ubegrænset/begrænset distance
	40.	nødt til at gå med stok
Trapper	41.	besvær med at gå ned ad trapper
	42.	besvær med at gå op ad trappe
	43.	besvær med at gå ned ad trapper med gelænder
	44.	besvær med at gå op ad trappe med gelænder
Stille	45.	besvær ved at stå stille
	46.	besvær med at sidde i hug
	47.	besvær med at ligge i seng
	48.	besvær med at sidde med bøjet knæ
Påklædning/hygiejne	49.	besvær med at tage strømper på
	50.	besvær med at tage strømper af
	51.	besvær med at vaske hår
Transfer	52.	besvær med at rejse dig fra siddende
	53.	besvær med at komme ind i en bil
	54.	besvær med at komme ud af i en bil
	55.	besvær med at komme i sengen
	56.	besvær med at komme ud af sengen
	57.	behov for hjælp til at komme ind/ud af seng
	58.	besvær med at komme ind/ud badekar, brusebad
	59.	besvær med at rejse/sætte sig fra toilet
	60.	besvær med at vende i seng
Bevægelse	61.	besvær med at gå ned i knæ /ned på hug
	62.	besvær med at ligge på knæ/ gå på knæ
	63.	besvær med at bøje ned til gulv
	64.	usikkerhed ved at dreje på knæ
	65.	usikkerhed ved at vride på knæ
	66.	besvær med at cykle
	67.	besvær med at tage ud at danse
	68.	besvær med at løbe efter små børn
	69.	besvær med at løbe efter bussen/toget
	70.	besvær med at hoppe fra en båd til kajen
	71.	bøje forover/bagover
	72.	vende eller dreje
	73.	begrænset i lettere aktiviteter
	74.	besvær med at bære tunge objekter
Arbejde	75.	sygemeldt
	76.	let arbejde
	77.	middeltungt arbejde (fx sygehjælper)

	78. deltid
	79. fuldtid
	80. skift af arbejde
	81. tungt arbejde (fx jord/beton)
Hjemmet	82. problemer med vanlige hobbies eller fritidsaktiviteter
	83. lette aktiviteter i hjemmet
	84. tunge aktiviteter i hjemmet
	85. støv af og vand blomster
	86. støvsugning og græsslåning
	87. besvær med tungt husarbejde
	88. besvær med let husarbejde
	89. besvær med havearbejde
	90. flytte bord, distance
	91. besvær med at gå på indkøb
	92. besvær med at bære indkøbsvarer
	93. bevæge dig rundt i en lille gyngende båd

Function in Sport and Recreation

Løb	94. motionsløb 3-4 x ugl.
	95. almindelig løb ligefrem ved sport
	96. løb med retningsskift
	97. løb med opbremsninger
	98. løb med drejende, vridende bevægelser
	99. løb med dreje eller vride på det skadede knæ
	100. orienteringsløb
	101. fuld konkurrence løb - lige ud
Hop	102. hop
	103. fuld konkurrence hop og landing
	104. hop på det skadede ben
	105. sidelæns hop fra det ene ben til det andet
Sportsgrene	106. deltage i konkurrence sport
	107. fodbold (fritidsniveau)
	108. fodbold (seriehold)
	109. fodbold (3. div. og nedad)
	110. elitefodbold (1. og 2. Division)
	111. elite: kontaktidræt (håndbold, basketball, ishockey…) atletik (hop), tennis, squash
	112. alpint skiløb
	113. Langrend skiløb
	114. svømning
	115. øvrig kontaktidræt, tennis (ikke elite)
	116. motions tennis/squash
	117. ridning (heste)
	118. motionscykling
	119. elite cykling
	120. cykling lang distance
Fysisk træning	121. hård fysisk træning kort tid efter skaden eller operation
	122. udspændingsøvelser
	123. styrkeøvelser til benene
	124. lidt begrænset dybe knæbøjninger
	125. normale ubegrænset dybe knæbøjninger

Psycho-social

Emotionelt	126. føler dig roligt og afslappet (tidsrum f.eks. sidste 4 uger)
	127. følt dig trist til mode
	128. frustration over at skulle huske knæet ved sportsaktivitet
	129. angst for kontaktsport
	130. generelle sikkerheds bekymringer
	131. bekymringer omkring din livsstil og aktiviteter med din familie
	132. manglende selvtillid pga din skade
	133. angst for genskade
	134. Problemer med arbejde eller ADL pga følelsesmæssige problemer
	135. fuld af energi
	136. bekymring for at skaden forværres af at dyrke sport/aktivitet
	137. angst for knæsvigt/giver efter ved sport
	138. bekymring for eksterne faktorer (i.e., vådt gulv, etc.)
	139. forsigtighed ved sport
Socialt	140. vanskeligt at se andre mennesker
Begrænsninger	141. vanskelighed ved at give dig helt under sport
	142. begrænsning i at dyrke din 1. prioriterede sport
	143. begrænsning i at dyrke din 2. prioriterede sport
	144. begrænset i at dyrke fitness og fysisk træning
	145. begrænsninger i livsnydelse
	146. tilbageholdenhed pga din skade
	147. accept af dine begrænsninger pga skaden
Forandringer	148. Ændret forventninger til din sport
	149. overvejelser om at dine konkurrencebehov ikke længere bliver opfyldte
	150. omlægning af din livsstil pga knæet
Bevidsthed af skaden	151. hvor ofte mindes problemet
	152. problemstørrelsen
	153. opmærksom på dine knæ problemer
	154. hvor tilfreds er du med dit knæ
	155. stole på knæet
	156. sammenligning af aktivitetsniveau før/efter skaden
	157. deltage i sport med/uden symptomer

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