The lingering impact of sport-related knee injuries on health-related quality of life in active youth

by

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Abstract

Background: It is assumed that youth who experience a knee injury while playing sports have an initial decline in health that resolves with time, leaving no lasting impact. Health-related quality of life (HRQoL) encompasses the physical, psychological, and social domains of health. It can represent overall health (*generic HRQoL*) or health relative to a specific condition or body part (e.g., *knee-specific HRQoL*). Our knowledge of how sport-related knee injuries impact HRQoL is mostly based on adults and one injury type [anterior cruciate ligament (ACL) rupture]. To appreciate the full consequence of sport-related knee injuries on active youth, a broader understanding of how these injuries impact HRQoL is needed.

Objectives: To improve our understanding of 1) how to measure HRQoL of active youth, 2) how HRQoL is altered by a youth sport-related knee injury at varying timepoints, and 3) what physical, psychological, and social consequences of injury are associated with HRQoL in active youth at varying timepoints.

Methods: This thesis consists of 4 studies: 1) a systematic review evaluating patient-reported outcome measures (PROMs) for measuring generic and condition-specific HRQoL of active youth according to COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) guidelines; 2) a secondary analysis of a historical cohort study comparing *generic and knee-specific HRQoL* between individuals with and without a 3-12-year history of a youth sport-related knee injury; 3) a preliminary analysis of a prospective cohort study describing differences in *knee-specific HRQoL* and associated health outcomes between youth with and without a sport-related knee injury over an initial 6-month period; and 4) a prospective cohort study comparing *knee-specific HRQoL* between youth with and without a sport-related knee injury and assessing the influence of associated health outcomes on this relationship over a 12-month period.

Results: The systematic review identified and evaluated 11 generic and 7 condition-specific HRQoL PROMs used in active youth. No existing PROM was deemed robust due to lacking sufficient measurement properties. Two generic and 1 upper extremity-specific HRQoL PROMs were judged as the most suitable based on sufficient structural validity and internal consistency. The historical and prospective cohort studies reveal that a wide range of youth sport-related knee injuries are associated with reduced *knee-specific HRQoL* at baseline, 6-month, 12-month and 3-12 year follow-ups compared to uninjured controls, regardless of sex. Conversely, no differences in *generic HRQoL* were found at 3-12 year follow-up. Exploratory analyses suggest that intermittent knee pain, knee muscle strength, physical activity, kinesiophobia, injury type, and baseline HRQoL may influence the relationship between knee injury and HRQoL.

Conclusions: Taken together, these studies reveal that youth who experience a wide range of sport-related knee injuries – not just ACL ruptures – experience significant and persistent deficits in *knee-specific HRQoL* but not *generic HRQoL* compared to uninjured controls. Intermittent knee pain, knee extensor strength, physical activity, kinesiophobia, and injury type may be potential determinants of HRQoL in this population. Novel contributions from this thesis can guide future development and evaluation of HRQoL PROMs and inform future efforts to better understand and optimize HRQoL following a youth sport-related knee injury.

Preface

This thesis is an original work by Christina Le under the supervision of Dr. Jackie L. Whittaker, Associate Professor in the Department of Physical Therapy at the University of British Columbia, Adjunct Associate Professor in the Department of Physical Therapy at the University of Alberta, and research scientist at Arthritis Research Canada; Dr. Carolyn A. Emery, Professor in the Faculty of Kinesiology at the University of Calgary; Dr. Stephanie R. Filbay, Senior Research Fellow in the Centre for Health, Exercise & Sports Medicine at the University of Melbourne; and Dr. Patricia J. Manns, Associate Dean in the College of Health Sciences at the University of Alberta.

The University of Alberta Research Ethics Board approved the research study in Chapters 4 and 5 (Ethics ID Pro00063773). The University of Calgary Conjoint Health Research Ethics Board approved the research study in Chapter 3 (Ethics ID E-25075). The study in Chapter 2 was published in the *Journal of Orthopaedic & Sports Physical Therapy*. The study in Chapter 3 was published in the *International Journal of Environmental Research and Public Health*. The study in Chapter 4 has been submitted for publication in the *Clinical Journal of Sport Medicine*. The study in Chapter 5 has been submitted for publication in the *Journal of Orthopaedic & Sports Physical Therapy*.

Dedication

I dedicate this dissertation to my family and especially my dad, Hoang Dang Le and grandma, Sen Thi Phen.

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List of Abbreviations

Abbreviation	Definition
ACL	Anterior cruciate ligament
ACL QOL	Anterior Cruciate Ligament Quality of Life questionnaire
ACLR	Anterior cruciate ligament reconstruction
ALQS	Athlete Life Quality Scale
ANOVA	Analysis of variance
BIA	Bioelectrial impedance analysis
BMI	Body mass index
COSMIN	COnsensus-based Standards for the selection of health Measurement INstruments
DPA	Disablement in the Physically Active scale
DPA-MSC	Disablement in the Physically Active scale-mental summary component
EQ-5D-5L	EuroQol-5D-5L
EQ VAS	EuroQol-visual analog scale
FAAM-S	Foot and Ankle Ability Measure sports subscale
FAI	Femoroacetabular impingement
FAST	Functional Arm Scale for Throwers
FMI	Fat mass index
GLTEQ	Godin Leisure-Time Exercise Questionnaire
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HAGOS	Copenhagen Hip and Groin Outcome Score
HOOS	Hip dysfunction and Osteoarthritis Outcome Score
HR	Hazard ratio
HRQoL	Health-related quality of life
ICC	Intra-class correlation coefficient
ICOAP	Measure of Intermittent and Constant Osteoarthritis Pain
iHOT	International Hip Outcome Tool
kg	Kilogram
KOOS	Knee injury and Osteoarthritis Outcome Score
LCL	Lateral collateral ligament
m	Metre
MCL	Medial collateral ligament
MDC	Minimal detectable change
MET	Metabolic equivalent
MIC	Minimal important change
MID	Minimal important difference
MRI	Magnetic resonance imaging
MVPA	Moderate-to-vigorous physical activity
NCAA	National Collegiate Athletic Association
N	Newton
n	Number of participants
OR	Odds ratio
QOL	Quality of life

PAR-Q	Physical Activity Readiness Questionnaire
PASS	Patient acceptable symptom state
PASS	Pediatric/Adolescent Shoulder Survey
PCL	Posterior cruciate ligament
PedsQL	Pediatric Quality of Life Inventory
PrE-OA	Alberta Youth Prevention of Early Osteoarthritis cohort
PROM	Patient-reported outcome measure
PROMIS	Patient-Reported Outcomes Measurement Information System
R^2	Coefficient of determination
RTS	Return to sport
SD	Standard deviation
SF-12	Medical Outcomes Study 12-Item Short-Form Health Survey
SF-36	Medical Outcomes Study 36-Item Short-Form Health Survey
TSK or TSK-17	Tampa Scale for Kinesiophobia
WHOQOL-BREF	World Health Organization Quality of Life instrument-abbreviated version
95%CI	95% confidence interval

CHAPTER 1: INTRODUCTION

It is assumed that youth who experience a sport-related knee injury have an initial decline in health-related quality of life (HRQoL) that resolves with time, leaving no lasting impact. However, our understanding about how a knee injury affects HRQoL is mostly based on studies that focus on adults who experience one specific injury [anterior cruciate ligament (ACL) rupture with subsequent ACL reconstruction (ACLR)] and lack an uninjured, comparison group. This leaves many important questions unanswered. What are the best methods to measure youth HRQoL? What is the short-and long-term impact of youth sport-related knee injuries on HRQoL? What factors influence HRQoL after a youth sport-related knee injury? Without the answers to these questions, we cannot determine if we need to or how to promote HRQoL during this critical life stage.

1.1 YOUTH SPORT-RELATED INJURIES

Youth who regularly participate in sports and recreational activities enjoy numerous health benefits such as improved cardiovascular health,[1, 2] motor competence,[3] cognitive functioning,[4] weight management,[1] and academic performance.[1] Unfortunately, youth who play sports also face an elevated risk of injury. In Canada, sport is the leading cause of injury in youth with approximately 1-in-3 youth seeking medical attention for a sport-related injury per year.[5-7] Sport-related injuries occur at rates of 60.9 and 65.7 injuries per 100 students for Canadian junior high and high school students, respectively.[6, 7]

Youth is a period that comprises biological growth and social transition from childhood to adulthood.[8] It is characterized as a critical time when "an individual acquires the physical, cognitive, emotional, social, and economic resources that are the foundation for later life health and wellbeing."[9] The definition of "youth" can vary but an age range of 10-24 years old[10] aligns with "contemporary patterns of adolescent growth."[8] Experiencing an injury that interrupts this important developmental phase can trigger health problems that are life-altering.[11]

1.2 YOUTH SPORT-RELATED KNEE INJURIES

Sport-related knee injuries are most prevalent between the ages of 15-24 years[12] and represent 15-20% of all sport-related injuries in Canadian youth.[6, 7] The most common sport-related knee injuries involve the medial collateral ligament (MCL; 36.1%) followed by the patella or patellar tendon (29.5%), ACL (25.4%), meniscus (23.0%), lateral collateral ligament (LCL; 7.9%), and posterior cruciate ligament (PCL; 2.4%).[13] Data from Australia suggests that the number of sport-related injuries requiring hospital treatment has grown 37% from 2004 to 2010.[14] The rising incidence of youth sport-related injuries is highly problematic because they have long-term health consequences and contribute to healthcare system burden.[15, 16]

1.3 HEALTH CONSEQUENCES OF SPORT-RELATED KNEE INJURIES

The short- and long-term consequences of sport-related knee injuries span the physical (i.e., functional status and capacity to perform tasks and activities[17]), psychological (i.e., cognition, behaviour, and affect[17, 18]), and social (i.e., relationships and participation in social networks[17, 18]) health domains. These injuries also increase the risk for future disease states including osteoarthritis.[19] In fact, there is strong evidence that many types of knee injuries increase the risk for osteoarthritis, including ACL or PCL sprains [hazard ratio (HR) 8.2; 95%CI 5.9, 11.4], meniscus tears (HR 7.6; 95%CI 5.5, 10.5), fractures (HR 7.0; 95%CI 4.2, 11.7), patella dislocations (HR 5.9; 95%CI 3.4, 10.1), cartilage injuries (HR 5.2; 95%CI 3.8, 7.0), MCL or LCL sprains (HR 4.9; 95CI 3.3, 7.3), and bony contusions (HR 3.2; 95%CI 2.2, 4.7).[19]

Despite this knowledge, researchers and clinicians have tended to focus on ACL ruptures. This may be due to the high costs of ACLR and lengthy rehabilitation associated with these injuries.[20, 21] As a result, most of what we know about the consequences of sport-related knee injuries comes from studies that involve within-group comparisons of individuals who experience an ACL rupture and subsequent ACLR. Only recently has preliminary evidence about the consequences of other intra-articular knee injuries (i.e., beyond ACL ruptures) started to emerge.[22]

The following sections and **Table 1.1** highlight what is known about the physical, psychological, and social consequences of sport-related knee injuries based on studies that include comparisons to uninjured controls or population norms. This overview focuses on the injury consequences relevant to this thesis and is not inclusive of all outcomes that have been assessed. The evidence is summarized by health domain, life stage (youth vs. adult), and time since injury or surgery. Additional information is provided in **Appendices A and B** for youth and adults, respectively.

Table 1.1: Overview of the Health Consequences of Sport-Related Knee Injuries by Time Since Injury and Life Stage

		Short-Term (0-2 Years)[a]						Medium-Term (2-5 Years)[a]						Long-Term (≥5 Years)[a]					
Health Domain	**Consequence**	**Youth**[b]			**Adult**[c]			**Youth**			**Adult**			**Youth**			**Adult**		
	Injury Type:																		
Physical	Pain																		
	Knee symptoms																		
	Knee muscle weakness																		
	Physical inactivity																		
	Obesity																		
Psychological	Kinesiophobia																		
Social	Social isolation																		

This table represents data from studies that compared outcomes between individuals with a sport-related knee injury to uninjured controls or population norms and found statistically significant between-group differences in mean or median scores. All studies are described in greater detail in **Appendices A and B**.

[a]Indicates time since knee injury or surgery
[b]Includes samples with a mean age between 10-24 years
[c]Includes samples with a mean age ≥25 years

Legend

Pooled Sample Size of Injured Individuals

Injury Type	<100	≥100	
			ACL rupture or ACLR
			Meniscus
			Any knee injury

1.3.1 Physical Health Consequences of a Sport-Related Knee Injury

Common physical health consequences associated with sport-related knee injuries include pain and other symptoms (e.g., swelling, stiffness), knee extensor and flexor muscle weakness, physical inactivity, and obesity.

1.3.1.1 Physical Health Consequences in Youth

In the first 2 years (i.e., short-term) following an ACL rupture or ACLR, there is consistent evidence that youth demonstrate greater pain and symptoms[23-25] and weaker knee extensor and flexor muscles[23, 26] compared to uninjured controls. There is also preliminary evidence that injured youth also have lower physical activity levels in the short-term.[27, 28] Between 2-5 years (i.e., medium-term) following ACL rupture or ACLR, we have consistent evidence of elevated knee pain and symptoms[24, 29-32] and preliminary evidence of lower physical activity levels,[33] including being less likely to meet national physical activity guidelines [≥150 minutes of moderate-to-vigorous physical activity (MVPA) per week], than controls.[34] At 5 years and beyond (i.e., long-term) an ACL rupture or ACLR, there is consistent evidence of greater knee pain and symptoms.[35-38] Conversely, little is known about knee muscle strength past the short-term after ACL rupture or ACLR or body composition or obesity at any timepoint.

Beyond ACL rupture and ACLR, 1 cohort study provides preliminary evidence of increased pain and other symptoms, reduced knee extensor strength, lower daily MVPA, and increased adiposity 3-10 years following a variety of youth sport-related knee injuries compared to uninjured controls.[22, 39, 40]

1.3.1.2 Physical Health Consequences in Adults

In the short-term following an ACL rupture or ACLR, there is consistent evidence that adults have reduced knee extensor and flexor strength compared to uninjured controls.[26, 41-44] In the medium-term, there is preliminary evidence of increased pain and other symptoms[45-47] and reduced knee flexor strength.[48] Finally, in the long-term, 1 cohort study reported greater knee pain and other symptoms compared to uninjured controls.[49] In contrast, we know little about physical activity and obesity outcomes in adults who have experienced an ACL rupture or ACLR in comparison to uninjured controls.

With respect to non-ACL injuries, adults who have a meniscus injury or surgery (meniscectomy or meniscal repair) report greater pain and other symptoms in the short-[50] and medium-term[47] relative to controls.

1.3.2 Psychological Consequences of Sport-Related Knee Injuries

Kinesiophobia or fear of re-injury is often reported after an ACL rupture.[18, 51-55] Kinesiophobia is defined as "an excessive, irrational, and debilitating fear of physical movement and activity resulting from a feeling of vulnerability to painful injury or re-injury."[56, 57]

1.3.2.1 Psychological Health Consequences in Youth

Few studies have compared kinesiophobia in youth with and without a sport-related knee injury. However, there is preliminary evidence that youth who have undergone ACLR report greater medium-[31] and long-term[36] kinesiophobia than uninjured controls.

1.3.2.2 Psychological Health Consequences in Adults

Following an ACL rupture or ACLR, greater short-term[58] and medium-term[46, 59, 60] kinesiophobia has been observed in adults compared to uninjured controls.

1.3.3 Social Consequences of Sport-Related Knee Injuries

No quantitative studies have examined the social consequences of a sport-related knee injury by comparing outcomes between injured and uninjured individuals. However, qualitative studies have described the social effects of these injuries, including the temporary or permanent removal from sports and recreational activities.[18, 61, 62]

1.3.3.1 Social Health Consequences in Youth

A qualitative study of youth with a severe sport-related injury (including an ACL rupture) revealed they have feelings of "no longer fitting in" with their teammates and are frustrated about not experiencing the joy of sport.[61] Similar feelings of loneliness and frustration of not being able to participate in sports are conveyed by youth who with an ACL rupture.[63]

1.3.3.2 Social Health Consequences in Adults

A literature review of adults' concerns during rehabilitation for a sport-related knee injury highlights feelings of disengagement, isolation from their sporting community (e.g., coaches, teammates, training partners), and perceived lack of social support.[62]

1.4 HEALTH-RELATED QUALITY OF LIFE

Health-related quality of life is a construct that encompasses the physical, psychological, and social domains of health and is influenced by an individual's perceptions, expectations, experiences, and beliefs (**Figure 1.1**).[64-66] Health-related quality of life is also described as "the degree to which [individuals] retain their ability to participate in valued activities within the family, in the workplace, and in the community."[67]

Figure 1.1: Visual Interpretation of Health-Related Quality of Life

1.4.1 Generic and Condition-Specific Health-Related Quality of Life

To gain a comprehensive understanding of HRQoL in individuals with health conditions, we must assess both generic and condition-specific HRQoL. This is typically achieved by obtaining responses to patient-reported outcome measures (PROMs) from the individual of interest rather than a proxy (e.g., parent, caregiver, healthcare professional).

Generic PROMs broadly measure HRQoL across different demographic groups, medical conditions, and healthcare interventions. The strength of generic PROMs is comparability or facilitating the comparison of HRQoL across different health conditions (e.g., knee vs. shoulder injury) or in response to different interventions (e.g., surgical vs non-surgical ACL treatment). However, generic PROMs tend to be less responsive (i.e., able to detect change over time) and more prone to ceiling effects than condition-specific PROMs.[67] Examples of commonly used generic HRQoL PROMs include the EuroQol-5D-5L (EQ-5D-5L)[68] and the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36).[69]

Conversely, condition-specific PROMs provide a more nuanced assessment of HRQoL relative to a particular health condition or disease. Condition-specific PROMs are developed to be responsive or capable of measuring small, meaningful changes in HRQoL for a specific population.[67] The main limitation of condition-specific PROMs is the inability to compare HRQoL across patient groups or conditions. “Knee-specific HRQoL” or “knee-related QOL” is the condition-specific HRQoL of interest for individuals with a sport-related knee injury and refers to one’s perception of their knee health. The Knee injury and Osteoarthritis Outcome Score (KOOS) knee-related QOL subscale[70] and Anterior Cruciate Ligament Quality of Life (ACL QOL) questionnaire[71] are the most widely used knee-specific HRQoL PROMs.

1.4.2 Selecting Health-Related Quality of Life Patient-Reported Outcome Measures

Selecting generic and/or condition-specific HRQoL PROMs should be based on the robustness of measurement properties (i.e., validity, reliability, and responsiveness), interpretability (i.e., ability to produce meaningful findings), and feasibility (i.e., easy to use; **Table 1.2**).[72-74]

Table 1.2: Definitions of Measurement Properties

Domain	Measurement Property	Definition
Validity		The degree to which a PROM assesses the construct(s) it intends to measure
	Content validity	The degree to which the content of a PROM reflects the construct to be measured (i.e., is relevant, comprehensive, and comprehensible)
	Structural validity	The degree to which the scores of a PROM adequately reflect the dimensionality of the construct to be measured
	Cross-cultural validity	The degree to which the performance of items on a translated or culturally adapted PROM adequately reflect the performance of items on the original version
	Construct validity	The degree to which the scores of a PROM are consistent with hypotheses, based on the assumption that the PROM validly measures the construct to be measured (e.g., scores of a generic HRQoL PROM hypothesized to have high positive correlation with scores of another generic HRQoL PROM)
	Criterion validity	The degree to which scores of a PROM adequately reflect a gold standard
Reliability		The degree to which a PROM is free from measurement error
	Reproducibility	The extent to which scores for patients who have not changed are the same for repeated measurements over time (test-retest reliability), by different persons on the same occasion (inter-rater reliability), or by the same person (intra-rater reliability)
	Internal consistency	The degree of interrelatedness among items of a PROM
	Reliability (test-retest)	The proportion of total variance in measurements that is due to "true" differences between individuals
	Measurement error	The systematic and random error of an individual's score that is not attributed to true chances in the construct to be measured
Responsiveness		The ability of a PROM to detect change over time in the construct to be measured
Interpretability[a]		The degree to which one can assign qualitative meaning (i.e., clinical or commonly understood connotations) to a PROM's scores or change in scores
Feasibility[a]		The ease of application of a PROM in its intended setting given various constraints (e.g., time, money)

Adapted from the COSMIN User Manual[72-75] and Mokkink et al. (2010)[76]
[a]An important characteristic of a PROM but not considered a measurement property

HRQoL, health-related quality of life; PROM, patient-reported outcome measure

Understanding the robustness of a PROM's measurement properties involves rating methodological quality, critically appraising the results, and synthesizing the findings of individual studies that have evaluated that PROM. The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) initiative has created evidence-based tools, the 2018 COSMIN Risk of Bias checklist[72] and the criteria for good measurement properties,[72-75, 77, 78] to facilitate the evaluation of validity, reliability, and responsiveness.

According to the COSMIN group, there is a hierarchy of measurement properties. Content validity is the most important measurement property as it reflects how relevant, comprehensive, and comprehensible a PROM is to a target population.[74, 78] The second most important properties are internal consistency, structural validity, and cross-cultural validity (if applicable) which represent the internal structure of a PROM, including how items are related and organized into subscales.[72, 78] As per the COSMIN Manual for Systematic Reviews of Patient-Reported Outcome Measures,[72-74] a suitable HRQoL PROM should possess sufficient content validity and internal consistency to accurately measure HRQoL.

No tools exist to rate interpretability or feasibility of PROMs, but a set of desired characteristics are listed in the COSMIN Manual for Systematic Reviews of PROMs.[72-74] Indicators of good interpretability include providing information on score distributions (e.g., floor and ceiling effects) and meaningful thresholds [e.g., minimal important change (MIC), minimal important difference (MID)].[72-74] Having MIC (i.e., average individual change in score over time within a group that is considered minimally important[79, 80]) and MID (i.e., difference in mean change scores over time between 2 groups that is considered minimally important[80]) values is extremely helpful for determining if changes in PROM scores over time are important to patients. Indicators of good feasibility include providing information about PROM completion (e.g., time to complete, required physical or mental abilities), administration (e.g., time to score, ease of scoring), and accessibility (e.g., copyright, costs).[72-74]

1.4.3 Measuring Health-Related Quality of Life of Active Youth

Special considerations must be taken when measuring HRQoL in unique populations, such as youth and, more specifically, active youth. Interviews and focus groups with youth have identified that some factors (e.g., mental health) that contribute to HRQoL overlap between youth and adult populations while others are unique to youth (e.g., supportive parents, quality of education).[81] It is also well-documented that high school and collegiate athletes report better generic HRQoL compared to non-athletes.[82, 83] Given these distinctions, it is important to use PROMs that have been developed for or validated in active youth populations when measuring their HRQoL.

1.5 HEALTH-RELATED QUALITY OF LIFE AFTER A SPORT-RELATED KNEE INJURY

Individuals who have a sport-related knee injury and encounter any associated physical, psychological, and/or social health consequences are likely to experience some decline in HRQoL. Similar to other outcomes, most of the evidence that exists related to HRQoL after a knee injury is based on within-group comparisons of individuals with an ACL rupture or ACLR. Few studies have compared generic or knee-specific HRQoL outcomes with uninjured controls or population norms nor considered injuries beyond ACL ruptures.

The following sections and **Figure 1.2** summarize what is known about generic and knee-specific HRQoL following a sport-related knee injury when compared to uninjured controls or population norms and organized by life stage (youth vs. adult) and time since injury or surgery. Additional information is provided in **Appendices C and D** for youth and adults, respectively.

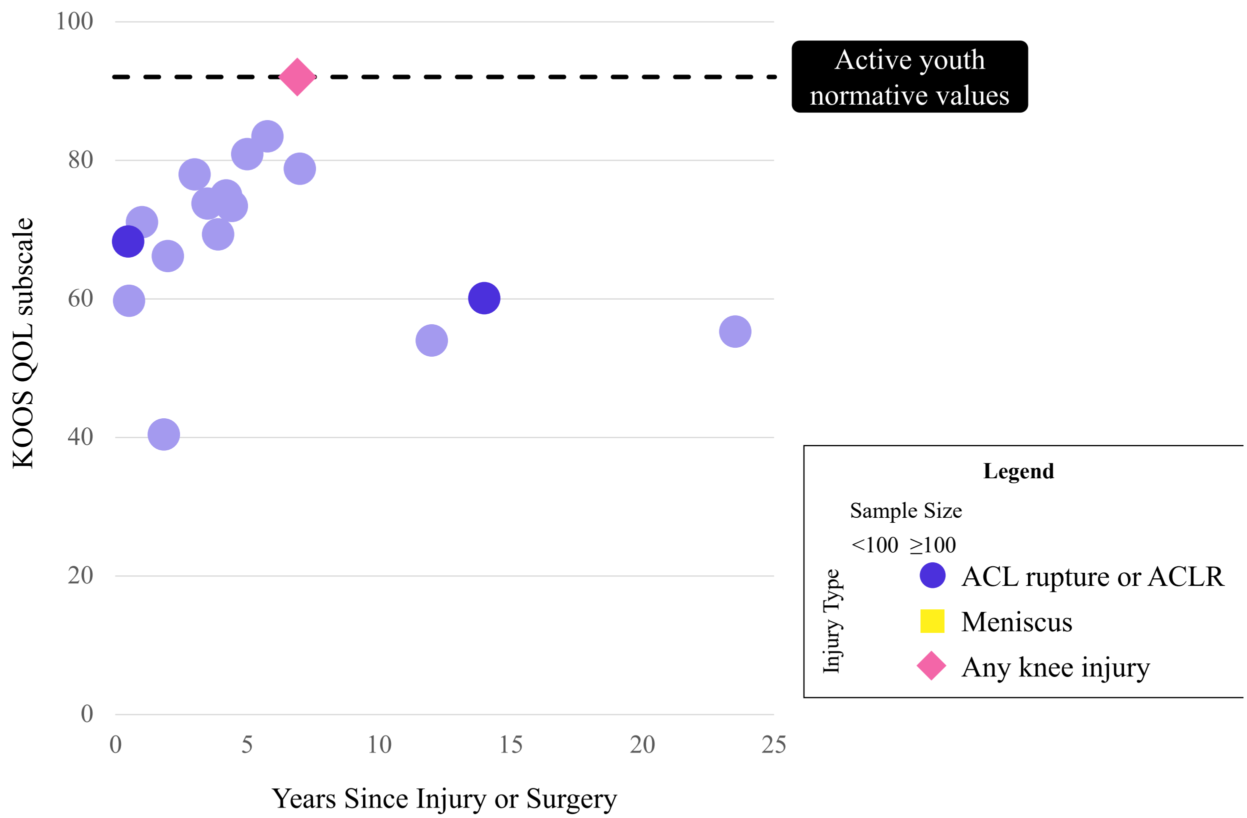

Figure 1.2: KOOS QOL Subscale Scores for Youth Cohorts with a Sport-Related Knee Injury

This figure represents data from studies that compared the Knee injury and Osteoarthritis Outcome Score QOL subscale (KOOS QOL) between youth with and without a sport-related knee injury and found statistically significant between-group differences in mean or median scores (0-100). Active youth normative values were obtained from Cameron et al. (2013).[84]

One study did not find significant differences in KOOS QOL scores at mean follow-up of 5.9 years between professional male soccer players who underwent an ACLR in their youth and a healthy control group of professional soccer players.[85]

1.5.1 Youth Health-Related Quality of Life after a Sport-Related Knee Injury

There is a paucity of studies comparing short- (0-2 years since injury) and medium-term (2-5 years) *generic HRQoL* following a youth sport-related knee injury. However, several studies have reported that over the long-term (≥5 years), youth who experience an ACL rupture or ACLR demonstrate similar generic HRQoL outcomes as uninjured controls.[35, 85-87]

With respect to *knee-specific HRQoL*, youth who undergo an ACLR report poorer knee-specific HRQoL in the short-,[23-25, 88] medium-,[24, 25, 29-32] and long-term[35-38, 87] after ACLR compared to uninjured controls. Specifically, it appears that short-term deficits in knee-specific HRQoL improve over the medium-term before declining again in the long-term (**Figure 1.2**). In contrast, 1 study reported no differences in long-term knee-specific HRQoL between professional male soccer players who had an ACLR in their youth and those who did not.[85] Beyond ACL ruptures, reduced knee-specific HRQoL is evident following a wide range of sport-related knee injuries at 3-10 years post-injury.[22]

1.5.2 Adult Health-Related Quality of Life after a Sport-Related Knee Injury

Adults with an ACL rupture or ACLR demonstrate short-term deficits in *generic HRQoL*[89] that are no longer detected in the medium- and long-term in comparison to uninjured controls.[46, 90, 91] Two systematic reviews including both youth and adults with an ACL rupture or ACLR also describe no differences in long-term generic HRQoL.[92, 93] Interestingly, a third systematic review reports lower physical domain scores of generic HRQoL over the long-term following a youth or adult ACL rupture or ACLR.[94]

Adults who experience an ACL rupture or ACLR demonstrate medium-[45, 46, 95] and long-term[49] deficits in *knee-specific HRQoL* compared to uninjured controls. Similarly, adults who experience a meniscus injury or surgery (meniscectomy or meniscal repair) report lower short-[96] and medium-term[47] knee-specific HRQoL than controls.

1.6 FACTORS ASSOCIATED WITH YOUTH HEALTH-RELATED QUALITY OF LIFE

Our ability to optimize generic and knee-specific HRQoL after a youth sport-related knee injury is contingent on knowing who experiences lower HRQoL (i.e., target population), identifying modifiable determinants of HRQoL (i.e., treatment targets), and implementing interventions that mitigate these modifiable determinants (i.e., treatments). This requires us to understand what factors have independent relationships with HRQoL (i.e., determinants). Non-modifiable determinants (e.g., sex) point to target populations while modifiable determinants (e.g., knee muscle strength) point to treatment targets and can inform actual treatments. Furthermore, we must understand what factors are independently associated with HRQoL and/or youth sport-related knee injuries and may modify or confound this relationship. This information will determine if it is necessary to stratify our reporting of the relationship between injury and HRQoL (effect modifier) or adjust our analyses (confounder).

The following sections and **Table 1.3** provide information about potential determinants of youth generic and knee-specific HRQoL. It is important to note that many of the studies that have assessed these factors as it relates to knee-specific HRQoL in this population are subject to selection bias due to convenience sampling and sample sizes. Therefore, this information should be interpreted with caution.

Table 1.3: Summary of Potential Determinants of Generic and Knee-Specific Health-Related Quality of Life in Youth with Direction of Association and Level of Supporting Evidence

Potential Determinant	Generic HRQoL	Knee-Specific HRQoL
Structural factors[a]		
Socioeconomic status	+	?
Healthcare accessibility and literacy	+	?
Education	+	?
Demographic factors		
Age	–	–
Sex/gender[b]	–	×
Sport participation	+	?
General health outcomes		
Pain	–	?
Physical activity	+	?
Muscle strength	?	?
Weight status[c]	+	?
Social support	+	?
Knee injury-related outcomes		
Knee pain and symptoms	?	–
Physical inactivity	?	–
Knee muscle weakness	?	?
Obesity	?	–
Kinesiophobia	?	–
Social isolation	?	?
Injury type	?	?

Associations are positive (+), negative (–), unknown (?), or no association (×)
Shading indicates Levels of Evidence as per the Oxford Centre for Evidence-Based Medicine 2011 for prognostic studies:[97] Level 1, systematic reviews of inception cohort studies (blue); level 2, inception cohort studies (yellow); level 3, cohort study or control arm of a randomized trial (orange), level 4, case-series, case-control, or poor quality prospective cohort study (red). Lastly, qualitative studies are shaded in purple. Studies are described in greater detail in sections 1.6.1 to 1.6.4.
[a]Defined as "fundamental structures of the nation state that generate social stratification" and include national wealth, income inequality, educational status, sexual or gender norms, or ethnic groups as per Viner et al. (2012).[98]
[b]Reference = female/girl
[c]Reference = healthy weight

HRQoL, health-related quality of life

1.6.1 Structural Factors

Structural factors represent "fundamental structures of the nation state that generate social stratification."[98] Structural factors that are associated with generic HRQoL in youth populations include socioeconomic status,[99, 100] healthcare access and literacy,[101] and education.[81, 98] How these factors mediate the relationship between a sport-related knee injury and youth HRQoL is unknown.

1.6.2 Demographic Factors

Demographic factors are characteristics that describe a population. Age, sex, and sport participation are demographic factors that have been associated with HRQoL in youth.

1.6.2.1 Age

Increasing age is associated with reduced generic HRQoL in youth[102] as well as reduced knee-specific HRQoL in youth who undergo an ACLR.[103, 104] Youth also have an elevated risk of experiencing a sport-related knee injury compared to adults.[12]

1.6.2.2 Sex

Females report worse generic HRQoL[105] than males. In contrast, sex does not appear to be associated with knee-specific HRQoL following an ACL rupture or ACLR.[92, 93, 106, 107] Females also demonstrate a higher risk of ACL ruptures than males.[108]

1.6.2.3 Sport Participation

Sport participation is positively associated with generic HRQoL in primary,[109] secondary,[109, 110] and university students.[111] However, the impact of sport participation on knee-specific HRQoL is less clear. Playing sports and recreational activities that require frequent cutting, pivoting, and jumping (e.g., soccer, basketball) is a known risk factor for ACL ruptures.[112]

1.6.3 General Health Outcomes

General health outcomes, such as pain, physical activity, muscle strength, weight status, and social support, are linked with HRQoL in uninjured youth. Specifically, the presence of pain[113, 114] and obesity[115, 116] is negatively associated with generic HRQoL, whereas physical activity[117, 118] and social support[98, 119] are positively associated with it. There is also preliminary evidence that strength training is associated with increased generic HRQoL in adolescents with obesity.[120] How these general health outcomes impact knee-specific HRQoL in youth is unknown.

1.6.4 Knee Injury-Related Outcomes

Common consequences of youth sport-related knee injuries that are potential determinants of HRQoL include knee pain and symptoms, physical inactivity, knee muscle weakness, obesity, kinesiophobia, and social isolation. Additionally, different injury types may have different relationships with HRQoL.

Greater kinesiophobia[53] and higher body mass index (BMI)[104] are negatively associated with knee-specific HRQoL at 3 and 10 years following ACLR, respectively. Increased knee pain and other symptoms are also negatively associated with knee-specific HRQoL 3-10 years following any sport-related knee injury.[121] Physical activity does not appear to be associated with knee-specific HRQoL in the first 1-2 years following an ACLR[122] or 3-12 years following any knee injury.[39]

The influence of knee muscle weakness and social isolation on knee-specific HRQoL has not been assessed in youth populations. We also lack evidence of how any of these common injury consequences influence generic HRQoL.

Knee injuries that involve lengthy rehabilitation (≥6 months) and possible surgery (e.g., ACL rupture, meniscus tear) may be associated with lower generic and knee-specific HRQoL than other injuries (e.g., MCL sprain, bony contusion). No studies to date have assessed the influence of injury type on generic or knee-specific HRQoL.

1.7 THE RELATIONSHIP BETWEEN GENERIC AND KNEE-SPECIFIC HEALTH-RELATED QUALITY OF LIFE

The strength and direction of the relationship between generic and knee-specific HRQoL has not been previously examined. Theoretically, reduced generic HRQoL may lead to reduced knee-specific HRQoL through determinants such as lower socioeconomic status and decreased access to healthcare. Conversely, reduced knee-specific HRQoL may trigger reduced generic HRQoL through determinants such as increased knee pain and other symptoms or lower physical activity levels.

1.8 KNOWLEDGE GAPS

To improve our understanding of the impact of sport-related knee injuries on HRQoL in active youth and move toward strategies to optimize HRQoL in this age group, we must:

- Identify robust (i.e., valid, reliable, responsive, interpretable, and feasible) PROMs to measure and monitor generic and knee-specific HRQoL in active youth.
- Compare changes in generic and knee-specific HRQoL in youth with a wide range of sport-related knee injuries and uninjured controls over the short- (0-2 years), medium- (2-5 years), and long-term (≥5 years)
- Identify potential determinants of HRQoL following a wide range of youth sport-related knee injuries

1.9 THESIS RATIONALE

The knee is one of the most commonly injured joints in youth who play sports.[6, 7] Experiencing a sport-related knee injury during this crucial, transitional life stage can have a profound and lasting effect on one's physical, psychological, and social health and, ultimately, HRQoL. Currently, our understanding of how a sport-related knee injury influences youth HRQoL is mostly derived from individuals with a single injury type – an ACL rupture – despite it only accounting for 25% of knee injuries.[13] Furthermore, our understanding of modifiable and non-modifiable determinants of HRQoL following a youth sport-related knee injury is limited.

Robust generic and condition-specific HRQoL PROMs can help us establish the burden of youth sport-related knee injuries and characterize recovery patterns. Identifying factors that are independently associated with youth HRQoL provides information about who may be most vulnerable to reduced HRQoL and what potential targets may be included in future treatment strategies. Poor generic and knee-specific HRQoL following a sport-related knee injury may impede youth from adopting healthy, active lifestyles that can be maintained throughout adulthood and add to the growing individual and societal burden of these injuries.

1.10 PURPOSE

The overarching purpose of this thesis is to better understand the HRQoL (generic and condition-specific) of active youth following a sport-related knee injury and examine the association between physical, psychological, and social consequences of injury and HRQoL compared to uninjured controls.

The specific objectives of this research include:

1. Identifying the most suitable existing PROMs for measuring generic and condition-specific HRQoL of active youth based on measurement properties, interpretability, and feasibility.
2. Assessing and comparing generic and knee-specific HRQoL and associated (physical) health outcomes between active youth with a sport-related knee injury and uninjured controls of similar age, sex, and sport participation at 3-12-year follow-up.
3. Describing the relationship between injury history and early changes in knee-specific HRQoL or associated (physical and psychological) health outcomes in active youth with a sport-related knee injury compared to uninjured controls of similar age, sex, and sport participation over a 6-month follow-up.
4. Assessing and comparing the relationship between injury history and knee-specific HRQoL of active youth with a sport-related knee injury and uninjured controls of similar age, sex, and sport participation and examining the influence of associated (physical, psychological, and social) health outcomes on this relationship over a 12-month follow-up.

1.11 THESIS FORMAT

Chapters 2 to 5 represent 4 separate manuscripts that have been published, are under review, or have been submitted to peer-reviewed journals for publication. Chapter 6 highlights novel contributions and provides directions for future research and clinical practice.

1.12 CANDIDATE CONTRIBUTIONS

Each study was devised and designed in a collaborative effort by Christina Le and Dr. Jackie Whittaker. The study in Chapter 3 was also devised and designed by Drs. Jackie Whittaker and Carolyn Emery. The PhD Candidate, Christina Le, was the primary author for preparing each full manuscript and her contributions are outlined below. All coauthors contributed to manuscript revisions and approved the inclusion of the joint work in this doctoral thesis.

Chapter 2: Le CY, Truong LK, Holt CJ, Filbay SR, Dennett L, Johnson JA, Emery CA, Whittaker JL. Searching for the holy grail: a systematic review of health-related quality of life measures for active youth. Journal of Orthopaedic and Sports Physical Therapy. 2021;51(10):478-491. doi: 10.2519/jospt.2021.10412

The Journal of Orthopaedic and Sports Physical Therapy is ranked in the 94th percentile for physical therapy, sports therapy, and rehabilitation journals.

Candidate contributions: Developed the research question, developed the search strategy with a librarian scientist, executed the search strategy, reviewed records and selected eligible studies, extracted data from included studies, evaluated patient-reported outcome measures from included studies, interpreted the results, drafted the full manuscript, and led manuscript revisions and responses to reviewers.

This work was presented at:

1. La Trobe Sport and Exercise Medicine Higher Degree Research Student Showcase, La Trobe University, Melbourne, Australia in October 2020 (oral presentation, online due to the COVID-19 pandemic)
2. World Physiotherapy Congress in April 2021 (poster presentation, online due to the COVID-19 pandemic)
3. Canadian Physiotherapy Association Congress in May 2021 (oral presentation, online due to the COVID-19 pandemic)

For this work, Christina Le was supported by The Arthritis Society Training Graduate PhD Salary Award (TGP-19-0400; $41 000 awarded over 2019-2021) and Canadian MSK Rehab Research Network Trainee Award (CIHR FRN: CFI-148081; $5 000 awarded in 2017).

Chapter 3: Le CY, Toomey CM, Emery CA, Whittaker JL. What does the future hold? Health-related quality of life 3-12 years following a youth sport-related knee injury. International

Journal of Environmental Research and Public Health. 2021;18:6877. doi: 10.3390/ijerph18136877 (open access)

The International Journal of Environmental Research and Public Health is ranked in the 75th percentile for public, environmental, and occupation health journals.

Candidate contributions: Developed the research question for previously collected historical cohort data, cleaned data, cleaned data, planned data analysis with a biostatistician, led data analysis, synthesized and interpreted the results, drafted the full manuscript, and led manuscript revisions and responses to reviewers.

This work was presented at:

1. Canadian Arthritis Research Conference in February 2021 (poster presentation, online due to the COVID-19 pandemic)

Funding for this work is the same as above.

Chapter 4: Le CY, Pajkic A, Losciale JL, Filbay SR, Emery CA, Manns PJ, Whittaker JL. Comparing short-term knee-specific health-related quality of life and associated health outcomes between youth with and without a sport-related knee injury. *In submission at the Clinical Journal of Sport Medicine*.

The Clinical Journal of Sport Medicine is ranked in the 84th percentile for physical therapy, sports therapy, and rehabilitation journals.

Candidate contributions: Contributed to ethics renewals and amendments, recruited participants, scheduled data collection, collected, entered, and cleaned data, planned and led data analysis, synthesized and interpreted the results, and drafted the full manuscript.

This work was presented at:

1. Osteoarthritis Research Society International World Congress in April 2021 (oral presentation, online due to the COVID-19 pandemic)
2. Faculty of Rehabilitation Medicine Research Day in June 2021 (oral presentation, online due to the COVID-19 pandemic)
3. Canadian Arthritis Research Conference in February 2022 (oral presentation, online due to the COVID-19 pandemic)

In addition to previously mentioned funding, Christina also received a Speaker Award ($1 000) for her presentation at the 2022 Canadian Arthritis Research Conference.

Chapter 5: Le CY, Filbay SR, Emery CA, Manns PJ, Whittaker JL. Youth with a sport-related knee injury exhibit significant and persistent knee-specific health-related quality of life deficits at 12-month follow-up compared to uninjured peers. *In submission at the Journal of Orthopaedic & Sports Physical Therapy*.

Candidate contributions: Contributed to ethics renewals and amendments, recruited participants, scheduled data collection, collected, entered, and cleaned data, planned and led data analysis, synthesized and interpreted the results, and drafted the full manuscript.

This work was presented at:

1. Osteoarthritis Research Society International World Congress, Berlin, Germany in April 2022 (poster presentation)
2. Arthritis Research Canada Trainee Retreat, Vancouver, Canada in October 2022 (oral presentation)

In addition to previously mentioned funding, Christina also received a Faculty of Graduate Studies and Research, University of Alberta Trainee Travel Award ($630) for her presentation at the 2022 Osteoarthritis Research Society International World Congress.

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CHAPTER 2: SEARCHING FOR THE HOLY GRAIL: A SYSTEMATIC REVIEW OF HEALTH-RELATED QUALITY OF LIFE MEASURES FOR ACTIVE YOUTH

The information has been peer-reviewed and published as Le CY, Truong LK, Holt CJ, Filbay SR, Dennett L, Johnson JA, Emery CA, Whittaker JL. Searching for the holy grail: a systematic review of health-related quality of life measures for active youth. Journal of Orthopaedic and Sports Physical Therapy. 2021;51(10):478-491. doi: 10.2519/jospt.2021.10412.

The original publication can be found in **Appendix E**. Minor revisions have been made to the wording (e.g., "young people" replaced with "youth") and formatting to remain consistent with the other chapters.

Publication metrics: 335 full-text downloads, 1 citation

Current evidence indicates active youth have unique HRQoL, yet many PROMs used to measure HRQoL of active youth were not originally developed for this population. To accurately assess the HRQoL of active youth, PROMs should possess sufficient measurement properties, interpretability, and feasibility. This chapter summarizes the search for suitable existing generic and condition-specific HRQoL PROMs for active youth.

ABSTRACT

Objective: To identify the most suitable existing PROMS for measuring generic and condition-specific of active youth with and without a musculoskeletal injury based on measurement properties, interpretability, and feasibility.

Study Design: Systematic review conducted and reported according to the COSMIN User Manual for systematic reviews of PROMs and PRISMA guidelines, respectively.

Methods: We searched MEDLINE, Embase, CINAHL, SPORTDiscus, PsycINFO, and Scopus from inception to April 30, 2020. Records with original data describing the evaluation of a PROM or PROM subscale in active youth (15-24 years old) with or without a musculoskeletal injury were included. Non-English studies and those including individuals with a cognitive, developmental, or systemic condition were excluded. The COSMIN User Manual guided our measurement property evaluation and interpretability and feasibility description.

Results: Of 6931 potential records, 21 studies were included. Eleven generic and 7 condition-specific PROMs were identified. No PROM received a final COSMIN recommendation of "A," because all lacked sufficient content validity. The 8-item Disablement in the Physically Active scale-mental summary component Short Form (DPA-MSC SF-8), Quality of Life Survey, and Functional Arm Scale for Throwers (FAST) were the most suitable existing PROMs, given their high-quality evidence of sufficient structural validity and internal consistency.

Conclusion: No definitively robust PROM for measuring generic or condition-specific HRQoL of active youth was identified. Until one exists, we recommend selecting the DPA-MSC SF-8, the Quality of Life Survey, or the FAST and applying mixed methods to best characterize the HRQoL of active youth.

2.1 INTRODUCTION

Health-related quality of life encompasses the physical, psychological, and social domains of health. It is influenced by an individual's perceptions, experiences, expectations, beliefs,[1] and environment.[2] Determinants of HRQoL that may be most relevant to youth include participating in sports,[3] having supportive parents,[1] and receiving a good education.[1] Youth athletes report higher HRQoL compared to non-athletes.[3, 4] Youth who participate in sports and recreational activities may experience greater physical (e.g., increased fitness), psychological (e.g., increased autonomy), and social (e.g., established feelings of community) health benefits than those who do not.[5-7] Active youth may also report higher HRQoL, given the association between socioeconomic status and sports participation.[8]

Despite the many benefits of sports participation,[9-12] active youth (15-24 years old)[13-15] face an increased risk of musculoskeletal injury.[16, 17] Sport-related injuries are associated with long-term consequences and can negatively impact HRQoL.[18-21] Youth athletes who experience a sport-related injury report lower HRQoL compared to uninjured peers,[4, 22] even after returning to sport.[23] A better understanding of how youth HRQoL changes after a sport-related injury may identify which health domains are most affected and guide patient-centred care.

Patient-reported outcome measures provide the patient's perspective of their health and can inform individual care.[24] Both generic and condition-specific PROMs are needed to build a complete picture of the HRQoL of active youth.[25] To accurately measure and monitor changes in HRQoL and evaluate an intervention's effectiveness following injury, a PROM must demonstrate acceptable content validity (i.e., relevant, comprehensive, and comprehensible to active youths).[26, 27] A PROM should be psychometrically robust (i.e., valid, reliable, and responsive), easy to interpret, and feasible to use in clinical and research settings.

2.1.1 Objective

Previous research aimed at understanding the HRQoL of active youth has relied heavily on PROMs developed in adult populations. Important information about the HRQoL of active youth and its determinants may have been missed or misunderstood. The objective of our systematic review was to identify the most suitable existing PROMS for measuring generic and condition-specific of active youth with or without a musculoskeletal injury based on measurement properties, interpretability, and feasibility.

2.2 METHODS

This review was registered in the PROSPERO database (CRD42019123282), conducted according to the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) Manual for Systematic Reviews of PROMs (version 1.0, 2018),[26-29] and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[30] The COSMIN Manual[26-29] is an internationally accepted guideline designed for systematic reviews examining PROMs.[26-28] It provides steps to rigorously evaluate measurement properties of PROMs which leads to identifying the most robust PROM(s) for a specific purpose.[27]

2.2.1 Information Sources and Search

Eligible records were identified by searching 6 online databases – MEDLINE (Ovid), Embase (Ovid), CINAHL Plus with Full Text (EBSCOhost), SPORTDiscus (EBSCOhost), PsycINFO (Ovid), and Scopus – from inception to April 30, 2020. Medical subject headings and key words were selected to capture the constructs of youth, physical activity, HRQoL, PROMs, and measurement properties. The final search strategy was determined in collaboration with a health sciences librarian scientist (L.D.) (**Appendix F**). Reference lists of included studies were hand searched for relevant records.

2.2.2 Eligibility Criteria

Records reporting original data about the HRQoL of active youth with or without a musculoskeletal injury and describing the development of a PROM or evaluation of at least 1 measurement property of a generic or condition-specific HRQoL PROM or PROM subscale were included. Generic HRQoL PROMs assessing overall HRQoL may be used to compare groups who differ in demographics, medical condition, or healthcare intervention received. Condition-specific HRQoL PROMs pertain to a particular patient population or health condition. The term *active youth* indicated a sample of individuals with a mean or median age of 15 to 24 years[13] who were identified as recreational, competitive, or elite athletes or individuals who regularly participated in light to vigorous physical activity. For the latter, authors had to report on minutes of physical activity per week or enrollment in physical education or fitness classes. Non-English records and those including nonhuman participants or individuals with a cognitive (e.g., brain injury), developmental (e.g., developmental delay), or systemic (e.g., diabetes, cancer) condition were excluded. Conference abstracts, editorials, commentaries, reviews, case series, case studies, and grey literature were also excluded.

2.2.3 Study Selection

Records were organized using reference management software (EndNote X8.2, Clarivate Analytics, Philadelphia, PA). After removing duplicates, titles and corresponding abstracts were independently reviewed by pairs of 2 reviewers (C.L. and L.T., C.H., S.F., Wasim Labban., or J.W.) blinded to the record author(s) and journal title using an Excel (Microsoft Corporation, Redmond, WA) workbook designed specifically for screening.[31]

Prior to title/abstract screening, all reviewers independently screened a random sample of 120 records to assess the applicability of the exclusion criteria. The agreement between reviewers and the senior author (J.W.) on these 120 records ranged between 69% and 83% (Cohen's κ = 0.28-0.66). Discrepancies were discussed and exclusion criteria clarified before title/abstract screening began in full.

If a record title of interest was found but the abstract was unavailable, the full text was retrieved to ensure potentially relevant studies were not missed. The full texts of relevant records were independently reviewed by 2 reviewers to determine final study selection. The senior author (J.W.) mediated any disagreements at all stages when primary reviewers could not reach consensus. If multiple records reported on the same measurement property from the same study, we included the first published record.

2.2.4 Data Extraction

Data extraction followed recommendations from the COSMIN User Manual[26-29] and included study characteristics (e.g., sample size, mean or median age, sex), PROM characteristics (e.g., target population, number of subscales and items, scoring), and information about measurement properties, interpretability, and feasibility (as described below). Initial data extraction was completed by the lead author (C.L.) then independently verified by a second reviewer. Disagreements were resolved by consensus or by the senior author (J.W.). Study authors were contacted for missing data or clarification as needed.

2.2.5 Measurement Property Evaluation

As per the COSMIN User Manual,[26-29] the evaluation of each measurement property (see **Table 1.2** for definitions) of included PROMs involved 4 steps outlined below (**Figure 2.1**). A hypothetical example of the evaluation process can be found in **Appendix G**.

2.2.5.1 Evaluate the Methodological Quality of Measurement Properties by Individual Study

First, we evaluated the methodological quality of individual studies that assessed a measurement property, using the COSMIN risk-of-bias checklist.[26-29] Checklist items were graded as "very good," "adequate," "doubtful," and "inadequate" and the final rating for the methodological quality of a measurement property was determined by taking the lowest rating of any item assessing that property (i.e., "the worst score counts"[26-29]).

2.2.5.2 Rate the Results of Measurement Properties by Individual Study

Second, we rated the result of individual studies that estimated a measurement property by applying the criteria for good measurement properties (**Appendix H**).[26-29, 32, 33] A rating of "sufficient (+)," "insufficient (–)," "inconsistent (±)," or "indeterminate (?)" was assigned to each measurement property.

2.2.5.3 Summarize the Evidence for Measurement Properties by PROM

Third, we qualitatively summarized the evidence for a measurement property of a PROM across studies (as appropriate) and rated the summarized results by applying the criteria for good measurement properties.[26-29, 32, 33] An overall rating of sufficient was assigned if at least 75% of the results were sufficient.[26-29] In the case of inconsistent results across studies, we re-examined each study for sample heterogeneity. If sample heterogeneity existed, we provided an overall rating for each subgroup (i.e., sex, sport type, competition level). If no heterogeneity was found, the measurement property received an overall rating of inconsistent.

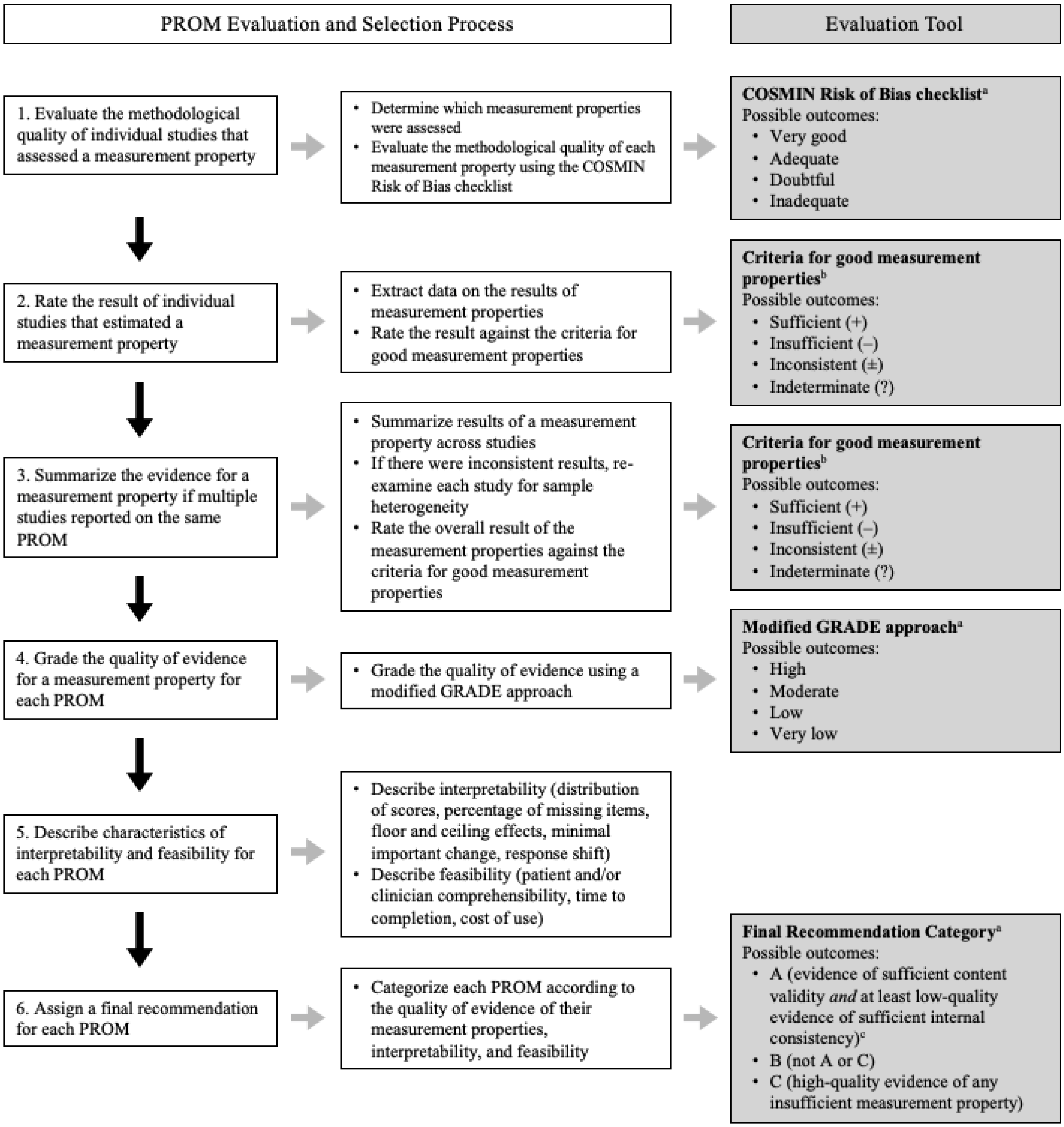

Figure 2.1: Patient-Reported Outcome Measure Evaluation and Selection Process

As recommended and adapted from the COSMIN User Manual.[26-29]
[a]References from the COSMIN User Manual[26-29]
[b]References from the COSMIN User Manual,[26-29] Prinsen et al. (2016),[32] and Terwee et al. (2007)[33]
[c]The instrument(s) with a final recommendation of 'A' and acceptable interpretability and feasibility were deemed the most suitable PROM(s)

2.2.5.4 Grade the Quality of Evidence for Measurement Properties by PROM

Fourth, we graded the quality of the evidence for each PROM measurement property as "high," "moderate," "low," or "very low" using a modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach (**Appendix I**).[26-29] The quality of evidence referred to the confidence that the overall results and ratings for each measurement property were trustworthy. As per the GRADE approach, the evidence was assumed to be high quality and possibly downgraded, based on 4 factors: 1) risk of bias (methodological quality of the studies), 2) inconsistency (inconsistency of summarized results), 3) imprecision (total sample size across studies), and 4) indirectness (inclusion of individuals beyond target population, for example, participants aged older than 24 years despite sample mean age of 18 years).[26-29]

2.2.6 HRQoL PROM Selection

2.2.6.1 Description of Interpretability and Feasibility

As no scoring scales exist for rating PROM interpretability or feasibility, we described characteristics of interpretability (distribution of scores, percentage of missing items, floor and ceiling effects, minimal important change, and response shift) and feasibility (patient and/or clinician comprehensibility, completion time, and cost of use) as outlined in the COSMIN User Manual.[26-29] Instruments containing information that would help clinicians and researchers interpret scores and minimize barriers for use in real-world settings were considered ideal.

2.2.6.2 Final Recommendation

All identified HRQoL PROMs were given a final recommendation of "A" (evidence for sufficient content validity and at least low-quality evidence for sufficient internal consistency), "B" (neither "A" nor "C"), or "C" (high-quality evidence for any insufficient measurement property), as per the COSMIN User Manual.[26-29] The emphasis on content validity and internal consistency in the final recommendation reflects the importance of a PROM's relevance, comprehensiveness, and comprehensibility to a target population as well as its internal structure, respectively.[26-29] Instruments categorized as "A" that had acceptable interpretability and feasibility were deemed the most suitable HRQoL PROMs.

2.3 RESULTS

2.3.1 Study Selection

Of 6931 records, 1834 duplicates were removed, 5097 unique records underwent title/abstract screening, 635 records were reviewed in full, and 21 studies were included in the analysis (**Figure 2.2**). We attempted to contact authors of 9 studies via e-mail to clarify sample characteristics and determine eligibility. Of the 9 studies, 1 was included and 8 were excluded (3 authors provided information proving that their study was ineligible due to age or activity level and 5 authors failed to respond after 2 attempts to contact over 30 days).

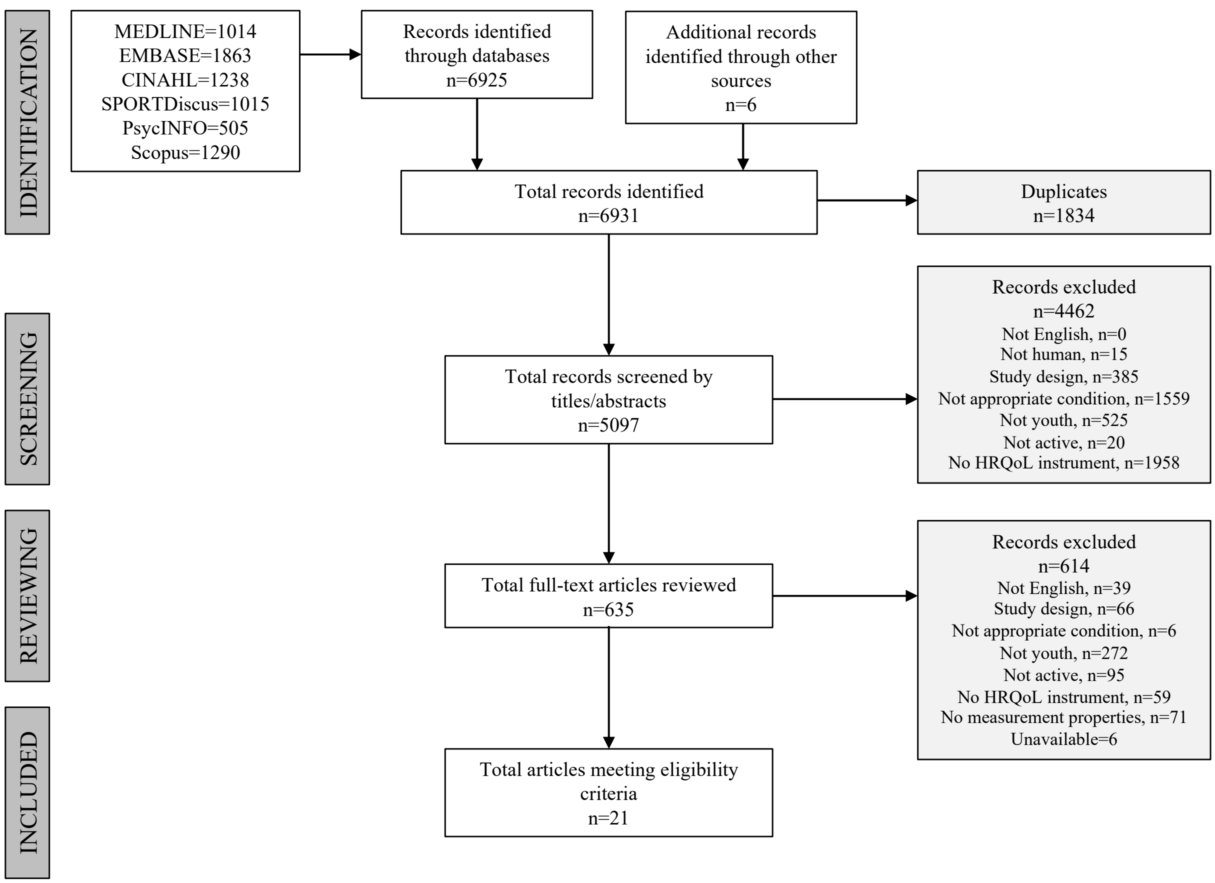

Figure 2.2: PRISMA Flow Chart

We identified 18 HRQoL PROMs across 21 included studies, including 11 generic[23, 34-45] and 7 condition-specific[46-53] PROMs. Eight generic and 5 condition-specific HRQoL PROMs were assessed in only 1 study. An overview of the studies, including the HRQoL PROM(s) evaluated and study sample characteristics, can be found in **Table 2.1**. Studies were published between 2007 and 2020 and included participants from 5 countries (United States,[23, 34-40, 43, 44, 46-48, 51-53] Australia,[49, 50] Brazil,[45] Croatia,[41] and Norway[42]). Competitive athletes (professional, collegiate, or high school athletes) were assessed in 7 studies[23, 34, 36, 47, 49, 51, 52] recreational athletes in 9 studies,[38, 39, 41-45, 50, 53] or both competitive and recreational athletes in 5 studies.[35, 37, 40, 46, 48] Ten studies examined uninjured active youth,[23, 34, 41-47, 52] 7 studies examined active youth with a musculoskeletal injury,[35, 36, 39, 40, 50, 51, 53] and 4 studies examined both.[37, 38, 48, 49]

2.3.2 Generic HRQoL Instruments

Eleven generic HRQoL PROMs were evaluated in 13 of 21 included studies (62%).[23, 34-45] These included the Athlete Life Quality Scale (ALQS),[34] Disablement in the Physically Active scale-mental summary component (DPA-MSC),[35-40] 10-item Disablement in the Physically Active scale-mental summary component Short Form (DPA-MSC SF-10),[37] 8-item Disablement in the Physically Active scale-mental summary component Short Form (DPA-MSC SF-8),[37] 52-item KIDSCREEN questionnaire (KIDSCREEN-52),[41] 10-item KIDSCREEN index (KIDSCREEN-10),[42] and Pediatric Quality of Life Inventory (PedsQL),[43] Quality of Life (QoL) Survey,[44] Medical Outcomes Study 36-Item Short-Form (SF-36),[23, 44] Medical Outcomes Study 12-Item Short-Form (SF-12),[40] and World Health Organization Quality of Life instrument-abbreviated version (WHOQOL-BREF).[44, 45] An overview of these generic HRQoL instruments is found in **Appendix J**. Three generic HRQoL PROMs were a subscale of a larger instrument, whereas 8 generic HRQoL PROMs were multidimensional, consisting of subscales that encompassed various health domains. Higher scores indicated better outcomes on all PROMs except for the DPA-MSC and its short-forms. All studies used self-completed administration (i.e., no proxy).

Table 2.1: Characteristics of Included Studies

Author, Year, and Country	HRQoL PROM	Language of PROM	Primary Objective	Sample	Physical Activity Description	HRQoL Definition	Measurement Properties Evaluated
Gentner et al., 2011, USA[34]	ALQS	English	Develop a PROM for assessing the QoL of athletes	159 NCAA Division I college athletes Age range: 18-22; 50% women	Participated in collegiate sports	"Mental, emotional, physical, and spiritual health and the possession of socially desirable attributes, life satisfaction, and positive feelings"	Content validity, structural validity, internal consistency, feasibility
Vela & Denegar, 2010, USA[35]	DPA-MSC	English	Estabilish standard values and evaluate measurement properties of the DPA	368 competitive and recreational athletes with and without an acute or persistent musculoskeletal injury Mean age (SD): 20.1±3.8; 55% women	Engaged in athletic, recreational, or occupational activities ≥3 times/week	"The psychosocial effects of injury"	Content validity, structural validity, internal consistency, test-retest reliability, criterion validity, responsiveness, interpretability
Houston et al., 2015, USA[36]	DPA-MSC	English	Evaluate the structural validity of the DPA	467 NCAA Division I and III athletes Mean age (SD): 19.5±1.3; 57% women	Participated in collegiate sports	"The physical, psychological and social components of health."	Structural validity, internal consistency, criterion validity, feasibility
Baker et al., 2019, USA[37]	DPA-MSC DPA-MSC SF-10 DPA-MSC SF-8	English	Re-evaluate the structural validity and establish a short-form version of the DPA	1592 physically active individuals with and without an acute, subacute, or persistent musculoskeletal injury Mean age (SD): 23±9; 49% women	Participated in athletic, recreational, or occupational activities ≥3 times/week	"Patients' perceptions of physical, psychological, and social subconstructs of their health status and recovery"	Structural validity, internal consistency,
White et al., 2018, USA[38]	DPA-MSC	English	Evaluate the internal consistency of the DPA	31 university students enrolled in a dance course with or without a history of a musculoskeletal injury Mean age (SD): 20.8±2.6; 100% women	Reported being physically active ≥30 minutes, 3 times/week	NR	Internal consistency
Powden et al., 2019. USA[39]	DPA-MSC	English	Evaluate the response shift phenomenon in individuals with chronic ankle instability	22 individuals with self-reported chronic ankle instability Mean age (SD): 24.91±7.33; 75% women	Scored >24 on the GLTEQ	NR	Internal consistency, interpretability, feasibility
Lorger et al., 2012, Croatia[41]	KIDSCREEN-52	Croatian	Identify factors that contribute to the QoL of youth athletes	343 youth athletes Mean age: 15.1; 56% women	Participated in organized individual and team sports	NR	Structural validity, internal consistency, feasibility
Sigvartsen et al., 2016, Norway[42]	KIDSCREEN-10	Norwegian	Describe QoL and physical activity across different physical education programs	156 high school students Mean age (SD): 16.1±0.8; 79% women	Reported being physically active for a mean of 2.0 hours/day, 2.4 times/week	NR	Internal consistency, feasibility

Zhang et al., 2018, USA[43]	PedsQL	English	Evaluate the relationship between HRQoL, individual factors, environmental factors, and physical activity	235 undergraduate women Mean age (SD): 21.0±1.7; 100% women	Reported a mean of 460.54 minutes/week of MVPA	"Comprehensive construct including physical and psychosocial health functioning"	Internal consistency, construct validity, feasibility
Gill et al., 2015, USA[44]	QoL survey, SF-36, WHOQOL-BREF	English	Evaluate the measurement properties of the QoL survey and compare it to the SF-36	446 university students enrolled in Fitness for Life classes Mean age (SD): 20.4±4.02; 67% women	Enrolled in a Fitness for Life class	"A subjective, multidimensional, integrative construct that reflects optimal well-being and positive health"	Structural validity, internal consistency, test-retest reliability, construct validity
Huffman et al., 2008, USA[23]	SF-36	English	Compare SF-36 scores of competitive athletes with an age-matched general population sample	696 NCAA Division I and II college athletes Mean age (range): 20.4, 17-23; 41% women	Participated in collegiate sports	NR	Internal consistency
Hoch et al., 2019 USA[40]	SF-12, DPA-MSC	English	Determine the relationship between the SF-12, DPA, and PROMIS-PF	100 collegiate or recreational athletes with a lower extremity musculoskeletal injury Mean age (SD): 20.40±2.19; %women not reported	Reported being physically active >90 minutes/week	NR	Construct validity, interpretability, feasibility
Cieslak et al., 2007, Brazil[45]	WHOQOL-BREF	NR	Describe HRQoL and physical activity	85 physical education students Mean age (SD): 20.74±2.79; 46% women	Classified as very active or active on the IQPA	"The individual's perception of his position in life in the context of culture and system of values and in relation to his objectives, expectations, patterns, and worries"	Internal consistency
Sauers et al., 2017, USA[46]	FAST	English	Develop an upper-extremity region-specific and population-specific PROM to measure HRQoL in throwing	830 baseball (men) and softball (women) athletes with and without a throwing injury Mean ages (SDs): 16.5±0.9, 19.5±1.1; 0-28% women	Participated in baseball or softball	"The physical, psychological, and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations, and perceptions"	Content validity, structural validity, internal consistency
Sauers et al., 2011, USA[47]	FAST	English	Evaluate relationships between upper extremity injury history, current pain rating, and HRQoL in softball pitchers	25 competitive high school and college softball pitchers (women) without a current musculoskeletal injury Mean age (SD): 18.3±2.0; 100% women	Participated in softball	"The physical, psychological, and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations, and perceptions"	Construct validity
Huxel Bliven et al., 2017, USA[48]	FAST	English	Evaluate the measurement properties of the FAST	557 baseball (men) and softball (women) players with and without a current	Participated in baseball or softball	NR	Test-retest reliability, measurement error, construct validity,

				musculoskeletal upper extremity injury Mean ages (SDs): 17.9±2.3, 18.2±2.1, 18.8±2.2, 20.0±2.2; 0-27% women			responsiveness, interpretability
Drew et al., 2017, Australia[49]	HAGOS QOL	English	Establish normative HAGOS scores in Australian Football	75 professional and semi-professional Australian football players (men) with and without current groin pain Mean age (SD): 23.1±3.1; 0% women	Participated in Australian football	NR	Structural validity, interpretability
Hinman et al., 2014, Australia[50]	HAGOS QOL, HOOS QOL, iHOT-33	English	Evaluate the test-retest reliability of hip-related PROMs in active youth with FAI	30 young adults with hip and/or groin pain Mean age (SD): 24±4; 50% women	Reported being physically active for a mean of 6 hours/week	NR	Test-retest reliability, measurement error, feasibility
Clapp et al., 2019, USA[51]	iHOT-12	English	Compare 2-year iHOT-12 scores of competitive athletes and nonathletes undergoing hip arthroscopy	59 professional, semi-professional, or college athletes who underwent hip arthroscopy for FAI Mean age (SD): 22.0±4.8; 63% women	Participated in competitive sports	NR	Interpretability
Hoch et al., 2015, USA[52]	KOOS QOL	English	Evaluate the test-retest reliability and estimate the MDC of the DPA, FAAM-S, and KOOS	16 NCAA Division I soccer players without a current musculoskeletal injury Mean ages (SDs): 19.7±1.0 (women), 19.9±0.9 (men); 56% women	Participated in soccer	"A person's function in everyday life and an evaluation of his or her physical, psychological, and social aspects of health derived from personal beliefs, preferences, experiences, and expectations"	Test-retest reliability, measurement error, feasibility
Edmonds et al., 2017, USA[53]	PASS	English	Evaluate the reliability and validity of the PASS	132 individuals with a shoulder injury Mean age (SD): 16±2; 30% women	Participated in a sport, including overhead throwing sports	N/A	Construct validity, responsiveness, interpretability, feasibility

ALQS, Athlete Life Quality Scale; DPA, Disablement of the Physically Active; DPA-MSC, DPA Mental Summary Component; DPA-MSC SF-10, DPA-MSC Short-Form 10; DPA-MSC SF-8, DPA-MSC Short-Form 8; FAAM-S, Foot and Ankle Ability Measure-Sport; FAI, femoroacetabular impingement; FAST, Functional Arm Scale for Throwers; GLTEQ, Godin Leisure Time Exercise Questionnaire; HAGOS QOL, Copenhagen Hip and Groin Outcome Score Quality of Life subscale; HOOS QOL, Hip dysfunction and Osteoarthritis Outcome Score Quality of Life subscale; HRQoL, health-related quality of life; iHOT-33, International Hip Outcome Tool-33; iHOT-12, International Hip Outcome Tool-12; IQPA, International Questionnaire of Physical Activity; KOOS QOL, Knee injury and Osteoarthritis Outcome Score Quality of Life subscale; MIC, minimal important change; MVPA, moderate-to-vigorous physical activity; NCAA, National Collegiate Athletic Association; NR, not reported; QoL survey, Quality of Life survey; PASS, Pediatric/Adolescent Shoulder Survey; PedsQL, Pediatric Quality of Life Inventory; PROM, patient-reported outcome measure; PROMIS-PF, Patient-Reported Outcomes Measurement Information System Physical Functioning subscale; SD, standard deviation; SF-36, Short-Form 36; SF-12, Short-Form 12; WHOQOL-BREF, World Health Organization Quality of Life abbreviated instrument

2.3.2.1 Content Validity

Two studies[34, 35] described the development of the ALQS and DPA-MSC (**Appendix K**). The ALQS[34] had very low-quality evidence for insufficient content validity because it did not address relevance, comprehensiveness, or comprehensibility in a sample of uninjured collegiate athletes (**Appendix M**). The development of the DPA-MSC[35] included qualitative interviews with injured competitive and recreational youth athletes but it was unclear if the athletes were asked about comprehensiveness or comprehensibility; therefore, it was rated as low-quality evidence for inconsistent content validity.

2.3.2.2 Structural Validity

Six studies[34-37, 41, 44] assessed the structural validity of 6 PROMs. The DPA-MSC was investigated across 3 studies.[35-37] In 1 study including injured active youth,[35] the DPA-MSC possessed high-quality evidence for insufficient structural validity; however, in studies with uninjured active youth[36] or both injured and uninjured active youth,[37] its structural validity was indeterminate. The DPA-MSC SF-10[37], DPA-MSC SF-8,[37] KIDSCREEN-52,[41] and QoL Survey[44] demonstrated moderate- or high-quality evidence for sufficient structural validity. The ALQS[34] demonstrated indeterminate structural validity.

2.3.2.3 Internal Consistency

Twelve studies[23, 34-39, 41-45] investigated the internal consistency of 10 PROMs. The DPA-MSC SF-10,[37] DPA-MSC SF-8,[37] and KIDSCREEN-52,[41] and QoL Survey[44] had high-quality evidence for sufficient internal consistency. The ALQS,[34] PedsQL,[43] SF-36,[23, 44] and WHOQOL-BREF[44] had indeterminate ratings, as they lacked sufficient structural validity in active youth. The DPA-MSC had very low-quality evidence for insufficient internal consistency in injured active youth[35, 39] but indeterminate findings in uninjured active youth[36] and in both injured and uninjured active youth.[38] The WHOQOL-BREF findings from 1 study[45] were not included in the qualitative summary due to poor overall study quality.

2.3.2.4 Test-Retest Reliability

Two studies[35, 44] examined the test-retest reliability of the 3 PROMs. The DPA-MSC[35] demonstrated very low-quality evidence for sufficient reliability due to imprecision (i.e., sample size fewer than 50), the QoL Survey[44] had moderate-quality evidence for sufficient reliability, and the SF-36[44] had indeterminate reliability.

2.3.2.5 Construct Validity

Four studies evaluated the construct (convergent) validity of the DPA-MSC,[38] PedsQL,[43] QoL survey,[44] and SF-12[40] compared to generic HRQoL, life satisfaction, physical functioning, physical activity, self-efficacy, and/or social support. All studies had indeterminate results because no a-priori hypotheses were provided.

2.3.2.6 Criterion Validity

Two studies[35, 36] evaluated the criterion validity of the DPA-MSC. The DPA-MSC demonstrated very low-quality evidence for sufficient criterion validity with a single global functioning item in injured active youth,[35] and high-quality evidence for insufficient criterion validity with the DPA total score in uninjured active youth.[36]

2.3.2.7 Responsiveness

One study[35] assessed the responsiveness of the DPA-MSC. The DPA-MSC[35] possessed low-quality evidence for sufficient responsiveness in active youth with an acute or persistent musculoskeletal injury.

2.3.2.8 Other Measurement Properties

No included studies assessed measurement error or cross-cultural validity (i.e., validity across ethnicities, languages, sexes, ages, or patient groups) of generic HRQoL PROMs.

2.3.2.9 Interpretability and Feasibility

Interpretability and feasibility characteristics for generic HRQoL PROMs are outlined in **Appendices N and O**. The minimal important change (MIC) for the DPA-MSC[35] was estimated to be 9 points for youth with an acute musculoskeletal injury and 6 points for youth with a persistent musculoskeletal injury, using anchor-based methods. The SF-36[23, 54] was reported to have a MIC of 10 points for domain scores and 5 points for summary component scores. The KIDSCREEN questionnaires (for commercial use), PedsQL, and SF-12 had a user fee.

2.3.2.10 Final Recommendation

All generic HRQoL PROMs except the DPA-MSC were given a final recommendation of "B" because none provided evidence for sufficient content validity in active youth (**Table 2.2**). The DPA-MSC was assigned a final recommendation of "C" due to high-quality evidence for insufficient structural validity[35] and criterion validity.[36] The DPA-MSC SF-10, DPA-MSC SF-8, and QoL Survey had high-quality evidence for sufficient structural validity and internal consistency, and the QoL survey also had moderate-quality evidence for sufficient test-retest reliability. With other generic instruments having indeterminate or inconsistent measurement properties, the DPA-MSC SF-10, DPA-MSC SF-8, and QoL survey were considered the most suitable existing generic HRQoL PROMs for active youth.

2.3.3 Condition-Specific HRQoL Instruments

Seven condition-specific HRQoL PROMs were evaluated in 8 of 21 studies (38%).[46-53] An overview of these instruments is found in **Appendix J**. Two PROMs were specific to the upper extremity [Functional Arm Scale for Throwers (FAST)[46-48] and Pediatric/Adolescent Shoulder Survey (PASS)[53]], 4 to the hip [Copenhagen Hip and Groin Outcome Score hip-related quality of life (HAGOS QOL) subscale,[49, 50] Hip dysfunction and Osteoarthritis Outcome Score hip-related quality of life (HOOS QOL) subscale,[50] 33-item International Hip Outcome Tool (iHOT-33),[50] and 12-item International Hip Outcome Tool (iHOT-12)[51]], and 1 to the knee [Knee injury and Osteoarthritis Outcome Score knee-related quality of life (KOOS QOL) subscale[52]]. Three condition-specific instruments were a subscale of a larger PROM. Higher scores reflected better HRQoL outcomes in all PROMs except for the FAST. All studies used self-completed administration.

2.3.3.1 Content Validity

Two studies[46, 53] described the content validity of the FAST and PASS (**Appendix L**). The FAST had low-quality evidence for inconsistent content validity because relevance, comprehensiveness, and comprehensibility were not established in uninjured competitive and recreational throwing athletes (**Appendix M**).[46] The PASS demonstrated very low-quality evidence for insufficient content validity because the study did not conduct interviews or focus groups in active youth with a shoulder injury.[53]

2.3.3.2 Structural Validity

Two studies[46, 49] examined the structural validity of 2 PROMs. The FAST[46] had high-quality evidence for sufficient structural validity, whereas the HAGOS QOL subscale[49] had indeterminate structural validity.

2.3.3.3 Internal Consistency

One study[46] evaluated internal consistency. The FAST[46] demonstrated high-quality evidence for sufficient internal consistency.

2.3.3.4 Test-Retest Reliability

Three studies[48, 50, 52] investigated the test-retest reliability of 5 PROMs. The HAGOS QOL subscale,[50] HOOS QOL subscale,[50] iHOT-33,[50] and KOOS QOL subscale[52] possessed very low-quality evidence for sufficient reliability due to imprecision. The FAST[48] had low-quality evidence for sufficient reliability due to a short test-retest interval (mean 4.5 days).

2.3.3.5 Measurement Error

Three studies[48, 50, 52] examined the measurement error for 5 PROMs. The FAST,[27] HAGOS QOL subscale,[50] HOOS QOL subscale,[50] iHOT-33,[50] and KOOS QOL subscale[21] all had indeterminate results as a MIC was not defined.

2.3.3.6 Construct Validity

Three studies[47, 48, 53] assessed the convergent validity of 2 PROMs. The FAST[47, 48] and PASS[53] had indeterminate results because no a-priori hypotheses were stated. The FAST[48] demonstrated low-quality evidence for sufficient known-groups validity between injured and uninjured active youth.

2.3.3.7 Responsiveness

Two studies[48, 53] assessed the responsiveness of 2 PROMs. The FAST[48] had low-quality evidence for sufficient responsiveness whereas the PASS had indeterminate responsiveness.[53]

2.3.3.8 Other Measurement Properties

No included studies assessed the criterion or cross-cultural validity of condition-specific HRQoL instruments.

2.3.3.9 Interpretability and Feasibility

Interpretability and feasibility characteristics for condition-specific HRQoL PROMs are described in **Appendices N and O**. There was missing data for the KOOS QOL subscale (11%)[52] and PASS (20.5%).[53] The MIC for the iHOT-12 was estimated as 12.1 points[51] using distribution-based methods. The MIC for the HAGOS QOL subscale and iHOT-33 was stated to be 10 to 15 points.[55, 56] All condition-specific HRQoL instruments were free to use.

2.3.3.10 Final Recommendation

All condition-specific HRQoL PROMs were given a final recommendation of "B" due to a lack of sufficient content validity in active youth (**Table 2.2**). The FAST (upper extremity) was the only instrument with high-quality evidence for sufficient structural validity and internal consistency. We judged the FAST to be the most suitable existing condition-specific HRQoL PROM for active youth.

Table 2.2: Overall Rating and Quality of Evidence for HRQoL

HRQoL PROM	Content Validity		Structural Validity		Internal Consistency		Test-Retest Reliability		Measurement Error		Construct Validity		Criterion Validity		Responsiveness		Final Recomm-endation[c]
	Rating[a]	Quality[b]	Rating	Quality	Rating	Quality	Rating	Quality	Rating	Quality	Rating	Quality	Rating	Quality	Rating	Quality	
Generic PROMs																	
ALQS	–	Very low	?	Mod	?	Low											B
DPA-MSC	±	Low	–/?	High/mod	–/?	Very low/high	+	Very low			?	Very low	+/–	Very low/high	+	Low	C
DPA-MSC SF-10[d]			+	High	+	High											B
DPA-MSC SF-8[d]			+	High	+	High											B
KIDSCREEN-52			+	Mod	+	High											B
KIDSCREEN-10					+	Very low											B
PedsQL					?	High					?	High					B
QoL survey[d]			+	High	+	High	+	Mod			?	Mod					B
SF-36					?	High	?	Mod									B
SF-12											?	Very low					B
WHOQOL-BREF					?	High											B
Condition-Specific PROMs																	
FAST[d]	±	Low	+	High	+	High	+	Low	?	Low	?/+	Very low/low			+	Low	B
HAGOS QOL			?	Very low			+	Very low	?	Very low							B
HOOS QOL							+	Very low	?	Very low							B
iHOT-33							+	Very low	?	Very low							B
iHOT-12																	B
KOOS QOL							+	Very low	?	Very low							B
PASS	–	Very low									?	Very low			?	Very low	B

Blank cells indicates no identified study evaluated the measurement property. Maroon cells indicate high-quality evidence for insufficient results; red cells indiciate low- or very low-quality evidence for any results; orange cells indicate any quality evidence for indeterminant results; yellow cells indicate moderate-quality evidence for sufficient results; and blue cells indicate high-quality evidence for sufficient results

[a]Overall rating of summarized results by PROM rated as 'sufficient (+),' 'indeterminate (?),' 'inconsistent (±),' or 'insufficient (–)' as per the COSMIN criteria for good measurement properties[66-71]

[b]Quality of evidence by PROM graded as 'high,' 'moderate,' 'low,' or 'very low' as per the modified GRADE approach[66-69]

[c]Final recommendation for a PROM categorized as 'A' (evidence of sufficient content validity and at least low quality evidence of sufficient internal consistency), 'B' (neither 'A' nor 'C'), or 'C' (high quality evidence of any insufficient measurement property)[66-69]

[d]Identified as most suitable existing HRQoL PROMs after evaluating measurement properties, interpretability, and feasibility

ALQS, Athlete Life Quality Scale; DPA, Disablement of the Physically Active; DPA-MSC, DPA-Mental Summary Component; DPA-MSC SF-10, DPA-MSC Short-Form 10; DPA-MSC SF-8, DPA-MSC Short-Form 8; FAST, Functional Arm Scale for Throwers; HAGOS QOL, Copenhagen Hip and Groin Outcome Score Quality of Life subscale; HOOS QOL, Hip dysfunction and Osteoarthritis Outcome Score Quality of Life subscale; HRQoL, health-related quality of life; iHOT-33, International Hip Outcome Tool-33; iHOT-12, International Hip Outcome Tool-12; KOOS QOL, Knee injury and Osteoarthritis Outcome Score Quality of Life subscale; QoL survey, Quality of Life survey; PASS, Pediatric/Adolescent Shoulder Survey; PedsQL, Pediatric Quality of Life Inventory; PROM, patient-reported outcome measure; SF-36, Short-Form 36; SF-12, Short-Form 12; WHOQOL-BREF, World Health Organization Quality of Life abbreviated instrument

2.3.4 Comparison of HRQoL PROMs Between Injured and Uninjured Active Youth

Of the 18 HRQoL PROMs identified, 5 were only evaluated in injured active youth (the SF-12,[40] HOOS QOL subscale,[50] iHOT-33,[50] iHOT-12,[51] and PASS[53]), 8 were only evaluated in uninjured active youth (the ALQS,[34] KIDSCREEN-52,[41] KIDSCREEN-10,[42] PedsQL,[43] QoL Survey,[44] SF-36,[23, 44] WHOQOL-BREF,[44, 45] KOOS QOL subscale[52]), and 5 were evaluated in both injured and uninjured active youth (the DPA-MSC,[35-40] DPA-MSC SF-10,[37] DPA-MSC SF-8,[37] FAST,[46-48] HAGOS QOL subscale[49, 50]). Of the instruments evaluated in both injured and uninjured active youth, there was limited overlap in measurement properties assessed. Only the DPA-MSC had the same measurement properties assessed across multiple studies involving different samples.[35-40] The structural validity and internal consistency of the DPA-MSC demonstrated insufficient results in injured active youth but indeterminate results otherwise (**Appendix M**).

2.4 DISCUSSION

We identified and evaluated 11 generic and 7 condition-specific HRQoL PROMs for active youth. The methodological quality, overall results ratings, and quality of evidence for measurement properties across different instruments were highly variable. Only 2 generic and 2 condition-specific HRQoL PROMs assessed content validity, and all demonstrated low- or very low-evidence for inconsistent or insufficient content validity. There was little information about interpretability and feasibility. Ultimately, no identified PROMs warranted a final recommendation of "A," suggesting that there is no suitable generic or condition-specific HRQoL PROM for active youth.

Lacking sufficient content validity undermines the methodological quality of a study and reduces confidence in its results.[26] The absence of sufficient content validity across PROMs used to assess the HRQoL of active youth is a serious limitation. We note that all PROM development studies[34, 35, 46, 53] identified in our review were published before the 2018 COSMIN risk-of-bias checklist[26-28] and would not have benefited from this resource to assess content validity.

Structural validity, internal consistency, and cross-cultural validity of a PROM describe how individual items within an instrument are related and organized into subscales.[28] The DPA-MSC SF-10 (generic),[37] DPA-MSC SF-8 (generic),[37] QoL Survey (generic)[44] and FAST (upper extremity-specific)[46, 47] were the only PROMs with high-quality evidence for sufficient structural validity and internal consistency and are therefore considered the most suitable existing HRQoL PROMs for active youth. Given that there is no difference in the items of the 2 DPA-MSC short-forms (i.e., the discrepancy in items lies in physical summary component), we recommend the DPA-MSC SF-8, as it requires less time to complete and score.

The absence of evidence of other measurement properties limits the ability of PROMs to monitor HRQoL over time. Establishing test-retest reliability, measurement error, and responsiveness allows clinicians and researchers to understand whether a change in PROM score truly reflects patients' perceived change of their HRQoL (i.e., not due to random error). Estimating a MIC is also important for determining if change scores are meaningful to patients.

This systematic review is the first to examine the quality of existing HRQoL instruments used in active youth. Although not specifically focused on active youth or musculoskeletal conditions, 1 previous review in 2008[57] identified 94 instruments with the KIDSCREEN (generic) and PedsQL (generic) demonstrating acceptable validity and reliability. In contrast, we found the KIDSCREEN-52 had moderate- or high-quality evidence for sufficient structural validity and internal consistency, while the PedsQL showed indeterminate ratings for internal consistency and construct validity. This suggests that both should be further examined to determine if they are suitable for active youth populations.

2.4.1 Research Recommendations

The ideal HRQoL PROM for active youth is psychometrically robust, easy to interpret, and applicable in clinical and research settings. Without an ideal instrument, researchers must re-evaluate existing HRQoL PROMs or develop a new HRQoL PROM for active youth. As instrument development requires immense time, effort, and resources, it may be prudent to first re-evaluate existing HRQoL PROMs.

Future studies examining measurement properties of HRQoL instruments should follow the COSMIN risk-of-bias checklist.[26-28] Content validity must be well established by seeking input from members of the target population who represent different manifestations of HRQoL (e.g., high and low HRQoL) and demographics (e.g., varying age, sex/gender, ethnicity). Then, other measurement properties can be assessed, starting with structural validity and internal consistency, to understand a PROM's internal structure. To address interpretability and feasibility, investigators should report missing item data, floor and ceiling effects, a MIC, time to complete and score, and costs.

Until a suitable HRQoL PROM is available, we propose using a mixed methods approach[58] where generic and condition-specific PROMs are used alongside qualitative methods to study the HRQoL of active youth. When possible, we recommend selecting the DPA-MSC SF-8 (generic), QoL Survey (generic), and FAST (upper extremity-specific) to measure HRQoL. Additionally, conducting interviews with youth from varying sports or activities, competition levels, and health statuses can provide a more in-depth understanding of what HRQoL means to active youth and what determinants are important to them.

2.4.2 Clinical Implications

Clinicians who wish to learn how to select a suitable PROM are encouraged to review the COSMIN risk-of-bias Checklist[26-28] and explore the COSMIN website resources. The most suitable PROM for clinical use is one that is easy to understand, requires minimal time to complete and score, and is free to use. To assess the HRQoL of active youth with musculoskeletal injuries, we recommend collating findings from generic and condition-specific PROMs and selecting the DPA-MSC SF-8 (generic), QoL Survey (generic), and FAST (upper extremity-specific) when appropriate. Clinicians may also review responses to individual items to spark conversations regarding a patient's perception of injury, facilitators of and barriers to rehabilitation, and strategies to improve recovery. Information from overall PROM scores and individual item responses can help clinicians tailor treatment plans to the individual athlete.

2.4.3 Strengths and Limitations

Adhering to the COSMIN User Manual[26-29] provided a standardized approach to evaluating measurement properties, interpretability, feasibility, and final recommendation. As the COSMIN User Manual[26-29] is a universal resource, the findings of this review can be compared to past and future research.

A limitation of using the COSMIN User Manual,[26-29] including the 2018 COSMIN risk-of-bias checklist, is that many studies (71%) were judged on more rigorous criteria that did not exist at the time of their design. This may have resulted in stricter ratings and final recommendations for PROMs developed or evaluated before 2018. Despite a comprehensive search strategy, our stringent inclusion criteria likely excluded some relevant PROMs. For example, using sample mean or median age excluded the ACL QOL questionnaire, a commonly used condition-specific PROM for youth athletes with an anterior cruciate ligament injury, because it was developed in a sample with a mean age of 27.6 years.[59] It is worth assessing other HRQoL PROMs like the ACL QOL questionnaire to determine their measurement properties, interpretability, and feasibility for active youth. We also acknowledge the heterogeneity of the included studies, with few studies assessing the same PROM. Finally, there is likely a difference in variability of PROM scores between injured and uninjured youth (i.e., injured youth tend to demonstrate greater variability) across studies which may limit the generalizability of measurement properties evaluated between the 2 groups.

2.5 CONCLUSIONS

No available HRQoL PROM has sufficient content validity for active youth. The DPA-MSC SF-8 (generic), QoL Survey (generic), and FAST (upper extremity-specific) are the most suitable existing HRQoL PROMs because they demonstrate high-quality evidence for sufficient structural validity and internal consistency. Until a definitively robust instrument is available, we recommend selecting the DPA-MSC SF-8, QoL Survey, and FAST; using multiple PROMs; and applying mixed methods to gain a holistic understanding of the HRQoL of active youth.

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CHAPTER 3: WHAT DOES THE FUTURE HOLD? HEALTH-RELATED QUALITY OF LIFE 3-12 YEARS FOLLOWING A YOUTH SPORT-RELATED KNEE INJURY

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The original publication can be found in **Appendix P**. Minor revisions have been made to the context (i.e., greater focus on HRQoL rather than osteoarthritis), wording (e.g., "knee-related QOL" replaced with "knee-specific HRQoL") and formatting to remain consistent with the other chapters.

Publication metrics: 855 full-text downloads, 1 citation

Previous research comparing medium- or long-term HRQoL outcomes in injured and uninjured youth is mostly focused on ACL ruptures or ACLR. However, youth are susceptible to experiencing knee injuries beyond ACL ruptures. If differences in generic and knee-specific HRQoL outcomes exist between injured youth with a wide range of sport-related knee injuries and uninjured peers, then the need to address HRQoL after any knee injury becomes clearer. This chapter summarizes generic and knee-specific HRQoL outcomes at 3-12 years following any traumatic, sport-related knee injury in youth and uninjured controls of similar age, sex, and sport participation.

ABSTRACT

Objective: To assess generic (EQ-5D-5L and EQ-VAS) or knee-specific (KOOS QOL) HRQoL in individuals with a 3-12 year history of a youth sport-related knee injury compared to uninjured controls. We also examined the influence of potential HRQoL determinants on the relationship between injury history and HRQoL.

Study Design: Cross-sectional analysis of a historical cohort study.

Methods: Generic (EQ-5D-5L index, EQ-VAS) and knee-specific (KOOS QOL) HRQoL were assessed in 124 individuals 3-12 years following youth sport-related knee injury and 129 uninjured controls of similar age, sex, and sport. We used linear regression to examine differences in HRQoL outcomes by study group (injured vs. uninjured). We used multivariable linear regression to explore the influence of sex, time since injury (years), injury type (ACL rupture vs. other), BMI, knee extensor and flexor strength, intermittent knee pain [Intermittent and Constant Osteoarthritis Pain (ICOAP) intermittent pain score, and moderate-to-strenuous physical activity [Godin Leisure-Time Exercise Questionnaire (GLTEQ)].

Results: Participant median (range) age was 23 years (14-29) and 55% were female. Injury history was associated with poorer KOOS QOL (-8.41; 95%CI -10.76, -6.06) but not EQ-5D-5L (-0.0074; -0.0238, 0.0089) or EQ-VAS (-3.82; -8.77, 1.14). Injury history (-5.14; -6.90, -3.38), worse ICOAP score (-0.40; -0.45, -0.36), and ACL rupture (-1.41; -2.77, -0.06) contributed to poorer KOOS QOL. Worse ICOAP score contributed to poorer EQ-5D-5L (-0.0024; -0.0034, -0.0015) and higher GLTEQ moderate-to-strenuous physical activity to better EQ-VAS (0.10; 0.03, 0.17).

Conclusions: Experiencing a previous sport-related knee injury is associated with poorer knee-specific but not generic HRQoL 3-12 years post-injury. Having increased knee pain and an ACL rupture may be negative influences on knee-specific HRQoL whereas increased knee pain and lower moderate-to-strenuous physical activity may be negative influences on generic HRQoL.

3.1 INTRODUCTION

Sport-related knee injuries are highly prevalent in youth[1, 2] and are associated with a variety of injury consequences, including increased pain,[3-9] decreased muscle strength,[3, 10] lower physical activity levels,[11-14] weight gain,[15] and reduced HRQoL.[16, 17] Currently, what we know about these consequences is largely embedded in studies examining ACL ruptures and ACLR. However, with only 25% of youth sport-related knee injuries involving the ACL,[18] we must examine the impact of injuries beyond ACL ruptures.

Health-related quality of life may serve as a valuable indicator of overall health following a youth sport-related knee injury because it is a multifactorial construct that encompasses the physical, psychological, and social health domains.[19] Assessing both generic and condition-specific (i.e., knee-specific) HRQoL is required to gain a thorough understanding of HRQoL after injury. Generic instruments are best for capturing generic HRQoL and allow for comparisons across different demographic groups or medical conditions. On the other hand, condition-specific HRQoL instruments offer a more nuanced understanding of a particular patient group or condition and are more responsive to change over time. Previous research has revealed that generic and knee-specific HRQoL deficits exist at least 2-5 years after an ACL rupture or ACLR.[5, 16, 17, 20]

How and to what extent a youth sport-related knee injury contributes to long-term HRQoL is unknown. Demographic factors such as female sex[21] and older age,[22, 23] are associated with worse generic HRQoL in healthy youth populations. Similarly, common injury consequences such as greater BMI,[24, 25] increased pain,[26, 27] and lower physical activity levels[28, 29] are also linked with worse generic HRQoL in uninjured youth. Determining how demographic factors and injury consequences influence the relationship between a youth sport-related knee injury and HRQoL may provide information to help address long-term HRQoL deficits.

3.1.1 Objectives

The objective of this study was to assess generic (EQ-5D-5L and EQ-VAS) and knee-specific (KOOS QOL) HRQoL in individuals with a 3-12 year history of a youth sport-related knee injury compared to uninjured controls. To further understand what factors may influence the relationship between injury history and HRQoL, factors possibly linked with HRQoL (i.e., sex, time since injury, type of injury, BMI, knee extensor strength, knee flexor strength, intermittent knee pain, and self-reported physical activity) were also examined.

3.2 METHODS

3.2.1 Study Design

This study was a cross-sectional analysis of data from the first follow-up (3-12 years post-injury) of the Alberta Youth Prevention of Early Osteoarthritis (PrE-OA) historical cohort study.

3.2.2 Ethics

Ethics approval was granted by the Conjoint Health Research Ethics Board at the University of Calgary, Canada (Ethics ID E-25075). Before testing, all participants provided informed consent/assent and completed a Physical Activity Readiness Questionnaire (PAR-Q, 2002).

3.2.3 Participants

The PrE-OA cohort consists of a convenience sample of individuals who sustained a youth (≤18 years old) sport-related knee injury 3-12 years previously and uninjured controls of similar age (within 12 months), sex, and sport at the time of injury. Information about cohort recruitment, injury diagnosis, and inclusion and exclusion criteria has been described previously.[15, 30] Briefly, injured and uninjured participants were recruited after being identified from previous cohort studies examining risk factors for sport injury, a university-based sport medicine centre database, or through collaborators and participants. Injured participants sustained a youth sport-related knee injury (clinical diagnosis of a ligament, meniscus, or other intra-articular tibiofemoral or patellofemoral injury) that required medical attention (e.g., physician, physiotherapist) and disrupted sport participation 3-12 years previously. Uninjured controls were included if they reported no previous knee injury resulting in time-loss from sport. Individuals were excluded if they were pregnant; reported non-steroidal anti-inflammatory use, cortisone injection, or other musculoskeletal injury that disrupted sport, school, or work participation within 3 months prior to testing; or had a diagnosis of arthritis or any medical conditions that prevented study participation (e.g., neurological conditions).

3.2.4 Procedures

These analyses examined data from the first follow-up (3-12 years post-injury) collected during 1 testing session at the University of Calgary between 2013-2017.[15, 30] Participants completed a battery of questionnaires (study questionnaire, EQ-5D, KOOS, ICOAP, and GLTEQ) then rotated through testing stations that measured their height, weight, and isometric knee strength. A secure, online database was used to store and manage data (REDCap 8.6.5, Vanderbilt University, Nashville, TN, USA).

A study questionnaire gathered participant information (i.e., age, sex), sport information (i.e., pre-injury main sport, sport participation in the last 12 months), and knee injury details as applicable (i.e., type of injury, injury date, subsequent injury or surgery; **Appendix Q**).

3.2.5 Outcomes

3.2.5.1 Generic Health-Related Quality of Life

The EQ-5D is a self-reported instrument that measures generic HRQoL (**Appendix R**).[31, 32] EQ-5D is a widely used health utility instrument that consists of 2 components: the EQ-5D-5L index and EQ-VAS scores. The EQ-5D-5L describes one's health state and is measured in 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Participants indicated their health state by selecting 1 of 5 levels of responses ranging from no problems to extreme problems for each dimension. Using the Canadian value set,[33] health states were converted into EQ-5D-5L index scores which range from -0.148 (worst health status) to 0.949 (best health status). The EQ-VAS evaluates health on a 20 cm vertical visual analog scale with anchors of 0 (worst health you can imagine) and 100 (best health you can imagine). The EQ-5D has been shown to have acceptable reliability[34] and validity[32, 34] across musculoskeletal conditions. Although the EQ-5D has not been validated for individuals following a knee injury, it has been previously applied to individuals following ACLR.[35] The MIC for Canadian EQ-5D-5L index scores is 0.056[36] but no MIC for the EQ-VAS in a comparable sample has been established. However, it should be noted that our analyses did not measure change in scores over time.

3.2.5.2 Knee-Specific Health-Related Quality of Life

The KOOS QOL is 1 of 5 subscales of the KOOS[37, 38] (**Appendix S**) and assesses knee-specific HRQoL. It consists of 4 items (awareness of knee problem, lifestyle modification, knee confidence, and overall knee difficulty) scored on a 5-point Likert scale. Subscale scores are converted into a score ranging from 0-100 with higher scores indicating better outcomes. The KOOS demonstrates sufficient internal consistency (pooled Cronbach's alpha=0.79), test-retest reliability [pooled intraclass correlation coefficient (ICC)=0.88], and measurement error (pooled standard error of measurement=5.9, pooled smallest detectable change=16.3) in ACL injured samples.[37, 39]

3.2.5.3 Body Mass Index

Body mass index (kg/m^2) was calculated from weight (to the nearest 0.1 kg) and height (to the nearest 0.1 cm, shoes removed) measurements using a scale and stadiometer (Model 402 KL, Pelstar, McCook, IL, USA).

3.2.5.4 Isometric Knee Extensor and Flexor Strength

Normalized isometric knee extensor and flexor strength of the injured (index) limb were measured using handheld dynamometry (Model 01163, Lafayette Instrument, Lafayette, IN, USA).[30] Prior to testing, all examiners were given a written description of testing and scoring. Each examiner practiced under the guidance of an experienced examiner over a minimum of 3 one-hour training sessions before testing study participants.[40] For knee extension, participants were seated with hips and knees in 90º and 60º flexion, respectively, and a handheld dynamometer placed 5 cm proximal to the distal tip of the lateral malleolus on the shin. For knee flexion, participants were in a prone position with the knee in 60º flexion and a dynamometer placed 5 cm proximal to the distal tip of the lateral malleolus on the calf. In all strength tests, the dynamometer was secured to the leg with an immovable strap. After a practice trial, participants completed 3 experimental trials consisting of 5 s of maximum effort pushing into the dynamometer followed by 15 s of rest. Peak isometric strength scores (N) were converted to peak torque (Nm; force x distance between joint line and dynamometer) and normalized to body weight (Nm/kg). Isometric knee muscle strength testing has sufficient intra- (pooled ICC >0.90)[41, 42] and inter-rater reliability (pooled ICC>0.84).[41]

3.2.5.5 Intermittent Knee Pain

Intermittent knee pain was assessed with the intermittent pain subscale of the ICOAP (**Appendix T**).[43] This subscale consists of six items that asks patients about "pain that comes and goes" over the past week. Each item is scored on a 5-point Likert scale, summed, and transformed to a subscale score ranging from 0-100 with lower scores indicating better outcomes. The ICOAP has not been evaluated in active youth populations but demonstrates sufficient internal consistency (Cronbach's alpha=0.93) and test-retest reliability (ICC=0.85) in individuals with knee osteoarthritis.[43]

3.2.5.6 Physical Activity

Physical activity participation was self-reported using the GLTEQ (**Appendix U**).[44] Participants reported the number of 15-minute bouts of mild (minimal effort), moderate (not exhausting), and strenuous (heart beats rapidly) physical activity in which they engaged over a typical 7-day period. The total activity in metabolic equivalents (METs) is calculated by multiplying the number of mild, moderate, and strenuous bouts by 3, 5, and 9, respectively, and then summing these values. One MET equals the amount of energy expended by an individual seated at rest. The GLTEQ has been validated to assess physical activity.[45, 46] Weekly moderate-to-strenuous METs were the focus of these analyses.

3.2.6 Data Analysis

Statistical analyses were performed using STATA (v12.1, Stata Corp., College Station, TX, USA). Descriptive statistics [median (range), proportion (95%CI)] were calculated for all participant characteristics and outcomes by study group (knee injury history or not).

3.2.6.1 Primary Objective

Separate univariable linear regression models (95%CI; clustered on sex and main sport type), were used to assess the association between previous injury history (yes vs. no) and each HRQoL outcome (EQ-5D-5L index, EQ-VAS, and KOOS QOL). The analysis was clustered on sex (females are at higher risk for a knee injury[47] and report lower generic HRQoL[21] than males) and sport (different sport/activity exposure is linked with injury risk[48] and generic HRQoL[49-51]) to control for some confounding.

3.2.6.2 Exploratory Objective

To better understand how a sport-related knee injury impacts HRQoL, we explored the influence of other factors on this relationship. Sex,[21] age,[22, 23, 52] BMI,[24, 25] strength training,[53] pain,[26, 27] and physical activity,[28, 29] have been previously linked with generic and/or knee-specific youth HRQoL. Injury type has yet to be examined but severe injuries (e.g., ACL rupture) which are associated with longer rehabilitation periods and possible surgery may have a greater impact on HRQoL than mild injuries (e.g., MCL sprain).

Separate multivariable linear regression models (95%CI; clustered on sex and main sport type) explored the association of injury history with each HRQoL outcome while examining 8 additional variables: sex, time since injury (years), injury type (ACL rupture vs. other), BMI (kg/m^2), normalized peak knee extensor and flexor strength (Nm/kg), intermittent knee pain (ICOAP intermittent pain subscale), and moderate-to-strenuous physical activity (GLTEQ weekly METs). Time since injury for uninjured participants was coded the same as that of matched injured participants on recruitment and indicate an equivalent injury-free time. Regression analyses began with models that included injury history (primary exposure variable), sex, time since injury, type of injury, BMI, knee extensor and flexor strength, intermittent knee pain, moderate-to-strenuous physical activity, and a two-way interaction term for injury history and sex. After evaluating the significance of the interaction term (i.e., likelihood ratio test, ≥0.05), we followed a backwards stepwise elimination approach where variables with a p-value <0.05 were retained and the most parsimonious model was reported. All assumptions for linear regression analyses were assessed and met.

3.3 RESULTS

Table 3.1: Participant Characteristics and Outcomes by Study Group

Characteristic	Uninjured (n=129)	Injured (n=124)
Sex (n, % female)	72 (56)	66 (53)
Age at injury (years)	–	16 (9-19)
Age at follow-up (years)	23 (14-29)	22 (16-29)
Time since injury (years)	–	6.7 (2.9-11.6)
Type of injury (n, % ACL rupture)	–	72 (56)
Subsequent injury (n, % yes)[a]	1 (0, 7)	33 (27)
Subsequent surgery (n, % yes)[b]	–	26 (21)
Radiographic osteoarthritis (n, % yes)[c]	0 (0, 0)	9 (7)
MRI-defined osteoarthritis (n, % yes)[d]	3 (1, 10)	25 (28)
Main sport (n, % soccer)	45 (35)	43 (35)
Sport participation in last 12 months (n, % yes)	123 (95)	110 (89)
EQ-5D-5L index	0.911 (0.634-0.949)	0.911 (0.561-0.949)
EQ-VAS	85 (20-100)	80 (10-100)
KOOS QOL	100 (83-100)	92 (64-100)
BMI (kg/m^2)	23.5 (18.1-33.1)	24.8 (18.6-38.9)
Knee extensor strength (Nm/kg)	1.92 (0.73-4.21)	1.84 (0.40-3.53)
Knee flexor strength (Nm/kg)	1.09 (0.38-2.08)	0.95 (0.37-2.09)
ICOAP intermittent pain	0 (0-33)	0 (0-54)
GLTEQ moderate-to-strenuous physical activity (METs/week)	45 (0-93)	42 (4-136)

Values represent median (range) unless otherwise indicated

[a]Any tibiofemoral or patellofemoral injury that resulted in seeking medical attention and time-loss from sport participation

[b]Any surgery to the index or non-index knee during the follow-up period

[c]Grade ≥2 on the Kellgren-Lawrence Grading System;[54] data available for 86 uninjured and 84 injured participants

[d]Met criteria for tibiofemoral (medial or lateral compartment), mixed tibiofemoral, or patellofemoral MRI-defined osteoarthritis as per Hunter et al. (2011);[55] data available for 88 uninjured and 87 injured participants

ACL, anterior cruciate ligament; BMI, body mass index; EQ-5D-5L, EuroQoL 5-dimension, 5-level; EQ-VAS, EuroQoL visual analog scale; GLTEQ, Godin Leisure-Time Exercise Questionnaire; ICOAP, Intermittent and Constant Osteoarthritis Pain Score; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; m, metre; MET, metabolic equivalent; MRI, magnetic resonance imaging; n, number of participants; N, Newton; 95%CI, 95% confidence interval

A total of 253 participants were recruited, including 124 youth with a previous sport- related knee injury and 129 uninjured controls. The median age of the participants at follow-up was 23 years (range 14-29) and 55% of the participants were females (**Table 3.1**). Soccer was the most common pre-injury sport (35%) with ice hockey (21%), basketball (12%), skiing or snowboarding (8%), football (5%), rugby (4%), running (4%), volleyball (4%), dance or gymnastics (2%), horseback riding or rodeo (2%), baseball (1%), figure skating (1%), lacrosse (1%), and field hockey (1%) also identified. Of the injured group, 69 participants (56%) sustained an ACL rupture, all of whom underwent ACLR [median time from injury to surgery 6.6 months (range 0.6-43.0) and median time from surgery to follow-up 5.9 years (range 3.9-11.4)]. Twenty participants (16%) had meniscus injuries, 15 (12%) had other ligament injuries (i.e., grade I-II ACL or PCL injury, grade I-III MCL or LCL injury), 18 had a patella subluxation or dislocation (15%), and 2 (2%) had a fracture. The median time since injury was 6.7 years (range 2.9-11.6).

For generic HRQoL, the median EQ-5D-5L index score for the uninjured and injured participants was 0.911 (range 0.634-0.949) and 0.911 (range 0.561-0.949), respectively, and the median EQ-VAS score for the uninjured and injured participants was 85 (range 20-100) and 80 (range 10-100), respectively. For knee-specific HRQoL, uninjured participants had a median KOOS QOL score of 100 (range 83-100) whereas injured participants had a median score of 92 (range 64-100). One injured participant did not complete the EQ-5D-5L and 3 injured participants did not complete the EQ-VAS.

Table 3.2: Univariable Linear Regression Models for Injury History and HRQoL Outcomes

Outcome	Injury History[a]	R^2	n
EQ-5D-5L	-0.0074 (-0.0238, 0.0089)	0.005	252
EQ-VAS	-3.82 (-8.77, 1.14)	0.022	250
KOOS QOL	**-8.41 (-10.76, -6.06)**	0.305	253

Values represent coefficient and 95%CI
All models accounted for clustering by sex and sport
Bolded font represents 95%CI does not encompass zero
[a]Reference = uninjured participants

EQ-5D-5L, EuroQoL 5-dimension, 5-level; EQ-VAS, EuroQoL visual analog scale; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; n, number of participants; R^2, coefficient of determination; 95%CI, 95% confidence interval

Univariable associations between injury history and HRQoL outcomes are summarized in **Table 3.2**. Injury history was not associated with EQ-5D-5L index (−0.0074, 95%CI −0.0238, 0.0089) or EQ-VAS scores (−3.82, 95%CI −8.77, 1.14). However, a negative association was found between injury history and KOOS QOL scores (−8.41, 95%CI −10.76, −6.06).

Table 3.3: Multivariable Linear Regression Models for Injury History and HRQoL Outcomes Considering Determinants of HRQoL and Osteoarthritis Disease

Model	Injury History[a]	Sex[b]	Time since Injury	ACL ‡	BMI (kg/m^2)	Extensor Strength (Nm/kg)	Flexor Strength (Nm/kg)	ICOAP	GLTEQ (MET/wk)	Injury x Sex	R^2
EQ-5D-5L	-0.0032 (-0.0170, 0.0107)	-0.0090 (-0.0227, 0.0047)	–	–	–	–	–	**-0.0024 (-0.0034, -0.0015)**	–	**0.0232 (0.0042, 0.0422)**	0.220
EQ-VAS	-3.47 (-7.98, 1.04)	–	–	–	–	–	–	–	**0.10 (0.03, 0.17)**	–	0.047
KOOS QOL	**-5.14 (-6.90, -3.38)**	–	–	**-1.41 (-2.77, -0.06)**	–	–	–	**-0.40 (-0.45, -0.36)**	–	–	0.587

Values represent coefficient and 95%CI
All models accounted for clustering by sex and sport
Bolded font represents 95%CI does not encompass zero
[a]Reference = uninjured participants
[b]Reference = female sex.
[c]Reference = no ACL rupture

ACL, anterior cruciate ligament rupture; BMI, body mass index; EQ-5D-5L, EuroQoL 5-dimension, 5-level; EQ-VAS, EuroQoL visual analog scale; GLTEQ, Godin Leisure-Time Exercise Questionnaire moderate-to-strenuous physical activity; ICOAP, Intermittent and Constant Osteoarthritis Pain intermittent pain subscale; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; m, metre; MET, metabolic equivalent; Nm, Newton-metre; R^2, coefficient of determination; wk, week; 95% CI, 95% confidence interval

Multivariable linear regression models that considered the influence of sex, time since injury, type of injury, BMI, knee extensor and flexor strength, intermittent knee pain, and moderate-to-strenuous physical activity on the relationship between youth sport-related knee injury history and HRQoL outcomes are summarized in **Table 3.3**. Regardless of injury history, higher levels of intermittent pain (ICOAP) were associated with poorer generic HRQoL (EQ-5D-5L index −0.0024, 95%CI −0.0034, −0.0015), and higher levels of moderate-to-strenuous physical activity (GLTEQ) were associated with better generic HRQoL (EQ-VAS 0.10, 95%CI 0.03, 0.17). A significant interaction between injury and sex suggested that injured males have slightly higher generic HRQoL (EQ-5D-5L index 0.0232, 95%CI 0.0042, 0.0422) than uninjured males. Finally, injury history (−5.14, 95%CI −6.90, −3.38), an ACL rupture (−1.41, 95%CI −2.77, −0.06), and higher levels of intermittent pain (ICOAP −0.40, 95%CI −0.45, −0.36) were associated with lower knee-specific HRQoL (KOOS QOL). No other associations were found.

3.4 DISCUSSION

We present a novel examination of generic and knee-specific HRQoL in individuals with a previous youth sport-related knee injury compared to uninjured controls of similar age, sex, and sport. Our findings indicate that a 3-12 year history of a youth sport-related knee injury is not associated with generic HRQoL but is negatively associated with knee-specific HRQoL. Exploratory analyses revealed that more intermittent knee pain or less self-reported moderate-to-strenuous physical activity are associated with worse generic HRQoL, regardless of injury history. Additionally, injury history, a previous ACL rupture, and more intermittent knee pain were associated poorer knee-specific HRQoL. These data imply that the potential determinants generic and knee-specific HRQoL following a youth sport-related knee injury may be distinct from one another; therefore, these 2 outcomes should be considered as unique parts of a broad construct.

The finding that generic HRQoL was not associated with a 3-12 year history of a previous youth sport-related knee injury is consistent with previous studies examining youth at 5-14 years after an ACL rupture or ACLR who reported no differences in generic HRQoL than uninjured controls.[56-59] Similar outcomes have been described in 2 systematic reviews of youth and adults at 5-23 years post-ACL rupture[17] or 5-16 years post-ACLR.[16] However, 1 recent meta-analysis suggests there may be a difference in the physical but not mental component of generic HRQoL (as measured by the SF-36) in youth and adults with a previous ACL rupture or ACLR and uninjured controls.[20]

It is plausible that the link between intermittent pain and generic HRQoL is explained by its physical (e.g., sleep disturbance[60]), psychological (e.g., depression[61]), and social (e.g., activity or hobby limitation[60]) manifestations. Physical inactivity may also influence generic HRQoL through its negative impact on physical (e.g., increased sedentary behaviour[29]), psychological (e.g., depression[62]), and social (e.g., isolation from sports/recreational community[63]) health. With that said, pain/discomfort is 1 of 5 items on the EQ-5D-5L, so the relationship detected between intermittent knee pain and generic HRQoL may be due to the exposure and outcome variables representing a similar construct. We must also note that generic HRQoL could be influenced by factors not assessed here, including but not limited to other injuries, medical conditions (e.g., anxiety, depression, diabetes), smoking status, healthcare access and literacy, and socioeconomic status. Although intermittent pain and moderate-to-strenuous physical activity are potential determinants of generic HRQoL of youth, the influence of other physical, psychological, and social health outcomes should be investigated.

Current evidence indicates that youth and adults with an ACL rupture or undergone ACLR demonstrate long-term deficits in knee-specific HRQoL.[5, 16, 17] Our findings move beyond previous research and suggest that these long-term deficits are also present in individuals who experienced a broad range of traumatic knee injuries that occurred in their youth. Taken together, these observations solidify the relationship between injury history and knee-specific HRQoL following a sport-related knee injury, regardless of age at injury and injury type.

Intermittent pain was identified as a potential determinant of knee-specific HRQoL, likely due to similar physical, psychological, and social manifestations as those mentioned above. Sustaining an ACL rupture may contribute to greater reductions in knee-specific HRQoL than other injuries considering it is associated with substantial physical impairments (e.g., knee muscle weakness[10, 64]), psychological consequences (e.g., heightened fear of reinjury[65-67]), and social limitations (e.g., isolation from sport community[63]) as well as a long rehabilitation period.

3.4.1 Research Recommendations

Further investigation is needed to determine the relationship between youth sport-related knee injuries and HRQoL (particularly, knee-specific HRQoL) at different timepoints. Understanding the trajectory of generic and, particularly, knee-specific HRQoL outcomes will help identify when HRQoL deficits are greatest and when future interventions should be delivered. Researchers should continue to explore potential determinants of generic and knee-specific

HRQoL and assess their association with HRQoL in the short-, medium- , and long-term after a youth sport-related knee injury. Additionally, we recommend engaging patients as research partners to ensure relevant constructs related to HRQoL are examined.

3.4.2 Clinical Implications

Clinicians should collect both generic and knee-specific HRQoL outcomes from their youth patients with knee injuries as these constructs seem to be unique. Given that knee pain and physical activity were associated with generic and/or knee-specific HRQoL, providing long-term maintenance strategies to manage these health outcomes may be beneficial. Clinicians may also want to emphasize these strategies in youth who have an ACL rupture and ACLR as they are more susceptible to greater knee-specific HRQoL deficits in the long-term.

3.4.3 Strengths and Limitations

The strengths of this study are the inclusion of uninjured controls of similar age, sex, and sport participation and a broad definition of knee injury (i.e., beyond an ACL rupture) confirmed at the time of injury. In contrast, this study was not specifically powered for our research questions. However, these preliminary findings can be used to inform an adequately powered study to fully address related objectives. Many of the participants in the Alberta Youth PrE-OA cohort may be from middle-to-high socioeconomic status given the recruitment sources and their ability to access organized sport, post-secondary education, and healthcare which limits the generalizability of our findings. Future studies should seek diverse and inclusive samples to better understand what happens to people from all backgrounds following a youth sport-related knee injury. It is important to highlight that the EQ-5D-5L and KOOS QOL subscale only consist of 5 and 4 items, respectively, and may not capture the breadth or complexity of generic and knee-specific HRQoL. Other alternative PROMs to consider using are the SF-36[68] (generic) and ACL QOL[69] (knee-specific) which assess multiple domains of HRQoL. However, the ACL QOL has only been validated in people with an ACL rupture. Using a self-reported measure of physical activity also introduces possible recall bias. When possible, accelerometry should be utilized as it is a more valid measure of physical activity. Lastly, only data on biological sex is available for the Alberta Youth PrE-OA study. Arguably, one's socially constructed gender has a greater influence on HRQoL and, therefore, both sex and gender should be examined going forward.[70]

3.5 CONCLUSIONS

The findings of this study suggest that generic and knee-specific HRQoL are distinct from one another and should both be measured in research and clinical practice. Injury history appears to be associated with knee-specific but not generic HRQoL. Based on exploratory analyses, intermittent knee pain and moderate-to-strenuous physical activity may be factors that influence generic HRQoL whereas injury history, injury type, and intermittent knee pain may be factors that influence knee-specific HRQoL. These findings can inform the design of future studies and strategies to improve long-term HRQoL in youth.

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CHAPTER 4: COMPARING SHORT-TERM KNEE-SPECIFIC HEALTH-RELATED QUALITY OF LIFE AND ASSOCIATED HEALTH OUTCOMES BETWEEN YOUTH WITH AND WITHOUT A SPORT-RELATED KNEE INJURY

The information has been submitted for peer-review and is reproduced from Le CY, Pajkic A, Losciale JM, Filbay SR, Emery CA, Manns PJ, Whittaker JL. Comparing short-term knee-specific health-related quality of life and associated clinical outcomes between youth with and without a sport-related knee injury. In submission at the Clinical Journal of Sport Medicine.

Having determined that youth sport-related knee injuries are associated with reduced knee-specific but not generic HRQoL at 3-12 years post-injury, we shift our attention to short-term changes in health outcomes. How early can we detect differences in knee-specific HRQoL between injured youth and uninjured peers? What factors may influence this relationship in the early stages of injury? This chapter describes knee-specific HRQoL and associated health outcomes over an initial 6-month follow-up following any traumatic, sport-related knee injury in youth and uninjured controls of similar age, sex, and sport participation.

ABSTRACT

Objective: To compare short-term changes in knee-specific HRQoL and associated health outcomes between youth with and without a sport-related knee injury.

Design: Prospective cohort study.

Methods: Participants included 93 youth (11-19 years old) who sustained an intra-articular, sport-related knee injury in past 4 months and 73 uninjured youth of similar age, sex, and sport. Main outcome measures included knee-specific HRQoL (KOOS QOL), knee extensor and flexor strength (dynamometry), physical activity (accelerometer), fat mass index (FMI; bioelectrical impedance), and kinesiophobia (Tampa Scale for Kinesiophobia, TSK-17) measured at baseline (within 4 months of injury) and 6-month follow-up. Wilcoxon rank-sum tests assessed between-group differences for all outcomes. Separate regression models assessed the association between injury history and change (baseline to 6-month follow-up) in knee-specific HRQoL and associated health outcomes, considering sex-based differences. The influence of injury type (ACL and/or meniscus vs. other), baseline values, and physiotherapy attendance on these relationships were also explored.

Results: Participant median age was 16 (range 11-20) years and 66% were female. Despite greater improvements in KOOS QOL scores (20; 95%CI 15, 25), injured participants demonstrated deficits at 6-month follow-up ($z=9.3$, $p<0.01$) compared to controls, regardless of sex. Similar findings were observed for knee extensor and flexor strength, physical activity, and TSK scores but not FMI. Participants with an ACL rupture and/or meniscus injury demonstrated smaller changes in KOOS QOL scores (-10.7; 95%CI -20.6, -0.7) than those with other knee injuries over the study period. In injured youth, lower baseline values were associated with greater changes in knee-specific HRQoL and all other outcomes.

Conclusions: Youth have worse knee-specific HRQoL, muscle strength, physical activity levels, and kinesiophobia early after a sport-related knee injury compared to controls. Despite improvements, these deficits persist 6 months later. Injury type and baseline values may influence the relationship between knee injuries and short-term knee-specific HRQoL.

4.1 INTRODUCTION

Youth who sustain a sport-related knee injury experience persistent deficits in HRQoL. Our previous research reveals that these deficits are seen in knee-specific but not generic HRQoL.[1] Currently, it is unclear how early knee-specific HRQoL of youth changes after an injury and what factors may influence it. A better understanding of short-term knee-specific HRQoL is essential for developing strategies to minimize the long-term burden of sport-related knee injuries in youth.

Generic HRQoL reflects overall physical, psychological, and social health.[2] Knee-specific HRQoL considers these domains as they pertain to the knee and can represent how one perceives their knee health during injury, recovery, and beyond. Preliminary evidence shows that youth have poorer knee-specific HRQoL as early as 6 months[3] after an ACLR compared to uninjured controls. While other studies have measured short-term knee-specific HRQoL, they often lack comparable, uninjured controls, making it difficult to know if early changes in knee-specific HRQoL are related to the knee injury or other factors (e.g., age, sex, sport/activity exposure).

Many factors have been linked with generic HRQoL in youth. For example, generic HRQoL is higher in youth who participate in resistance training,[4] are physically active,[5] maintain a healthy weight,[6] and have lower anxiety.[7] Conversely, youth who experience a knee injury often encounter consequences such as knee muscle weakness,[8] physical inactivity,[9] adiposity,[10] and kinesiophobia (i.e., fear of movement or re-injury)[11] which may impact knee-specific HRQoL. Understanding how these associated health outcomes change early after injury will help us determine which are most relevant to knee-specific HRQoL in this population.

4.1.1 Objectives

The objective of this study was to compare knee-specific HRQoL and associated health outcomes (i.e., knee extensor and flexor strength, physical activity, adiposity, and kinesiophobia) over a 6-month period after injury between youth with an intra-articular, sport-related knee injury and uninjured youth of similar age, sex, and sport. The influence of sex, injury type, baseline values, and physiotherapy attendance was also explored.

4.2 METHODS

4.2.1 Study Design

This was a prospective cohort study comparing osteoarthritis-related health outcomes between youth with a sport-related knee injury and uninjured controls of similar age, sex, and sport biannually (baseline, 6, 12, 18, and 24 months) over 2 years. This paper focuses on data collected at baseline and 6-month follow-up.

4.2.2 Ethics

Ethics approval was granted by the University of Alberta Health Research Ethics Board, Health Panel, Edmonton, Canada (Ethics ID Pro00063773). Participants provided written consent and assent (when applicable) and completed a PAR-Q (2002)[12] before testing.

4.2.3 Participants

Participants were youth (11-19 years old) who sustained a first-time, traumatic, intra-articular, sport-related knee injury in the past 4 months and uninjured youth of similar age, sex, and sport who contributed baseline and 6-month data by May 1, 2021. We selected an age range of 11-19 years because of the high prevalence of youth who sustain sport-related knee injuries.[13-15] Knee injury was defined as an intra-articular knee injury (clinical diagnosis of a ligament, meniscus, or other intra-articular tibiofemoral or patellofemoral injury) that occurred while participating in a sport or recreational activity, required medical consultation (e.g., physiotherapist, physician), and disrupted regular sports participation on at least 1 occasion in the previous 4 months. Injury type was categorized based on clinical examination and diagnostic imaging and surgical reports when available.

Uninjured participants had no history of a knee injury and were of similar age (within 12 months), sex, and main sport (played most frequently) as injured participants. Exclusion criteria included pregnancy, other time-loss injury in the 4 months preceding baseline testing, arthritis diagnosis, or any condition preventing participation in functional tests (e.g., neurological conditions). Uninjured participants who experienced a sport-related knee injury during the study were withdrawn and given the option to re-enroll as an injured participant if eligible.

4.2.3.1 Sample Size

The full cohort study sample size was based on the ability to detect a clinically meaningful between-group difference in percent fat mass [uninjured mean 20.2%, injured mean 23.4%, common standard deviation (SD) 7.03%], physical activity (uninjured mean 153 minutes/week, injured mean 121 minutes/week, common SD 75 minutes/week), triple single leg hop distance (uninjured mean 489% of leg length, injured mean 450%, common SD 92%), and isometric knee extension strength asymmetry (uninjured mean 0.995, injured mean 0.892, common SD 0.23)[16, 17] with multivariate analyses, adjusted for a 10% drop out over 2 years (1-β=0.8, α=0.05).

4.2.4 Recruitment

Participants were recruited through regional sport medicine or physiotherapy clinics, local community sport organizations, social media, and word of mouth between December 2016 and September 2020. Additionally, injured participants were asked to share study information with uninjured teammates to identify uninjured controls of similar age, sex, and sport.

4.2.5 Procedures

Participants were assessed at baseline (within 4 months of injury) and approximately 6 months later. At each visit, participants were emailed a unique URL to a series of questionnaires hosted on a secure data management system (REDCap 8.6.5, Vanderbilt University, Tennessee, USA) [18] and attended an in-person testing session. Questionnaires included a bespoke study questionnaire adapted from the Alberta PrE-OA cohort [e.g., participant characteristics (age, sex, main sport), injury details (injury type, date of injury), sport and activity participation, physiotherapy attendance; **Appendix V**],[16] KOOS, and TSK. At in-person testing, participants rotated through stations measuring height (to the nearest 0.1 cm without shoes on a stadiometer, Model 402KL, Pelstar, McCook, Illinois, USA), weight, body composition, and knee extensor and flexor strength then were given an accelerometer to monitor their physical activity over 8 days. Study personnel included physiotherapists and undergraduate students who underwent formal training to minimize inter-rater variability during data collection.

4.2.6 Outcomes

4.2.6.1 Knee-Specific Health-Related Quality of Life

The KOOS comprises 42 items in 5 subscales: knee-related symptoms, pain, function in daily living, function in sport and recreation, and knee-related QOL (**Appendix S**). Specifically, the KOOS QOL subscale contains 4 items (i.e., awareness of a knee problem, lifestyle modification, knee confidence, and overall knee difficulty). Items are scored on a 5-point Likert scale and subscale scores are transformed to 0-100 where higher scores indicate better outcomes. The KOOS demonstrates sufficient internal consistency (pooled Cronbach's alpha=0.72-0.93) and test-retest reliability (pooled ICC=0.84-0.89) in individuals with an ACL rupture.[19, 20]

4.2.6.2 Isokinetic Knee Muscle Strength

Normalized concentric peak knee extensor and flexor torque were tested at a velocity of 90°/second through a range of 0±2° to 90±2° with participants seated in 90° of hip flexion and straps secured across the chest and thighs (BTE PrimusRS, Hanover, Maryland, USA). After a practice trial and 1 minute rest, participants performed 3 repetitions of knee extension and flexion with maximal effort while receiving verbal encouragement. The peak torque (Nm) across repetitions for the injured limb was normalized to body weight (Nm/kg) and recorded. Isokinetic dynamometry is considered the gold standard for measuring muscle strength[21] and has acceptable test-retest reliability (pooled correlation coefficients>0.9).[22]

4.2.6.3 Physical Activity

An accelerometer (ActiGraph GT3X, Pensacola, Florida, USA) was worn on the right anterior superior iliac spine (waist) for 8 days, only removed for bathing, water activities (e.g., swimming), or activities that may damage it (e.g., wrestling). A log was kept to record non-wear times as well as the duration and intensity (i.e., light, moderate, or vigorous) of any activities performed when the accelerometer was off (**Appendix W**). This log was used to validate non-wear time. Self-reported physical activity during non-wear periods was manually added to the extracted accelerometer data. Non-wear periods and physical activity intensity cut-points were determined by the Choi[23] and Evenson children [24, 25] algorithms, respectively. Data were valid if there was ≥5 days with ≥10 hours of wear time per day.[26] Total physical activity (sum of light, moderate, and vigorous activity) and sedentary time were recorded. The ActiGraph is a valid measure of physical activity in youth.[27]

4.2.6.4 Adiposity

Using bioelectrical impedance analysis (BIA; Tanita Body Composition Analyzer MC-780U, Arlington Heights, Illinois, USA), participants stood barefoot on footplate electrodes and gripped hand electrodes while the resistance to a low energy, high frequency electrical signal (50 kHz, 500 μA) was measured. The BIA unit estimates body mass (kg) and fat mass (kg) from which FMI (kg/m^2) was calculated.

4.2.6.5 Kinesiophobia

The TSK-17 consists of 17 items scored on a 4-point Likert scale (**Appendix X**). Scores range from 17-68 where lower scores indicate better outcomes (less fear of movement or re-injury). Although the TSK has not been validated in individuals with a knee injury, it is commonly used to measure kinesiophobia after an ACL rupture.[28, 29]

4.2.7 Data Analysis

Statistical analyses were performed using STATA (v12.1, College Station, Texas, USA). We reported the number of interested, screened, eligible, and enrolled participants and summarized differences in age, sex, and sport of participants and non-participants. The proportion of non-participation and loss to follow-up were summarized by study group (injured or uninjured). Descriptive statistics (median, mean, or proportion) were calculated for participant characteristics and outcomes at baseline, follow-up, and change from baseline to follow-up by study group. Univariable estimates ($p<0.05$) were made to compare all outcomes between study groups at baseline and follow-up based on data distribution (e.g., t-test for parametric data, Wilcoxon rank-sum test for non-parametric data).

For all analyses, we used backwards stepwise selection beginning with full models and removing variables with the highest p-value until all remaining variables were significant ($p<0.05$). Beta coefficients and variance explained by the models (R^2) were reported. We decided a-priori to retain sex in all models regardless of the backwards elimination process to assess if sex-based differences in knee-specific HRQoL observed in injured adults[30] are also present in youth. Participants with missing data for a particular outcome were removed from analyses for that outcome. Variables of interest were selected based on previous research (relationship with generic or knee-specific HRQoL) and the authors' clinical experience. All models were assessed for multicollinearity and linear regression assumptions were assessed and met.

4.2.7.1 Primary Objective

A multivariable linear regression model (95%CI; clustered on sex and to control for confounding effect) was used to assess the association between injury history (yes vs. no) and change (baseline to 6-month follow-up) in knee-specific HRQoL (KOOS QOL) with sex (female vs. male) as an additional variable of interest. Separate regression models were also used to assess the association between injury history and each associated clinical outcome [i.e., normalized knee extensor and flexor peak torque (Nm/kg), total physical activity (minutes/week), FMI (kg/m^2), and kinesiophobia (TSK)] and sex.

4.2.7.2 Exploratory Objective

To further understand the change in all outcomes in the injured group only, we explored the influence of injury type, physiotherapy attendance, and baseline values. Injury type[1] and baseline values[31] have been previously linked with knee-specific HRQoL. We grouped ACL ruptures and/or meniscus injuries together to reflect greater injury severity (often requiring ≥3 months of rehabilitation[32, 33]) and possibly greater impact on knee-specific HRQoL. After receiving input from physiotherapists and considering the heterogeneity of injury types included in this cohort, a cut-off point of 5 physiotherapy visits was used to identify individuals who participated in a comprehensive rehabilitation program.

In the injured group only, separate regression models explored the influence of sex, injury type (ACL rupture and/or meniscus injury vs. other), physiotherapy attendance (<5 or ≥5 visits), and baseline values of each respective outcome on short-term change from baseline to follow-up.

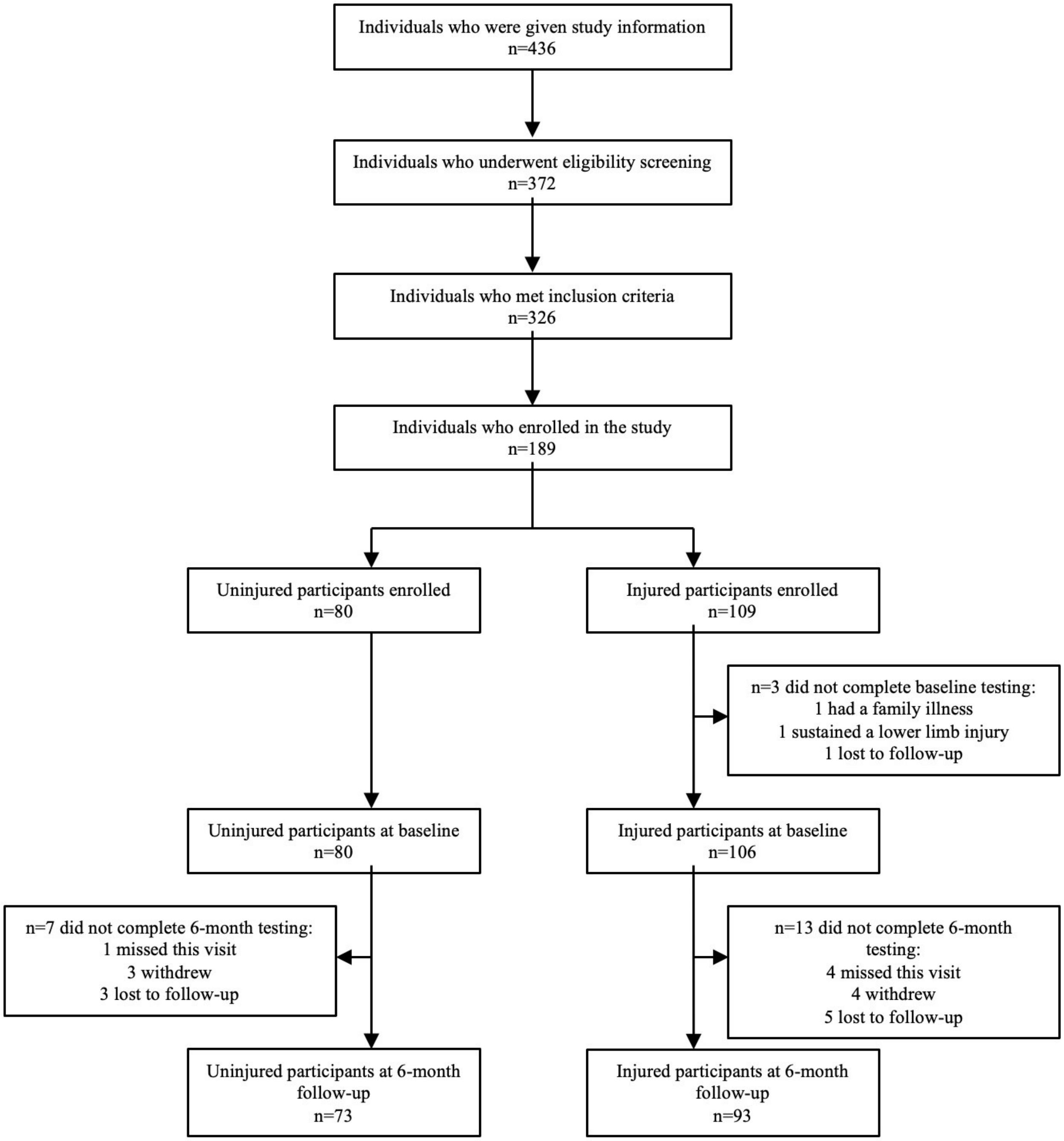

Figure 4.1: Participant Enrollment and Flow Chart (Baseline and 6-Month Follow-up)

4.3 RESULTS

Participant enrollment is outlined in **Figure 4.1**. Age, sex, main sport, and injury history did not differ between participants [median (range) age 16 (11-20) years, 114 (60%) females, 64 (34%)

played soccer, 109 (58%) injured] and non-participants [median (range) age 16 (11-19) years, 126 (50%) females, 47 (21%) played soccer, 82 (61%) injured].

We enrolled 189 participants (109 injured, 80 uninjured) but 3 injured participants did not complete baseline testing and 20 participants (13 injured, 7 uninjured) did not complete follow-up testing (**Figure 4.1**). Consequently, we had baseline and 6-month follow-up data for 93 (85%) injured and 73 (91%) uninjured participants. Furthermore, 6 injured and 9 uninjured participants only completed the online questionnaires at follow-up (reasons for missing data can be found in **Appendix Y**). One uninjured participant experienced a sport-related knee injury during the study period and was re-enrolled as an injured participant.

Table 4.1: Participant Characteristics by Study Group.

Characteristic	Uninjured (n=73)	Injured (n=93)
Sex (n, % female)	50 (69)	60 (65)
Age at injury (years)	–	16 (11-20)
Age at baseline (years)	17 (11-20)	16 (11-20)
BMI (kg/m^2)	22 (15-36)	23 (16-41)
Time from injury to baseline (months)	–	1 (0-4)
Time from baseline to follow-up (months)	6 (4-9)	6 (5-9)
Injury type (n, % ACL rupture)	–	48 (52)
Main sport (n, % soccer)	27 (37)	27 (29)
Main sport level (n, % club)[a]	53 (73)	54 (58)
KOOS symptoms (0-100)	96 (68-100)	64 (29-100)
KOOS pain (0-100)	100 (64-100)	75 (25-100)
KOOS ADL (0-100)	100 (78-100)	90 (35-100)
KOOS sport & recreation (0-100)	100 (60-100)	58 (0-100)
MVPA (minutes/week)	411 (90-1261)	271 (58-879)
Sedentary time (minutes/week)	8007 (5322-9280)	8018 (4307-9616)
Sport participation at baseline (minutes/week)[b]	460 (83-1597)	617 (37-1910)
Physiotherapy attendance (n, % ≥5 visits)	–	50 (54)

Values represent median (range) unless otherwise indicated
[a]Categories included recreational, club, school, varsity, provincial, or national
[b]Self-reported sport participation over the previous year

ACL, anterior cruciate ligament; ADL, activities of daily living; BMI, body mass index; kg, kilogram; KOOS, Knee injury and Osteoarthritis Outcome Score; m, metre; MVPA, moderate-to-vigorous physical activity; n, number of participants; 95%CI, 95% confidence interval

Participant characteristics are summarized in **Table 4.1**. Of the injuries reported, 53% were an ACL rupture, 17% other tibiofemoral ligament injury (any PCL, MCL, or LCL injury or partial ACL injury), 22% patellar subluxation or dislocation, 4% isolated meniscus tear, 3% intra-articular bony contusion, and 1% intra-articular fracture. For the injured group, the median (range) time from injury to follow-up was 8 months (5-11) and 50 participants (of which 34 had ACL ruptures) attended ≥5 physiotherapy visits for their knee injury during the study period. Of the 48 participants who ruptured their ACL, 24 (50%) underwent ACL reconstruction prior to 6-month follow-up [median time from injury to surgery 4.1 months (range 0.6-7.1) and median time from surgery to follow-up 3.9 months (range 1.2-8.4)].

Table 4.2: By Study Group, All Outcomes at Baseline, Follow-Up, and 6-Month Change.

	Uninjured (n=73)			**Injured (n=93)**		
Outcome	**Baseline Median (Range)**	**Follow-Up Median (Range)**	**Change Mean (95%CI)**	**Baseline Median (Range)**	**Follow-Up Median (Range)**	**Change Mean (95%CI)**
Primary Outcome						
KOOS QOL (0-100)	100[a] (56-100)	100[b] (31-100)	0 (-13, 13)	38 (0-100)	56 (0-100)	19 (-13, 63)
Associated Health Outcomes						
Peak knee extensor torque (Nm/kg)	1.94[a] (0.77-2.31)	1.90[b] (1.29-2.89)	0.04 (-0.28, 0.32)	1.37 (0.28-2.23)	1.71 (0.49-2.55)	0.28 (-0.57, 1.00)
Peak knee flexor torque (Nm/kg)	1.32[a] (0.56-2.21)	1.35[b] (0.80-2.69)	0.05 (-0.34, 0.40)	1.02 (0.17-2.23)	1.23 (0.41-2.27)	0.26 (-0.29, 0.92)
Total physical activity (minutes/week)	1992[a] (925-3265)	1722[b] (820-2682)	-241 (-1015, 573)	1730 (464-2972)	1531 (200-2748)	-189 (-1105, 657)
FMI (kg/m^2)	3.9 (0.4-10.9)	4.8 (0.4-10.7)	0.3 (-1.1, 1.8)	4.3 (0.5-21.5)	4.9 (0.6-20.3)	0.5 (-1.2, 2.1)
TSK (17-68)	35[a] (25-47)	34[b] (20-47)	-1 (-11, 12)	40 (22-56)	37 (22-55)	-3 (-12, 9)

[a]Significant difference from the injured group at baseline (Wilcoxon rank-sum tests): KOOS QOL z=10.9, p<0.01; peak knee extensor torque z=7.0, p<0.01; peak knee flexor torque z=5.8; p<0.01, total physical activity z=3.5, p<0.01; TSK z=-4.9, p<0.01
[b]Significant difference from the injured group at follow-up (Wilcoxon rank-sum tests): KOOS QOL z=9.2, p<0.01; peak knee extensor torque z=4.3, p<0.01; peak knee flexor torque z=2.4, p=0.02; total physical activity z=2.5, p=0.01; TSK z=-2.9, p<0.01

FMI, fat mass index; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; n, number of participants; Nm, Newton-metre; TSK, Tampa Scale for Kinesiophobia; 95%CI, 95% confidence interval

Table 4.3: By Injury Type, All Outcomes at Baseline, Follow-Up, and 6-Month Change

Outcome		ACL Rupture (n=48)	Other Ligament Injury[a] (n=17)	Patellofemoral Injury[b] (n=19)	Meniscus Tear (n=4)	Bony Contusion (n=3)	Fracture (n=1)
Primary Outcome							
KOOS QOL (0-100)	Baseline	31 (0-63)	38 (0-88)	50 (0-88)	63 (56-69)	75 (38-100)	6[d]
	Follow-up	44 (13-94)	59 (25-100)	66 (0-100)	100 (56-100)	94 (94-100)	100[d]
	Change[c]	17 (-19, 56)	25 (-6, 69)	15 (-19, 44)	34 (-6, 44)	25 (0, 56)	94[d]
Associated Health Outcomes							
Peak knee extensor torque (Nm/kg)	Baseline	1.36 (0.40-2.23)	1.58 (0.50-2.05)	1.06 (0.28-2.18)	1.54 (0.76-1.94)	1.37 (1.35-1.91)	N/T
	Follow-up	1.61 (0.84-2.44)	1.88 (0.52-2.55)	1.62 (0.49-2.21)	1.74 (1.72-1.88)	1.58 (1.32-1.84)	2.30[d]
	Change	0.30 (-0.98, 1.04)	0.19 (-0.57, 0.67)	0.40 (0.03, 1.57)	0.11 (-0.20, 0.55)	0.03 (-0.07, 0.21)	N/A
Peak knee flexor torque (Nm/kg)	Baseline	1.02 (0.28-2.23)	1.16 (0.38-1.84)	0.71 (0.17-1.92)	1.01 (0.74-1.34)	1.03 (0.88-1.29)	N/T
	Follow-up	1.11 (0.61-2.03)	1.43 (0.41-2.27)	1.30 (0.43-2.06)	1.00 (0.96-1.27)	1.03 (0.97-1.63)	1.57[d]
	Change	0.24 (-0.29, 0.92)	0.20 (-0.57, 1.05)	0.44 (-0.05, 1.12)	-0.05 (-0.23, 0.17)	0.15 (-0.31, 0.75)	N/A
Total physical activity (minutes/week)	Baseline	1743 (700-2708)	1839 (464-2510)	1680 (1010-2336)	1635 (1437-2031)	2335 (681-2972)	1364[d]
	Follow-up	1529 (653-2748)	1439 (200-2364)	1586 (1073-2615)	2437[d]	1823 (1032-2614)	1313[d]
	Change	-220 (-814, 541)	-207 (-2032, 870)	-95 (-987, 549)	883[d]	-831 (-1303, -358)	-51[d]
FMI (kg/m^2)	Baseline	4.4 (0.5-21.5)	4.0 (1.8-7.6)	4.4 (1.0-18.1)	6.5 (0.8-10.1)	4.4 (1.4-5.5)	3.3[d]
	Follow-up	4.7 (0.6-20.3)	4.5 (2.2-7.8)	5.5 (1.0-14.4)	7.6 (0.9-7.7)	4.6 (3.0-6.1)	3.7[d]
	Change	0.4 (-1.5, 2.1)	0.5 (-4.9, 1.7)	0.7 (-1.2, 2.7)	0.8 (0.1, 1.8)	0.8 (0.3, 1.5)	0.4[d]
TSK (17-68)	Baseline	43 (22-56)	38 (27-51)	41 (31-52)	34 (27-37)	35 (31-40)	37[d]
	Follow-up	37 (22-51)	38 (30-52)	40 (28-55)	33 (23-37)	28 (24-38)	31[d]
	Change	-4 (-13, 5)	-1 (-10, 9)	-1 (-10, 12)	-2 (-4, 0)	-5 (-7, -2)	-6[d]

[a]Includes a PCL, MCL, or LCL injury of any grade or partial ACL injury
[b]Includes a patellofemoral subluxation or dislocation
[c]Value represents change from baseline to 6-month follow-up
[d]Value only represents one participant so no range or 95%CI is presented

ACL, anterior cruciate ligament; FMI, fat mass index; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; LCL, lateral collateral ligament; MCL, medial collateral ligament; n, number of participants; N/A, not applicable; N/T, not tested as per physician's orders; Nm, Newton-metre; PCL, posterior cruciate ligament; TSK, Tampa Scale for Kinesiophobia; 95%CI, 95% confidence interval

Baseline, follow-up, and mean change (95%CI) values for all outcomes are summarized by study group in **Table 4.2** and by injury type in **Table 4.3**. Injured participants had significantly worse KOOS QOL scores, peak knee extensor and flexor torque, weekly total physical activity, and TSK scores compared to uninjured participants at baseline and follow-up (Wilcoxon rank-sum tests; **Table 4.2**). No between-group differences in FMI were found at either testing timepoint.

Table 4.4: Multivariable Linear Regression Models for Injury History, Sex, and Short-Term Change in All Outcomes.

Outcome Change	Injury History[a]	Sex[b]	R^2	n
Primary Outcome				
KOOS QOL (0-100)	**20 (15, 25)**	-5 (-10, 2)	0.204	164
Associated Health Outcomes				
Knee extensor peak torque (Nm/kg)	**0.24 (0.09, 0.40)**	0.00 (-0.14, 0.14)	0.110	135
Knee flexor peak torque (Nm/kg)	**0.21 (0.12, 0.29)**	0.05 (-0.10, 0.19)	0.096	135
Total physical activity (minutes/week)	53 (-69, 175)	-17 (-196, 163)	0.003	129
FMI (kg/m^2)	0.2 (-0.2, 0.6)	0.3 (-0.2, 0.7)	0.024	148
TSK (17-68)	**-2.2 (-4.3, -0.2)**	1.1 (-0.8, 3.1)	0.039	164

Values represent coefficient and 95%CI
All models included clustering by sex and sport
Bolded font represents 95%CI does not encompass zero
[a]Reference = uninjured participants
[b]Reference = female sex

FMI, fat mass index; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; n, number of participants; Nm, Newton-metre; R^2, coefficient of determination; TSK, Tampa Scale for Kinesiophobia; 95%CI, 95% confidence interval

Although there were no within-group differences for any outcomes from baseline to follow-up (**Table 4.2**), a multivariable linear regression model demonstrated that injured participants had greater increase in KOOS QOL scores (20; 95%CI 15, 25) compared to uninjured participants over the study period, regardless of sex (**Table 4.4**). Similarly, injured participants demonstrated greater improvements in peak knee extensor (0.24 Nm/kg; 95%CI 0.09, 0.40) and flexor (0.21 Nm/kg; 95%CI 0.12, 0.29) torque and TSK scores (-2.2; 95%CI -4.3, -0.2) compared to uninjured participants, regardless of sex. Although weekly total physical activity was significantly different between study groups at baseline and follow-up, injury history was not found to be associated with short-term change in physical activity. Injury history was also not associated with change in FMI.

Table 4.5: In the Injured Group, Exploratory Multivariable Linear Regression Models Examining the Influence of Sex, Injury Type, Physiotherapy Attendance, and Baseline Values on Short-Term Change in All Outcomes.

Outcome Change	Sex[a]	Injury Type[b]	Physiotherapy Attendance[c]	Baseline Values	R^2	n
Primary Outcome						
KOOS QOL (0-100)	–	**-10.7 (-20.6, -0.7)**	–	**-0.4 (-0.7, -0.2)**	0.158	91
Associated Health Outcomes						
Knee extensor peak torque (Nm/kg)	–	–	–	**-0.55 (-0.71, -0.39)**	0.408	71
Knee flexor peak torque (Nm/kg)	**0.17 (0.001, 0.34)**	–	–	**-0.52 (-0.71, -0.33)**	0.309	71
Total physical activity (minutes/week)	–	–	–	**-0.7 (-0.9, -0.4)**	0.335	68
FMI (kg/m^2)	–	–	–	**-0.1 (-0.2, -0.01)**	0.058	85
TSK (17-68)	–	–	–	**-0.4 (-0.5, -0.2)**	0.186	91

Values represent coefficient and 95%CI
All models included clustering by sex and sport
Bolded font represents 95%CI does not encompass zero
[a]Reference = female sex
[b]Reference = no ACL rupture and/or meniscus injury
[c]Reference = less than 5 physiotherapy visits

ACL, anterior cruciate ligament; FMI, fat mass index; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; n, number of participants; Nm, Newton-metre; R^2, coefficient of determination; TSK, Tampa Scale for Kinesiophobia 95%CI, 95% confidence interval

In injured participants only, multivariable linear regression models exploring the influence of sex, injury type, physiotherapy attendance, and baseline values on outcome change are summarized in **Table 4.5**. Changes in all outcomes were significantly and inversely associated with baseline values. When baseline values were considered, participants with an ACL rupture and/or meniscus injury demonstrated smaller changes in KOOS QOL scores (-10.7; 95%CI -20.6, -0.7) than those with other knee injuries and males demonstrated a larger change in peak knee flexor torque (0.17Nm/kg; 95%CI 0.001, 0.34) than females over the study period (assuming other variables remain constant).

4.4 DISCUSSION

We believe this is the first study to assess short-term knee-specific HRQoL and associated clinical outcomes in youth who have experienced a sport-related knee injury compared to uninjured controls. Despite short-term improvements, knee-specific HRQoL deficits are evident early after a knee injury and persist 6 months later. A similar pattern was observed for knee extensor and flexor strength and kinesiophobia. Our exploratory analyses suggest that short-term changes in knee-specific HRQoL are influenced by injury type and baseline values but not sex or physiotherapy attendance. Injured youth with lower knee-specific HRQoL, knee muscle strength, physical activity, and adiposity as well as higher kinesiophobia at baseline demonstrate the greatest short-term improvements.

Our novel findings identify early deficits in knee-specific HRQoL of youth with a broad range of knee injuries compared to uninjured peers. This builds on evidence of knee-specific HRQoL deficits at 6-months post-ACLR.[3] By comparing to uninjured controls of similar age, sex, and sport or activity participation, we are confident that the identified differences can be attributed to experiencing a knee injury.

We also found that youth with an ACL rupture and/or meniscus injury and higher baseline values may demonstrate less short-term improvement in knee-specific HRQoL early after injury. ACL and meniscus injuries are characterized by longer periods of reduced function than other injury types, so less change in knee-specific HRQoL is unsurprising. However, the difference in KOOS QOL change score from baseline to follow-up between youth with or without an ACL rupture and/or meniscus injury may not be clinically relevant considering the MIC for the KOOS QOL is 18.[34] Higher baseline values may indicate smaller room for growth and also less change. However, lower baseline values have been linked with worse long-term knee-specific HRQoL following ACLR,[31] suggesting more work is needed to understand the influence of baseline values. Sex and physiotherapy attendance were not found to impact short-term change in knee-specific HRQoL. Our findings about sex and knee-specific HRQoL are consistent with previous research[35] whereas physiotherapy attendance has yet to be assessed. Despite these contributions, injury type and baseline values only explained 15.8% of the variance in knee-specific HRQoL changes, so further research is required to identify other potential determinants.

Understanding how associated clinical outcomes change after a knee injury can determine what outcomes may influence knee-specific HRQoL. Over the study period, injured youth demonstrated positive changes in knee muscle strength and kinesiophobia but not physical activity or adiposity relative to uninjured peers. Weaker knee extensors, lower physical activity, and higher adiposity have been detected 6 months,[36] 2-3 years,[9] and 3-10 years,[10] respectively, after ACLR or intra-articular knee injury. Kinesiophobia has not been examined against a comparison group. Perhaps physical activity and adiposity changes manifest over the long-term, but knee muscle strength and kinesiophobia vary shortly after injury and their influence on knee-specific HRQoL warrants further exploration.

4.4.1 Research Recommendations

Future research should focus on how to improve knee-specific HRQoL early after a sport-related knee injury in youth. Identifying modifiable determinants of knee-specific HRQoL can inform evidence-based interventions. We have highlighted the importance of considering a wide range of knee injuries as opposed to ACL ruptures alone (25.4% of knee injuries in youth[15]) and including comparable, uninjured controls. Researchers should seek to understand why knee-specific HRQoL differs between injury types and how this may inform treatment strategies.

4.4.2 Clinical Implications

Clinicians should assess, monitor, and manage knee-specific HRQoL and associated outcomes in youth immediately after a sport-related knee injury, especially ACL or meniscus injuries. Accounting for baseline values can help clinicians estimate the amount of short-term change they expect to see in their patients. Alongside using PROMs, clinicians can ask patients how they feel about their overall knee health to thoroughly capture knee-specific HRQoL.

4.4.3 Strengths and Limitations

Our study strengths include comparing to controls, controlling for confounding by age, sex, and activity participation, and considering sex-based differences. To best describe short-term health changes, we performed univariable comparisons of key outcomes which may increase the probability of spurious findings. Twenty-eight (30%) injured participants were also patients of study physiotherapists which may augment retention (e.g., participants feel more comfortable attending follow-up visits with familiar research staff) but also introduce limitations (e.g., physiotherapists implicitly encourage familiar participants more than others). Our ability to detect sex differences may have been affected by a greater proportion of males withdrawing or being lost to follow-up. Our definition of physiotherapy attendance may lead to misclassification bias despite basing it on clinical experience and considering different injury types. Capturing exercise adherence (e.g., percentage of exercises completed) may be more helpful to understand how rehabilitation can impact health outcomes following injury. We acknowledge that gender (sociocultural construct) may have been more relevant to include in our analyses than sex (biological variable). Finally, the last 13 months of our study overlapped with the COVID-19 pandemic. As per the CONSERVE statement,[37] **Appendix Z** summarizes the impact, mitigation strategies, and study modifications due to COVID-19.

4.5 CONCLUSION

Youth demonstrate reduced knee-specific HRQoL after a sport-related knee injury compared to uninjured controls. Despite greater short-term improvements, injured youth report persisting knee-specific HRQoL deficits over a 6-month period. Early changes in knee-specific HRQoL appear to be influenced by injury type and baseline status but not sex. Future studies should focus on identifying modifiable determinants of knee-specific HRQoL in injured youth to inform treatment strategies. Shortly after injury, possible factors of interest may include knee muscle strength, physical activity, and kinesiophobia but not adiposity.

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CHAPTER 5: YOUTH WITH A SPORT-RELATED KNEE INJURY EXHIBIT SIGNIFICANT AND PERSISTENT KNEE-SPECIFIC HEALTH-RELATED QUALITY OF LIFE DEFICITS AT 12-MONTH FOLLOW-UP COMPARED TO UNINJURED PEERS

The information has been submitted for peer-review and is reproduced from Le CY, Filbay SR, Emery CA, Manns PJ, Whittaker JL. Youth with a sport-related knee injury exhibit significant and persistent knee-specific health-related quality of life deficits at 12-month follow-up compared to uninjured peers. In submission at the Journal of Orthopaedic & Sports Physical Therapy.

Preliminary analysis from the previous chapter suggests that youth who experience a sport-related knee injury report reduced knee-specific HRQoL than uninjured controls at baseline (within 4 months of injury) and 6-month follow-up. Injury type and baseline values have also been identified as possible factors that may influence knee-specific HRQoL and warrant further investigate. Building off of these findings, this chapter summarizes knee-specific HRQoL at approximately 6 and 12 months (i.e., over a typical rehabilitation timeframe) following any traumatic, sport-related knee injury in youth and uninjured controls of similar age, sex, and sport participation using more robust statistical analyses. We also further examine factors identified as potential determinants of HRQoL from the previous chapters.

ABSTRACT

Objective: To compare knee-specific HRQoL between youth with and without an intra-articular, sport-related knee injury at baseline (within 4 months post-injury), 6-month, and 12-month follow-up and to assess the relationship between associated health outcomes and knee-specific HRQoL.

Design: Prospective cohort study.

Methods: We recruited 86 injured and 64 uninjured youth of similar age, sex, sport participation. Knee-specific HRQoL was assessed with KOOS QOL subscale. Multivariable linear regression (95%CI; clustered on sex and sport) compared KOOS QOL between study groups (injured vs. uninjured) at all timepoints, considering sex-based differences. We also explored the association of injury type [anterior cruciate ligament (ACL) rupture and/or meniscus injury vs. other], knee extensor strength (isokinetic dynamometry), MVPA (accelerometer), intermittent knee pain (ICOAP intermittent pain subscale), fear of re-injury (TSK-17), and RTS (yes vs. no) with knee-specific HRQoL (KOOS QOL).

Results: Participant median (range) age was 16.7 (10.9-20.1), 67% were female, and 57% of injuries were ACL ruptures. Injured participants had lower mean KOOS QOL scores at baseline (-61; 95%CI -66, -56), 6-month (-41; 95%CI -46, -35), and 12-month follow-up (-34; 95%CI -41, -26), regardless of sex. Knee extensor strength, MVPA, ICOAP, and baseline KOOS QOL were associated with 12-month KOOS QOL, regardless of injury history or sex. In injured youth, ACL rupture and/or meniscus injuries and higher 6-month TSK scores were associated with worse 12-month KOOS QOL.

Conclusions: Youth with a sport-related knee injury exhibit significant and persistent knee-specific HRQoL deficits at 12-month follow-up. Knee extensor strength, physical activity, pain, and fear of re-injury may contribute to knee-specific HRQoL.

5.1 INTRODUCTION

Youth with a sport-related knee injury are believed to experience reduced knee-specific HRQoL. Previous studies have described knee-specific HRQoL after an injury, but they focus on within-group comparisons of individuals with ACL ruptures or ACLR.[1-3] Few studies have considered youth, prospective changes, injuries beyond the ACL, or comparison to uninjured peers. This has left a gap in understanding if, and to what extent, a sport-related knee injury affects youth knee-specific HRQoL and what factors might contribute to this relationship.

Knee-specific HRQoL encompasses how one perceives their physical, psychological, and social health as it pertains to their knee. This makes knee-specific HRQoL a valuable indicator of knee health. After a knee injury in adults, female sex,[4] weaker quadriceps and hamstring muscles,[5] lower physical activity,[6] higher fear of re-injury,[7] failure to RTS,[8] and lower baseline knee-specific HRQoL (i.e., status shortly after injury)[9] are associated with poorer knee-specific HRQoL. There is also evidence from uninjured youth that female sex,[10] lower participation in aerobic and resistance training,[11, 12] and pain[13] are associated with poorer generic HRQoL.

Currently, we do not know how knee-specific HRQoL changes in youth with a sport-related knee injury over a typical rehabilitation period (up to 12 months depending on injury type[14-17]) relative to uninjured youth. Comparing injured youth and uninjured peers of similar demographics (e.g., age, sex, sport/activity participation) at different timepoints during rehabilitation will allow us to determine if and how sport-related knee injuries impact knee-specific HRQoL.

5.1.1 Objectives

The primary objective of this study was to compare knee-specific HRQoL between youth with a sport-related knee injury and uninjured controls of similar age, sex, and sport participation at baseline, 6-month, and 12-month follow-up while considering sex-based differences. The secondary objective was to assess the association of injury history, sex, and 12-month knee extensor strength, physical activity, and intermittent knee pain with 12-month knee-specific HRQoL. In injured youth only, we explored the association of sex, injury type, and 6-month knee extensor strength, physical activity, intermittent knee pain, fear of re-injury, and RTS status with 12-month knee-specific HRQoL.

5.2 METHODS

5.2.1 Study Design

This is a longitudinal cohort study comparing health-related outcomes in youth with and without a sport-related knee injury. We followed the STROBE guidelines for reporting.[18]

5.2.2 Ethics

Ethics approval was granted by the University of Alberta Health Research Ethics Board, Health Panel, Edmonton, Canada (Ethics ID Pro00063773). Participants provided written consent or assent (when applicable) and completed a PAR-Q (2002)[19] before testing.

5.2.3 Participants

Participants included a convenience sample of youth (11-19 years old) who sustained a sport-related, intra-articular knee injury in the previous 4 months and uninjured youth of similar age, sex, and main sport (i.e., sport played most frequently). An intra-articular knee injury was defined as a clinical diagnosis of a ligament, meniscus, or other intra-articular tibiofemoral or patellofemoral injury that occurred while participating in a sport or recreational activity, required medical consultation (e.g., physiotherapist, physician), and disrupted regular sports participation on at least 1 occasion. Injury type was classified based on clinical examination and diagnostic imaging and/or surgical reports when available.

Uninjured participants were eligible if they had no previous knee injury and were of similar age (≤12 months), sex, and main sport as an injured participant. Exclusion criteria for all participants included pregnancy, other time-loss injury ≤4 months of baseline testing, arthritis diagnosis, or any medical condition preventing participation in functional tests (e.g., neurological conditions). Uninjured participants who experienced a knee injury during the study period were withdrawn and given the option to re-enrol as an injured participant if eligible. Individuals lost to follow-up were replaced with participants of similar age, sex, and sport to augment the cohort.

5.2.3.1 Sample Size

A sample size of 120 participants (60 per study group) for our primary objective was based on the ability to detect an 8.4-point between-group difference on the Knee injury and Osteoarthritis Outcome Score (KOOS) QOL subscale,[20] allowing for 1 covariate (sex) over 3 timepoints (baseline, 6-month, 12-month follow-up; $1-\beta=0.8$, $\alpha=0.05$). We then aimed to recruit 142 participants (71 per group) to allow for a 15% drop-out (**Appendix AA**).

5.2.4 Recruitment

Recruitment occurred between December 2016-September 2020. Injured participants were recruited through regional sport medicine or physiotherapy clinics, local sport organizations, social media, and word of mouth. Uninjured participants were recruited through injured participants (e.g., teammates), local sport organizations, social media, and word of mouth.

5.2.5 Procedures

Participants were assessed at baseline (within 4 months post-injury), 6-month, and 12-month follow-ups. At each assessment, participants completed online questionnaires and attended in-person testing. Questionnaires included a bespoke study questionnaire[21] (e.g., demographics, injury type, RTS status; **Appendix V**), KOOS, ICOAP, and TSK. At in-person testing, participants rotated through stations measuring anthropometrics (stadiometer, Model 402KL, Pelstar, Illinois, USA) and isokinetic strength then were given an accelerometer to wear for 8 days. A secure, online research platform was used to administer the questionnaires and store data (REDCap 8.6.5, Vanderbilt University, Tennessee, USA).[22]

5.2.6 Outcome Measures

5.2.6.1 Knee-Specific Health-Related Quality of Life

Knee-specific HRQoL was assessed with the KOOS QOL subscale (**Appendix S**).[23] This subscale contains 4 items asking about awareness of a knee problem, lifestyle modification, knee confidence, and overall knee difficulty. Items were scored on a 5-point Likert scale and transformed to a score between 0-100 (higher scores indicate better outcomes). The KOOS demonstrates sufficient internal consistency (pooled Cronbach's alpha=0.72-0.93) and test-retest reliability (pooled ICC=0.84-0.89) in ACL-injured individuals.[23, 24] We used a KOOS QOL patient acceptable symptom state (PASS) score of 72 derived from individuals (mean age 29.74 years) at 12 months post-ACLR[25] to help interpret our findings.

5.2.6.2 Isokinetic Knee Extensor Strength

Normalized concentric peak knee extensor torque was tested at 90º/second through a range of 0±2º to 90±2º with participants seated in 90º of hip flexion and straps secured across the chest and thighs (BTE PrimusRS, Hanover, Maryland, USA). After a practice trial and 1 minute rest, participants performed 3 maximal effort repetitions of knee extension and flexion bilaterally while receiving verbal encouragement. Peak torque (Nm) across repetitions was normalized to body weight (Nm/kg) and recorded. Isokinetic dynamometry is the gold standard for measuring muscle strength[26] and has acceptable test-retest reliability (pooled intraclass correlation coefficient>0.9).[27]

5.2.6.3 Physical Activity

Physical activity was measured using an accelerometer (ActiGraph GT3X; Pensacola, Florida, USA) worn on the right waist for 8 days. Participants removed it for bathing, water activities, or activities that may damage it (e.g., volleyball) and kept a log of the duration and intensity (i.e., light, moderate, vigorous) of non-wear time activities (**Appendix W**). The log was used to validate non-wear time and self-reported, non-wear time activities were added to the accelerometer data. Non-wear period algorithms and physical activity intensity cut-points were determined by Choi et al (2011)[28] and Evenson Children (2008),[29, 30] respectively. Data were examined in 60-second epochs and considered valid if there was a minimum of 5 days with ≥10 hours of wear time per day.[31] Weekly minutes of MVPA were recorded. Accelerometry is a valid measure of physical activity in youth.[32]

5.2.6.4 Intermittent Knee Pain

Intermittent knee pain was assessed with the ICOAP intermittent pain subscale (**Appendix T**).[33] Six items asked about knee pain that "comes and goes" over the past week. Each item was scored on a 5-point Likert scale, summed, and transformed to a score between 0-100 (lower scores indicate better outcomes). Although not evaluated in youth, the ICOAP has sufficient internal consistency (Cronbach's alpha=0.93) and test-retest reliability (ICC=0.85) in adults with knee osteoarthritis.[33]

5.2.6.5 Fear of Re-Injury

Fear of re-injury was assessed with the TSK-17 which has 17 items scored on a 4-point Likert scale (**Appendix X**).[34] Items were summed and scores ranged from 17-68 (lower scores indicate better outcomes). The TSK has not been validated in youth with a knee injury but it is often used to measure fear of re-injury in ACL-injured individuals.[35, 36]

5.2.6.6 Return to Sport

Return to sport status (yes vs. no) was determined from the response to the question, "Since the start of the study, have you attempted to train (practice) or compete (game) in your main sport?" Following a knee injury, RTS may act as a surrogate for restoring social support. That is, successful RTS likely represents less isolation and improved social health as individuals renew previous relationships with teammates and coaches.[37] Conversely, failure to RTS may represent greater isolation due to an inability to fully participate in one's usual social environment.[37] Therefore, successful RTS was defined as returning to training or competition as it likely reflects improved social health of injured participants.

5.2.7 Data Analysis

Statistical analyses were performed using STATA (v12.1, College Station, Texas, USA). The number of interested, screened, eligible, and enrolled participants were reported. Differences in age, sex, and sport between those who did and did not participate were summarized. Loss to follow-up was summarized by study group (injured or uninjured). Participants with missing data were removed from the analysis for that particular outcome and timepoint. Descriptive statistics (median, mean, proportion) were calculated for participant characteristics and outcomes at all timepoints by study group.

For all analyses, we used backwards stepwise selection beginning with full models and removing variables with the highest p-value until all remaining variables were significant ($p<0.05$). Beta coefficients and variance explained by the models (R^2) were reported. We decided a-priori to retain sex in all models regardless of the backwards elimination process to assess if sex-based differences in knee-specific HRQoL observed in injured adults[4] are also present in youth. Participants with missing data for a particular outcome were removed from analyses for that outcome. Variables of interest were selected based on previous research (relationship with generic or knee-specific HRQoL) and the authors' clinical experience. All models were assessed for multicollinearity and linear regression assumptions were assessed and met.

5.2.7.1 Primary Objective

Separate multivariable linear regression models (95%CI; clustered on sex and sport) compared *knee-specific HRQoL* (KOOS QOL score) between youth with a sport-related knee injury and uninjured controls at baseline, 6-month, and 12-month timepoints. We also assessed the relationship between sex (female/male) and *knee-specific HRQoL* in these models. We clustered the analysis on sex and sport to control for some confounding.

5.2.7.2 Secondary Objective

A multivariable linear regression model (95%CI; clustered on sex and sport) assessed the relationship between injury history (yes vs. no) and 12-month knee-specific HRQoL (primary outcome) while examining 5 additional variables of interest that may help further explain this relationship: sex, baseline KOOS QOL scores, 12-month peak knee extensor torque (Nm/kg), 12-month MVPA (minutes/week), and 12-month intermittent knee pain (ICOAP intermittent score).

5.2.7.3 Exploratory Objective

In injured youth only, a multivariable linear regression model (95%CI) explored the association of sex with 12-month knee-specific HRQoL (primary outcome) while examining 7 additional variables: injury type (ACL and/or meniscus injury vs. other knee injury), baseline KOOS QOL scores, 6-month peak knee extensor torque, 6-month MVPA, 6-month intermittent knee pain, 6-month fear of re-injury (TSK score), and 6-month RTS status (yes vs. no).

5.3 RESULTS

After giving study information to 436 individuals, 372 were screened for eligibility, 326 met inclusion criteria, and 189 enrolled in the study (80 uninjured, 109 injured; **Figure 5.1**). Demographics were similar between non-participants [median (range) age 16 (11-19) years, 50% females, 21% soccer players, and 61% injured] and participants [median (range) age 16 (10-20) years, 60% females, 34% soccer players, 58% injured].

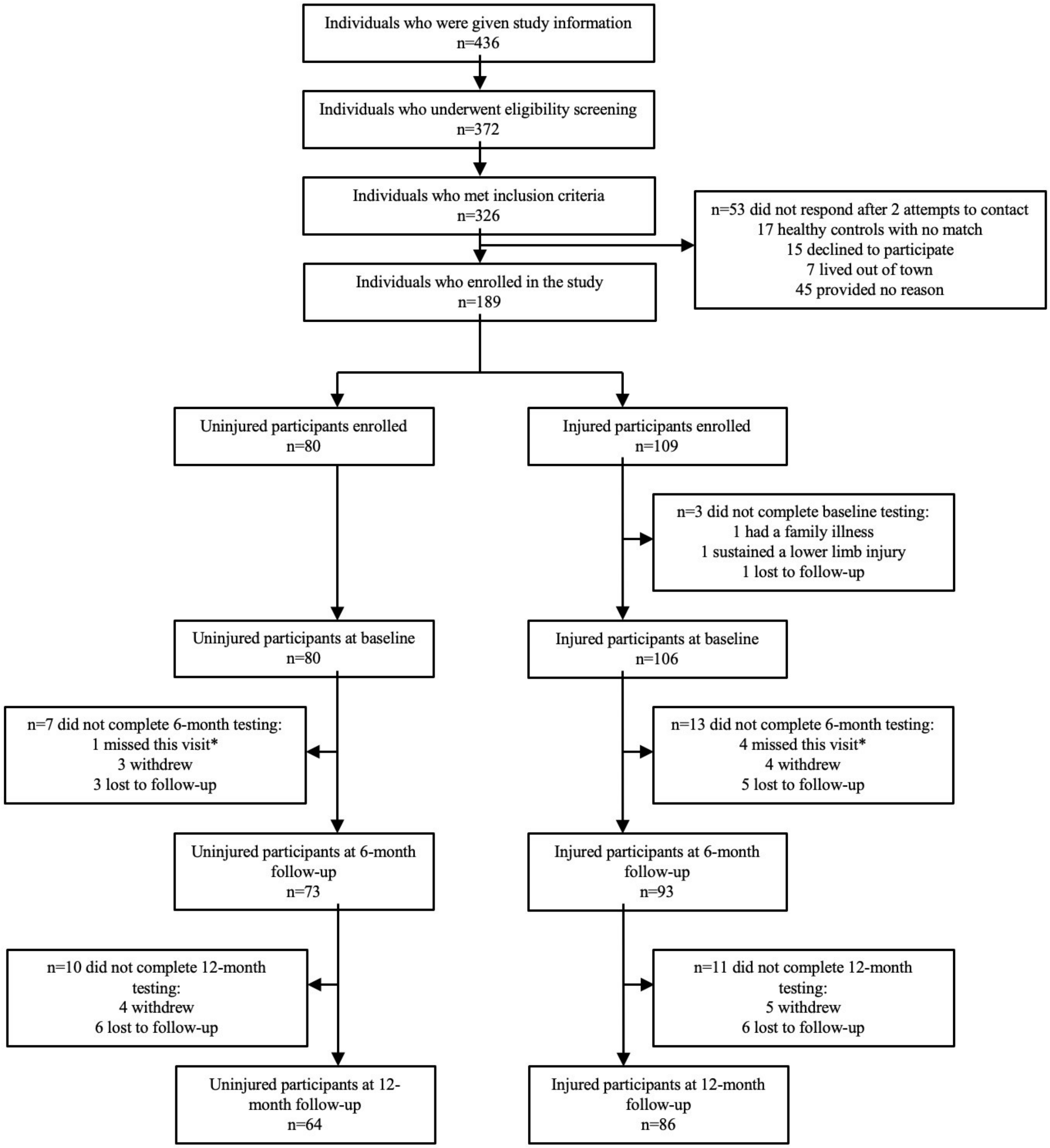

Figure 5.1: Participant Flow Chart (Baseline, 6-Month, and 12-Month Follow-Up)

*These participants returned for 12-month testing

Of the 189 participants who enrolled, 150 (64 uninjured, 86 injured) participants completed baseline, 6-month, and 12-month testing (79%). Three injured participants did not complete baseline testing and 36 participants (16 uninjured, 20 injured) did not complete 12-month testing. Characteristics of participants who withdrew or were lost to follow-up and reasons for missing data at all timepoints are summarized in **Appendices AB and AC**, respectively.

Table 5.1: Participant Characteristics at Baseline.

Characteristic	Uninjured (n=64)	Injured (n=86)
Sex (n, % female)	47 (73)	54 (63)
Age at injury (years)	–	16.2 (11.0-19.7)
Age at baseline (years)	16.7 (10.9-20.1)	16.4 (11.2-19.9)
BMI (kg/m^2)	22.0 (14.5-36.4)	22.6 (15.9-41.1)
Type of injury (n, % ACL rupture)	–	48 (56)
Injury to baseline (months)	–	1.3 (0.3, 4.5)
Baseline to 6-month follow-up (months)	6.0 (4.3-9.1)	6.3 (4.9-9.1)
Baseline to 12-month follow-up (months)	12.1 (10.9-16.4)	12.4 (10.7-15.7)
Main sport (n, % soccer)	23 (36)	25 (29)
Main sport level (n, % club)[a]	48 (75)	50 (58)

Values represent median (range) unless otherwise noted
[a]Categories included recreational, club, school, varsity, provincial, national

ACL, anterior cruciate ligament; BMI, body mass index; CI, confidence interval; kg, kilogram; m, metre; n, number of participants

Participant characteristics are summarized in **Table 5.1**. Knee injuries included ACL rupture (56%), other tibiofemoral ligament injury (16%), patellar subluxation/dislocation (20%), isolated meniscus injury (3%), intra-articular bony contusion (3%), and intra-articular fracture (1%). Soccer was the most commonly played sport (32%). Of the 48 participants who ruptured their ACL, 36 (75%) underwent ACL reconstruction prior to 12-month follow-up [median time from injury to surgery 4.5 months (range 0.6-13.1) and median time from surgery to 12-month follow-up 9.2 months (range 1.2-15.9)].

Table 5.2: By Study Group, Outcome and Variables of Interest at Baseline, 6-Month, and 12-Month Follow-Up.

	Uninjured (n=64)			Injured (n=86)		
Outcome or Variable of Interest	**Baseline[a]**	**6-Month[a]**	**12-Month[a]**	**Baseline[a]**	**6-Month[a]**	**12-Month[a]**
KOOS QOL (0-100)	100 97-100[b] 56-100[c]	100 94-100[b] 69-100[c]	100 97-100[b] 56-100[c]	38 19-50[b] 0-100[c]	53 38-75[b] 0-100[c]	69 44-8[b] 0-100[c]
MVPA (minutes/week)	429 281-547[b] 110-1261[c]	295 212-381[b] 97-567[c]	363 248-466[b] 60-1054[c]	271 184-363[b] 58-824[c]	216 153-325[b] 10-716[c]	276 188-396[b] 53-1291[c]
Peak knee extensor torque (Nm/kg)	1.93 1.70-2.09[b] 0.77-2.31[c]	1.90 1.72-2.09[b] 1.29-2.89[c]	1.91 1.69-2.05[b] 1.46-2.44[c]	1.37 1.03-1.76[b] 0.28-2.23[c]	1.71 1.43-1.90[b] 0.49-2.55[c]	1.77 1.49-2.00[b] 0.87-2.73[c]
ICOAP intermittent (0-100)	0 0-0[b] 0-42[c]	0 0-0[b] 0-29[c]	0 0-0[b] 0-50[c]	33 21-54[b] 0-96[c]	10 0-29[b] 0-75[c]	4 0-17[b] 0-71[c]
TSK (17-68)	36 32-40[b] 25-47[c]	34 30-39[b] 20-46[c]	35 30-40[b] 21-52[c]	41 37-46[b] 22-56[c]	37 34-42[b] 22-55[c]	34 30-40[b] 20-48[c]
RTS (% yes)	–	–	–	–	49[d] (38, 60)	62[d] (51, 72)

[a]All values represent median and [b]interquartile range or [c]minimum-maximum range due to the non-parametric data distribution.
[d]Proportion and 95% confidence interval

ICOAP, Intermittent and Constant Osteoarthritis Pain; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; MVPA, moderate-to-vigorous physical activity; n, number of participants; Nm, Newton-metre; RTS, return to sport; TSK, Tampa Scale for Kinesiophobia; –, not applicable

All outcomes are summarized at each timepoint and by study group in **Table 5.2** and by injury type in **Table 5.3**. At 12 months, 45% of injured participants met or exceeded the KOOS QOL PASS score compared to 95% of uninjured participants.[25]

Table 5.3: By Injury Type, Outcome and Variables of Interest at Baseline, 6-Month, and 12-Month Follow-Up.

Outcome		ACL Rupture (n=48)	Other Ligament Injury[a] (n=14)	Patellofemoral Injury[b] (n=17)	Meniscus Tear (n=3)	Bony Contusion (n=3)	Fracture (n=1)
Primary Outcome							
KOOS QOL (0-100)	Baseline	25 (0-63)	34 (0-63)	44 (0-88)	63 (56-69)	75 (38-100)	6[d]
	6-month	44 (13-94)	56 (25-100)	63 (0-100)	100 (100-100)	94 (94-100)	100[d]
	12-month	50 (6-100)	81 (31-100)	75 (0-100)	100 (88-100)	100 (100-100)	100[d]
Associated Health Outcomes							
MVPA (minutes/week)	Baseline	248 (58-824)	237 (81-616)	270 (88-495)	382 (287-616)	299 (62-520)	178[d]
	6-month	200 (35-716)	216 (10-630)	225 (102-458)	N/A	292 (91-949)	102[d]
	12-month	254 (38-796)	214 (183-514)	336 (139-1291)	438 (411-466)	281 (201-360)	169[d]
Peak knee extensor torque (Nm/kg)	Baseline	1.34 (0.40-2.23)	1.69 (0.50-2.05)	1.35 (0.28-2.18)	1.91 (0.76-1.94)	1.37 (1.35-1.91)	N/T
	6-month	1.63 (0.84-2.44)	1.86 (0.52-2.55)	1.77 (0.49-2.21)	1.81 (1.74-1.88)	1.58 (1.32-1.84)	2.30[d]
	12-month	1.70 (0.87-2.25)	1.78 (1.48-2.38)	1.90 (0.98-2.73)	2.00 (1.15-2.08)	1.56 (1.45-1.67)	2.03[d]
ICOAP intermittent (0-100)	Baseline	42 (0-88)	38 (0-83)	29 (4-96)	13 (0-33)	29 (0-29)	0[d]
	6-month	15 (0-54)	17 (0-75)	12 (0-71)	0 (0-0)	0 (0-0)	0[d]
	12-month	8 (0-71)	2 (0-50)	8 (0-46)	0 (0-8)	0 (0-0)	0[d]
TSK (17-68)	Baseline	44 (22-56)	38 (28-51)	40 (31-52)	32 (27-35)	35 (31-40)	37[d]
	6-month	38 (22-51)	38 (30-52)	40 (28-55)	31 (23-34)	28 (24-38)	31[d]
	12-month	34 (20-48)	34 (26-41)	36 (22-47)	31 (28-33)	32 (25-38)	32[c]
RTS[c] (% yes)	6-month	43 (29, 59)	79 (46, 94)	100 (100, 100)	100 (100, 100)	100 (100, 100)	100[d]
	12-month	53 (39, 67)	86 (52, 97)	94 (63, 99)	100 (100, 100)	100 (100, 100)	100[d]

[a]Includes a PCL, MCL, or LCL injury of any grade or partial ACL injury
[b]Includes a patellofemoral subluxation or dislocation
[c]Value represents proportion and 95%CI
[d]Value only represents one participant so no range or 95%CI is presented

ACL, anterior cruciate ligament; FMI, fat mass index; ICOAP, Intermittent and Constant Osteoarthritis Pain; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; LCL, lateral collateral ligament; MCL, medial collateral ligament; MVPA, moderate-to-vigorous physical activity; n, number of participants; N/A, not applicable; N/T, not tested as per physician's orders; Nm, Newton-metre; PCL, posterior cruciate ligament; RTS, return to sport; TSK, Tampa Scale for Kinesiophobia; 95%CI, 95% confidence interval

Table 5.4: Primary Multivariable Linear Regression Models Examining the Association of Injury History and Sex with KOOS QOL Scores at All Timepoints.

Outcome	Injury History[a]	Sex[b]	R^2	n
Baseline KOOS QOL	**-61 (-66, -56)**	1 (-5, 7)	0.74	149
6-month KOOS QOL	**-41 (-46, -35)**	-3 (-10, 5)	0.50	145
12-month KOOS QOL	**-34 (-41, -26)**	1 (-6, 8)	0.37	149

Values represent coefficient and 95%CI
All models accounted for clustering by sex and sport
Bolded font represents 95%CI does not encompass zero
[a]Reference = uninjured participants
[b]Reference = females

KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; R^2, coefficient of determination; 95%CI, 95% confidence interval

Injured youth had lower KOOS QOL scores than uninjured youth at all timepoints, regardless of sex. The magnitude of the KOOS QOL difference decreased over time [baseline: -61 (95%CI -66, -55), 6-month follow-up: -41 (95%CI -46, -36), and 12-month follow-up: -33 (95%CI -40, -26); **Table 5.4**]. The variance of KOOS QOL scores explained by injury history and sex decreased from 74% at baseline to 50% at 6 months and 37% at 12 months.

Table 5.5: Secondary Multivariable Linear Regression Model Examining the Association of Injury History, Sex, Baseline KOOS QOL Scores, 12-Month MVPA, 12-Month Peak Knee Extensor Torque, and 12-Month ICOAP Intermittent Pain Scores with 12-Month KOOS QOL Scores.

Outcome	Injury History[a] (Primary Exposure)	Sex[b]	Baseline KOOS QOL (0-100)	12-Month MVPA (min/week)	12-Month Knee Ext. Strength (Nm/kg)	12-Month ICOAP Intermittent[c] (0-100)	R^2	n
12-Month KOOS QOL	-7.0 (-16.1, 2.2)	-4.6 (-10.1, 1.0)	**0.3 (0.1, 0.5)**	**0.02 (0.01, 0.03)**	**10.0 (2.6, 17.4)**	**-1.0 (-1.3, -0.7)**	0.70	115

Values represent coefficient and 95%CI
This model accounted for clustering by sex and sport
Bolded font represents 95%CI does not encompass zero
[a]Reference = uninjured participants
[b]Reference = females
[c]Reverse scoring (lower scores indicate better outcomes)

Ext., extensor; ICOAP, Intermittent and Constant Osteoarthritis Pain measure; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; min, minute; MVPA, moderate-to-vigorous physical activity; n, number of participants; Nm, Newton-metre; QOL, quality of life; r^2, coefficient of determination; 95%CI, 95% confidence interval

Regardless of injury history and sex, greater baseline KOOS QOL scores (0.3; 95%CI 0.1, 0.5), 12-month normalized peak knee extensor torque (10.0; 95%CI 2.6, 17.4), and 12-month weekly MPVA minutes (0.02; 95%CI 0.01, 0.03) as well as lower 12-month ICOAP scores (-1.0; 95%CI -1.3, -0.7) were associated with higher 12-month KOOS QOL scores (R^2 0.70; **Table 5.5**).

Table 5.6: Exploratory Multivariable Linear Regression Model (Injured Youth Only) Examining the Association of Sex, Injury Type, Baseline KOOS QOL Scores, 6-Month MVPA, 6-Month Peak Knee Extensor Torque, 6-Month ICOAP Intermittent Pain Scores, 6-Month TSK Scores, and 6-Month RTS Status with 12-Month KOOS QOL Scores.

Outcome	Sex[a]	Injury Type[b]	Baseline KOOS QOL (0-100)	6-Month MVPA (min/week)	6-Month Knee Ext. Strength (Nm/kg)	6-Month ICOAP Intermittent[c] (0-100)	6-Month TSK[c] (17-68)	6-Month RTS[d]	R^2	n
12-Month KOOS QOL	2.7 (-7.7, 13.1)	**-20.8 (-30.9, -10.7)**	–	–	–	–	**-1.7 (-2.5, -1.0)**	–	0.33	81

Values represent coefficient and 95%CI
This model accounted for clustering by sex and sport
Bolded font represents 95%CI does not encompass zero
[a]Reference = females
[b]Reference = no ACL or meniscus injury
[c]Reverse scoring (higher scores indicates worse outcomes)
[d]Reference = no RTS

Ext., extensor; ICOAP, Intermittent and Constant Osteoarthritis Pain measure; kg, kilogram; KOOS, Knee injury and Osteoarthritis Outcome Score; min, minute; MVPA, moderate-to-vigorous physical activity; n, number of participants; Nm, Newton-metre; QOL, quality of life; r^2, coefficient of determination; RTS, return to sport; TSK, Tampa Scale for Kinesiophobia; 95%CI, 95% confidence interval

When considering injured participants only, having an ACL and/or meniscus injury (-20.8; 95%CI -30.9, -10.7) and higher 6-month TSK scores (-1.7; 95%CI -2.5, -1.0) were negatively associated with 12-month KOOS QOL scores (**Table 5.6**). No associations were found for sex, baseline KOOS QOL scores, or 6-month peak knee extensor torque, weekly MVPA minutes, and ICOAP scores

5.4 DISCUSSION

This is the first study to identify deficits in knee-specific HRQoL at baseline (within 4 months post-injury), 6-month, and 12-month follow-up of youth with a broad range of intra-articular, sport-related knee injuries compared to uninjured controls. Although knee-specific HRQoL improved over time, significant deficits persisted at 12-month follow-up. The injury also contributed less to knee-specific HRQoL as time progressed. No sex-based differences in knee-specific HRQoL were found. The relationship between injury and 12-month knee-specific HRQoL disappeared when baseline knee-specific HRQoL, knee extensor strength, physical activity, and intermittent pain were considered, revealing the complexity of this construct. Among injured youth, an ACL and/or meniscus injury and increased fear of re-injury may contribute to worse knee-specific HRQoL.

Our study has contributed to the trajectory of knee-specific HRQoL following a sport-related knee injury in youth. Previous research demonstrates knee-specific HRQoL deficits at 6 months,[38, 39] 12 months,[39] and 24 months[40] after ACLR compared to uninjured youth. However, these deficits are *not* unique to ACL injury or surgery and can be detected following various intra-articular knee injuries. It is evident that injured youth experience worse knee-specific HRQoL than their peers which is concerning given how many years youth may live with these deficits.

One key finding is that the knee injury explained less variance in knee-specific HRQoL over time while other factors may emerge as potentially important contributors. This might be due to youth gradually learning to cope with or overcome physical, psychological, and social injury consequences. Perhaps general aspects of knee health contribute more to knee-specific HRQoL over time. This hypothesis is supported by our secondary model that found injury history was not associated with 12-month knee-specific HRQoL. Instead, youth who had higher baseline knee-specific HRQoL, stronger quadriceps, increased physical activity, and less intermittent pain reported greater knee-specific HRQoL. This aligns with previous research indicating that generic HRQoL of uninjured youth is associated with being physically fit and active[11] and pain-free.[13]

We did not find a relationship between sex and knee-specific HRQoL in youth with a sport-related knee injury at any timepoint. Sex-based differences may not have been detected as our sample had more females than males.

Our exploratory findings suggest that youth with an ACL and/or meniscus injury and heightened fear of re-injury at 6 months reported worse knee-specific HRQoL at 12 months which is consistent with previous research.[7, 20] These youth are possibly at greater risk of having persistent knee-specific HRQoL deficits and should be targeted with future treatment strategies.

5.4.1 Research Recommendations

This study demonstrates how including uninjured controls of similar demographics is essential to understanding how knee-specific HRQoL is unique to injured youth, including what factors may influence it. We mostly examined physical factors (e.g., knee muscle strength, physical activity), so future research should assess how psychological (e.g., confidence, depression) and social (e.g., social support) factors contribute to knee-specific HRQoL.[41] Examining these factors in adequately powered models can inform future interventions. Lastly, researchers should understand how gender (sociocultural construct) impacts knee-specific HRQoL and aim to recruit an equal number of girls/women and boys/men to assess gender-based differences.

5.4.2 Clinical Implications

From our findings, we recommend measuring knee-specific HRQoL early and often after a sport-related knee injury. To thoroughly understand knee-specific HRQoL, clinicians can use credible patient-reported outcome measures (e.g., KOOS, ACL QOL questionnaire[42]) and directly ask patients about their physical, psychological, and social health. Patients with an ACL and/or meniscus injury, low baseline QOL values, and elevated fear of re-injury should be closely monitored as they may experience persistent knee-specific HRQoL deficits. Until further research is performed, treatment strategies focused on increasing quadriceps strength and MVPA while decreasing knee pain may be a good starting point to improve knee-specific HRQoL.

5.4.3 Strengths and Limitations

Our strengths include having uninjured controls of similar demographics, which allowed us to control for some confounding by age, sex, and sport participation, and assessing sex-based differences. Twenty-nine (34%) injured participants were also patients of study physiotherapists which may augment retention but also introduce implicit bias favouring these participants (e.g., being more encouraging with familiar participants). Despite using many participant retention strategies (e.g., email and text reminders, parking reimbursement), a larger proportion of males withdrew or were lost to follow-up and possibly prevented us from identifying sex-based differences. As knee-specific HRQoL is more likely to be associated with gender than sex, not capturing and considering gender is a limitation. Lastly, the final 13 months of our study overlapped with the COVID-19 pandemic. Following the CONSERVE statement,[43] we summarized the impact, mitigation strategies, and study modifications due to COVID-19 in **Appendix Z**.

5.5 CONCLUSION

Youth who experience a sport-related knee injury demonstrate significant and persistent knee-specific HRQoL deficits at 12-month follow-up compared to uninjured controls. Over time, the injury contributed less to knee-specific HRQoL while modifiable factors like knee extensor strength, physical activity, and intermittent pain emerged as potentially important contributors. Youth with an ACL or meniscus injury, low baseline knee-specific HRQoL, and heightened fear of re-injury may be susceptible to poor knee-specific HRQoL. As knee-specific HRQoL reflects knee health, restoring it should be a main goal of rehabilitation.

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CHAPTER 6: DISCUSSION AND CONCLUSIONS

The overarching purpose of this doctoral research is to better understand 1) how to measure HRQoL of active youth, 2) how HRQoL is altered by a youth sport-related knee injury, and 3) what physical, psychological, and social consequences of injury are associated with HRQoL in active youth. The 4 studies presented in chapters 2 to 5 address these aims, contribute novel information about HRQoL of youth who experience a sport-related knee injury, and provide considerations for future research and clinical practice on this topic. The chapter summaries below highlight these contributions.

6.1 CHAPTER SUMMARIES

6.1.1 Chapter 2: Searching for the Holy Grail: A Systematic Review of Health-Related Quality of Life Measures for Active Youth

Objective: To identify the most suitable existing PROMs for measuring generic and condition-specific HRQoL of active youth with and without a musculoskeletal injury based on measurement properties, interpretability, and feasibility.

This systematic review identified and evaluated 18 (11 generic and 7 condition-specific) PROMs that have been used to assess HRQoL of active youth. We concluded that no robust HRQoL PROM currently exists to measure generic or condition-specific HRQoL of youth, including those who experience a sport-related knee injury, due to a lack of sufficient measurement properties and adequate information about interpretability or feasibility. In particular, none of the identified PROMs had sufficient content validity which indicates that they may not be relevant, comprehensive, and comprehensible to active youth. With that said, 2 generic (DPA-MSC SF-8 and QoL Survey) and 1 condition-specific (FAST for the upper extremity) HRQoL PROMs were judged to be the most suitable existing PROMs for active youth as they demonstrated sufficient structural validity and internal consistency.

6.1.2 Chapter 3: What Does the Future Hold? Health-Related Quality of Life 3-12 Years Following a Youth Sport-Related Knee Injury

Objectives: To assess generic and knee-specific HRQoL in individuals with a 3-12 year history of a youth sport-related knee injury compared to uninjured controls and to examine what variables may influence the relationship between injury history and HRQoL.

This secondary analysis of data from the Alberta Youth PrE-OA cohort study revealed that youth with a previous sport-related knee injury report worse *long-term knee-specific* but similar generic HRQoL compared to uninjured controls of similar age, sex, and sport participation. These findings suggest that generic and knee-specific HRQoL may be distinct constructs with different trajectories and determinants following a youth sport-related knee injury. Exploratory analyses showed that *long-term generic HRQoL* may be negatively associated by intermittent knee pain and lower physical activity levels, regardless of injury history. Conversely, *long-term knee-specific HRQoL* may be negatively associated with a previous sport-related knee injury, especially an ACL rupture with subsequent ACLR, and intermittent knee pain. No evidence of an association between time since injury, BMI, and knee extensor or flexor strength and generic or knee-specific HRQoL was found.

6.1.3 Chapter 4: Comparing Short-Term Knee-Specific Health-Related Quality of Life and Associated Health Outcomes between Youth with and without a Sport-Related Knee Injury

Objectives: To compare changes in knee-specific HRQoL and associated health outcomes over a 6-month period between youth with and without a recent sport-related knee injury and to explore the influence of sex, injury type, baseline values, and physiotherapy attendance on the relationship between injury history and knee-specific HRQoL.

This preliminary analysis of data from a prospective, inception cohort study showed that youth with a wide range of sport-related knee injuries demonstrate poorer *short-term knee-specific HRQoL*, knee extensor and flexor weakness, and heightened kinesiophobia compared to uninjured controls. Although these outcomes improved over the study period, deficits remained at 6-month follow-up. Sex did not appear to influence the relationship between injury history and *early changes in knee-specific HRQoL* or associated health outcomes. In exploratory analyses of data from injured youth only, *short-term changes in knee-specific HRQoL* were negatively associated with having an ACL rupture and/or meniscus injury (vs. other intra-articular knee injuries) and lower baseline knee-specific HRQoL. No evidence of an association between sex or physiotherapy attendance and early changes in knee-specific HRQoL was found.

6.1.4 Chapter 5: Youth with a Sport-Related Knee Injury Exhibit Significant and Persistent Knee-Specific Health-Related Quality of Life Deficits at 12-Month Follow-Up Compared to Uninjured Peers

Objectives: To compare knee-specific HRQoL between youth with and without a sport-related knee injury at baseline, 6-month, and 12-month follow-up and to assess the association of injury history, sex, and other health outcomes associated with HRQoL with 12-month knee-specific HRQoL.

This prospective, inception cohort study demonstrated that active youth with a wide range of sport-related knee injuries exhibit poorer *knee-specific HRQoL after a 12-month follow-up period*, despite reporting improvements over time and regardless of sex. By including an uninjured control group, this cohort study revealed that injury history explained less variance in *short-term knee-specific HRQoL* as time since injury progressed. Additionally, the relationship between injury history and knee-specific HRQoL at 12-month follow-up disappeared when we factored in other variables of interest. Specifically, higher baseline knee-specific HRQoL, greater knee extensor strength, higher levels of physical activity, and lower intermittent knee pain were positively associated with *knee-specific HRQoL at 12-month follow-up*. In exploratory analyses of data from injured youth only, ACL rupture and/or meniscus injury (vs. other intra-articular knee injuries) and higher kinesiophobia at 6-month follow-up were negatively associated with *knee-specific HRQoL at 12-month follow-up*. No evidence of an association between knee extensor strength, MVPA, intermittent pain, and RTS status at 6-month follow-up and knee-specific HRQoL at 12-month follow-up was found.

6.2 GENERAL DISCUSSION

The following sections highlight the novel contributions of this doctoral research pertaining to measuring HRQoL of active youth, understanding the trajectory of HRQoL of youth with a sport-related knee injury, and identifying potential determinants of their HRQoL.

6.2.1 Measuring Health-Related Quality of Life after a Youth Sport-Related Knee Injury

Two key discussion points arise from this thesis regarding the measurement of HRQoL following a youth sport-related knee injury:

1. The lack of robust PROMs to measure HRQoL in active youth.
2. Generic and knee-specific HRQoL are unique constructs.

Chapter 2 presents novel information about the paucity of robust PROMs to measure generic and knee-specific HRQoL in active youth. Due to unproven measurement properties of available PROMs, we must cautiously interpret and apply the findings of studies that have assessed generic or knee-specific HRQoL in active youth, including the research contained in Chapters 3-5. Nonetheless, the evidence to date should not be abandoned entirely as “the absence of evidence is not evidence of absence.”

Many items and domains on PROMs commonly used to assess generic HRQoL of adults (e.g., EQ-5D-5L,[1] EQ-VAS[1], SF-36[2]) and generic HRQoL of youth (e.g., KIDSCREEN-52,[3] PedsQL[4]) are likely relevant to active youth. For example, the SF-36 captures pain which is a potential determinant of generic HRQoL of active youth[5] and the PedsQL has domain for school functioning which is important to consider for general youth.[6] However, these PROMs do not include aspects of generic HRQoL that may be important to active youth, such as participating in preferred sports or recreational activities or receiving support from teammates or coaches. With that said, a major strength of generic HRQoL PROMs is the ability to compare findings across different populations or conditions. Therefore, we must further evaluate the measurement properties of commonly used generic HRQoL PROMs in active youth populations.

Despite the lack of evidence for measurement properties in active youth, certain knee-specific PROMs may be promising for this population, including the KOOS QOL subscale[7] and ACL

QOL questionnaire.[8] All 4 items of the KOOS QOL (i.e., awareness of your knee problem, lifestyle modifications, lack of knee confidence, and general knee difficulty) are relevant for measuring knee-specific HRQoL in adults following an ACL rupture or ACLR[9] and may be relevant to active youth following an ACL rupture or ACLR as well. As it has been widely used, a notable benefit of the KOOS QOL is the ability to compare knee-specific HRQoL across demographic groups and injury/condition types. It has demonstrated sufficient measurement properties in adults with an ACL rupture, focal cartilage lesion, or osteoarthritis.[10, 11] A critique of the KOOS QOL is that it might lack comprehensiveness as it only consists of 4 items. Conversely, the ACL QOL is considered more comprehensive for measuring knee-specific HRQoL of active youth. The ACL QOL captures physical, psychological, and social aspects of HRQoL in 32 items spread over 5 domains (i.e., symptoms and physical complains, work-related concerns, recreational activities and sports participation, lifestyle, and social and emotional concerns). These items are relevant to adults with chronic ACL deficiency[8] and many are also likely relevant to active youth. With that said, the ACL QOL requires adapting for youth populations and knee injuries beyond ACL ruptures.

The findings from chapter 3 reinforce the concept that generic and knee-specific HRQoL represent distinct constructs with different trajectories and potential determinants following a youth-sport related knee injury. Previous systematic reviews describe long-term deficits in knee-specific HRQoL following an ACL rupture or ACLR.[12, 13] However, the evidence of long-term generic HRQoL is less consistent with deficits reported in 1 review[14] but not others.[12, 13] It should be noted that our ability to compare differences in the trajectory of generic and knee-specific HRQoL of active youth may be hindered by ceiling effects that can occur when measuring generic HRQoL over the long-term (≥5 years since injury).[15] Regarding potential determinants, our findings propose that having a previous knee injury and lower physical activity levels may influence knee-specific but not generic HRQoL. Taken together, these findings underscore the need to measure and monitor both generic and knee-specific HRQoL at regular intervals following youth sport-related knee injuries to gain a better understanding of their unique trajectories and determinants.

6.2.2 Mapping Health-Related Quality of Life after a Youth Sport-Related Knee Injury

Three key discussion points arise from this thesis regarding the trajectory of HRQoL following a youth sport-related knee injury:

1. The importance of including an uninjured comparison group.
2. The importance of including knee injuries beyond ACL ruptures and ACLR.
3. The magnitude of the relationship between youth sport-related knee injuries and HRQoL.

One of the key strengths of the research contained in chapters 3-5 is including uninjured controls of similar age, sex and sport or activity participation. Understanding how a sport-related knee injury impacts generic and knee-specific HRQoL of youth (i.e., signal) is a primary aim of this work. However, the natural changes to biology and social roles that epitomize the life stage of youth (i.e., noise) are also likely to impact HRQoL. By including an uninjured comparison group, we were able to control for some confounding that might stem from these natural changes (i.e., enhanced the signal-to-noise ratio) which instills more confidence in our conclusion that youth sport-related knee injuries are associated with significant short- and long-term knee-specific HRQoL. In particular, knee-specific HRQoL following a youth sport-related knee injury seems to improve with time since injury where the greatest improvements occur over an initial 12-month period then more gradual improvements are observed between 3-12 years post-injury (**Figure 6.1**). Considering the similar trajectories of knee-specific HRQoL following any sport-related knee injury or ACL rupture and ACLR, we must assess this construct beyond 10 years to determine if it also declines. Although we are unable to comment on short-term changes in generic HRQoL, it does not appear to be negatively impacted over the long-term.

It should be noted that there are limitations to using knee-specific HRQoL PROMs in uninjured populations as these PROMs are intended for use in individuals with knee injuries or conditions. For example, the item "How often are you aware of your knee problem?" of the KOOS QOL subscale used in chapters 3-5 may be challenging to answer if one does not have a knee injury. However, other items in the KOOS QOL, such as "Have you modified your lifestyle to avoid potentially damaging activities to your knee?" or "In general, how much difficulty do you have with your knee?", are likely relevant and comprehensible to both injured or uninjured individuals.

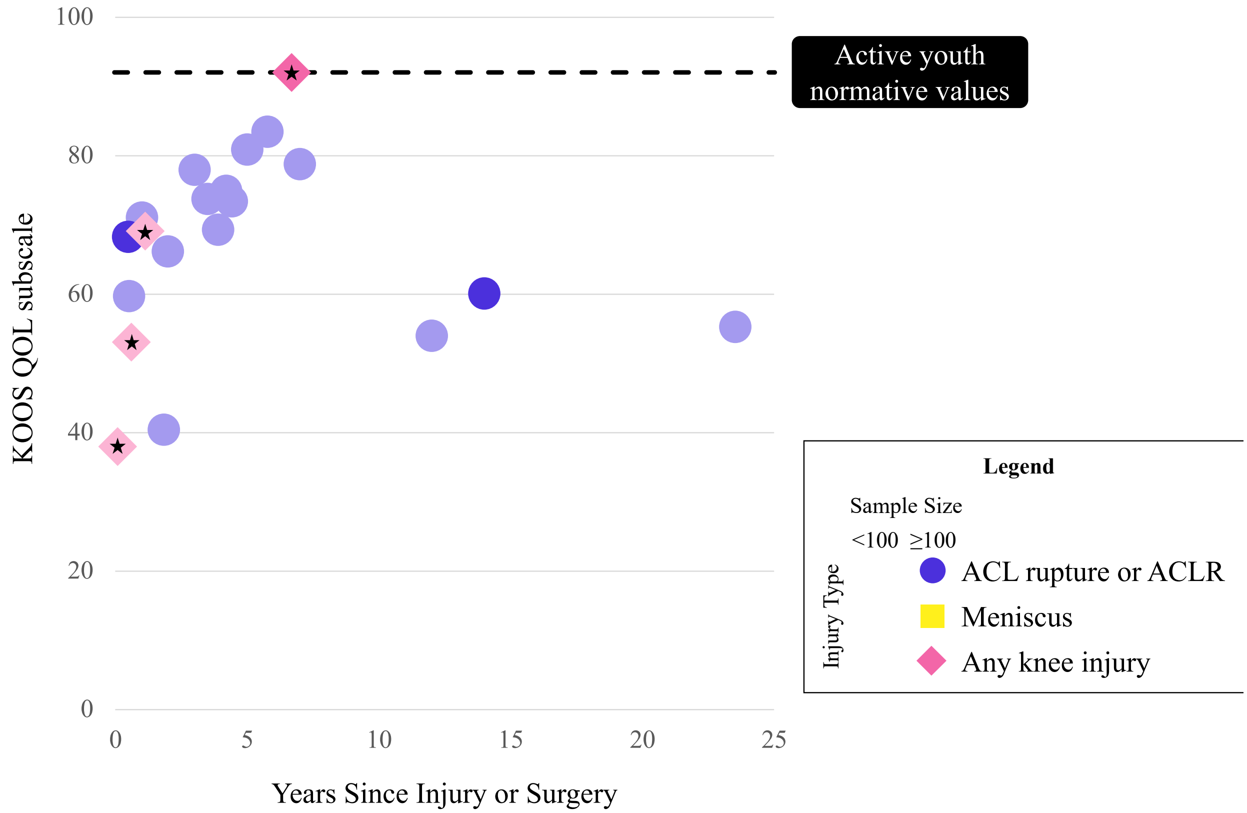

Figure 6.1: Updated KOOS QOL Subscale Scores for Youth Cohorts with a Sport-Related Knee Injury to Include Novel Contributions from this Thesis

The novel contributions from this doctoral research are represented by the graph points with stars.

Data is from studies that found significant between-group differences in mean or median KOOS QOL subscale scores (0-100) between youth with a sport-related knee injury and uninjured controls. Active youth normative values were obtained from Cameron et al. (2013).[16]

A novel contribution of the research summarized in chapters 3-5 is establishing a relationship between a wide range of youth sport-related knee injuries – including ACL ruptures, ACLRs, meniscus injuries, collateral ligament sprains, patella subluxations or dislocations, intra-articular bony contusions, and intra-articular fractures – and knee-specific HRQoL. While various youth sport-related knee injuries are linked with knee-specific HRQoL, the relationships between different injury types and knee-specific HRQoL are likely unique. Specifically, our exploratory analyses confirm what has only been speculated up to this point: that ACL ruptures and meniscus injuries likely have the greatest negative impact on knee-specific HRQoL compared to other knee injuries. However, when we consider that a wide range of sport-related knee injuries are also associated with an elevated risk of osteoarthritis,[17, 18] we should encourage future research to investigate the long-term consequences of *all* youth sport-related knee injuries.

The studies presented in chapters 3-5 also provide an estimate of the magnitude of the relationship between youth sport-related knee injuries and HRQoL. Whereas previous studies have compared HRQoL of injured youth to uninjured controls or population norms with univariable statistics [i.e., t-tests,[19-24] analysis of variance (ANOVA),[25-29] Mann-Whitney U tests,[30-32] Kruskal-Wallis tests[33]], we have used regression analyses which not only detect statistically significant between-group differences, but also provide an estimate of the magnitude of the between-group difference. Our analyses reveal that youth sport-related knee injuries result in short-term deficits in knee-specific HRQoL and underscore how substantial, and very likely meaningful, these deficits are.[34] Furthermore, our primary regression model in chapter 5 demonstrated that injury history explains less variance in knee-specific HRQoL with greater time since injury,[34] alluding to the complexity of HRQoL. Moving forward, future studies should account for time since injury in statistical analyses to better understand how HRQoL may change over time.

6.2.3 Identifying Potential Determinants of Health-Related Quality of Life After a Youth Sport-Related Knee Injury

Three key discussion points arise from this thesis regarding the potential determinants of HRQoL following a youth sport-related knee injury:

1. Sex may not be a determinant of generic or knee-specific HRQoL.
2. Intermittent knee pain, physical activity levels, and injury type are potential determinants of knee-specific HRQoL.
3. The importance of adjusting for baseline (i.e., post-injury) knee-specific HRQoL values in future research.

We did not find any evidence that sex influences generic or knee-specific HRQoL[5, 34, 35] following a youth sport-related knee injury (**Table 6.1**).[5] This observation is consistent with systematic reviews involving youth and adults with an ACL rupture or ACLR[12, 13, 36, 37] and reinforces the argument that sex may not be a determinant of HRQoL after a knee injury. This is not surprising as sex is a biological construct comprising of features such as chromosomes, hormone levels, and reproductive anatomy.[38] Perhaps we should assess the influence of gender on HRQoL. Gender refers to "socially constructed roles, behaviours, expressions, and identities."[38] As HRQoL incorporates an individual's perceptions, experiences, expectations, and beliefs, gender possibly has a greater impact on HRQoL than sex. For example, the gender differences observed in social relationships (where men focus on independence while women seek support)[39] may affect how one perceives their social health and overall HRQoL following an injury.

Table 6.1: Potential Determinants of Health-Related Quality of Life Following a Youth Sport-Related Knee Injury Assessed at Various Timepoints in this Thesis.

	Timepoint							
	Baseline		6 Months		12 Months		3-12 Years	
Potential Determinant	**Generic HRQoL**	**Knee-specific HRQoL**	**Generic HRQoL**	**Knee-specific HRQoL**	**Generic HRQoL**	**Knee-specific HRQoL**	**Generic HRQoL**	**Knee-specific HRQoL**
Primary outcome								
Injury history[a]		–ve		–ve		–ve		–ve
Demographic factors								
Sex[b]								
Knee injury-related outcomes								
Intermittent knee pain						–ve	–ve	–ve
Knee muscle strength						+ve		
Physical activity levels						+ve	+ve	
Obesity								
Kinesiophobia						–ve[g,h]		
RTS[c]								
Injury type[d]				–ve[f,g]		–ve[g]		–ve
Baseline values				–ve[f,g]		+ve		
Time since injury								
Physiotherapy attendance[e]								

Red cells indicate a negative association was found; blue cells indicate a positive association was found; grey cells indicate that an association was assessed but not found; and blank cells indicate that an association was not assessed.

[a]Reference = uninjured participants
[b]Reference = female sex
[c]Reference = successful return to main sport training or competition
[d]Reference = ACL rupture and/or meniscus injury
[e]Reference = attended <5 physiotherapy visits
[f]The outcome was change in HRQoL from baseline to 6-month follow-up.
[g]Analysis only included injured participants.
[h]The association was found between the variable of interest at 6-month follow-up and HRQoL at 12-month follow-up.

+ve, positive association; –ve, negative association; HRQoL, health-related quality of life; RTS, return to sport

Findings from chapters 3-5 provide preliminary evidence that intermittent knee pain, lower MVPA, knee extensor weakness, and kinesiophobia are potentially negative determinants of generic or knee-specific HRQoL at varying timepoints following a youth sport-related knee injury (**Table 6.1**). Establishing the link between *intermittent* knee pain, *moderate-to-vigorous* physical activity, knee *extensor* strength, and fear of re-injury in adequately powered studies is essential to determine if these variables represent treatment targets for optimizing HRQoL. The relationship between these variables and HRQoL appear to change with time, so identifying when these relationships have the greatest magnitude of effect can inform the timing of treatments. We also have preliminary evidence that youth with an ACL rupture or meniscus injury experience the worst deficits in knee-specific HRQoL which indicates they might be a target population of future treatment strategies. However, we must remember that youth with any traumatic, sport-related knee injury demonstrate persistent knee-specific HRQoL deficits and may also benefit from these treatment strategies. Although we found no association between obesity, RTS status, time since injury, or physiotherapy attendance and HRQoL, our analyses were exploratory and more research is required to investigate these relationships.

Baseline knee-specific HRQoL appeared to influence the relationship between youth sport-related knee injuries and short-term knee-specific HRQoL (**Table 6.1**).[34, 35] Therefore, researchers should consider adjusting for baseline HRQoL values in future longitudinal studies. Specifically, baseline HRQoL values should be considered when calculating sample size and building regression models.

6.3 FUTURE DIRECTIONS

The following sections describe implications for future research and clinical practice based on the current evidence, including this doctoral work.

6.3.1 Research Implications

Future research should seek to (re-)assess the measurement properties of commonly used generic and knee-specific HRQoL PROMs when used in active youth. Establishing sufficient content validity is of the highest priority. This includes gathering qualitative data that can be used to ascertain the degree to which a PROM is relevant, comprehensive, and comprehensible to active youth. Future evaluation should be guided by the evidence-based COSMIN methods to ensure that measurement properties are rigorously assessed and interpretability and feasibility characteristics are thoroughly described. These COSMIN tools, which are free to download on their website, can also be leveraged to guide the development of new HRQoL PROMs. Until robust PROMs are identified, researchers should consider selecting commonly used generic (e.g., EQ-VAS, SF-36, PedsQL) and knee-specific (e.g., KOOS QOL, ACL QOL) HRQoL PROMs as their findings can be compared across different demographic groups. Additionally, qualitative methodology can be employed to better understand what HRQoL means to active youth and how it might change after a sport-related knee injury.

There are still gaps to be filled about the trajectory of generic and knee-specific HRQoL following a youth sport-related knee injury. We currently lack information on the short- and medium-term generic HRQoL and long-term (particularly >10 years as seen in **Figure 6.1**) knee-specific HRQoL trajectories. Researchers should focus on these timepoints when comparing generic and knee-specific HRQoL in injured and uninjured youth. Furthermore, it is imperative that future studies include youth with *a wide range of sport-related knee injuries* and *uninjured controls* to better understand the burden of knee injuries in this vulnerable population. A true grasp of this burden requires moving beyond ACL ruptures and examining the impact of all knee injuries on youth HRQoL.

Identifying modifiable and non-modifiable determinants of generic or knee-specific HRQoL following a youth sport-related knee injury can inform targets of future treatment strategies and treatment target populations, respectively. Intermittent knee pain, MVPA, knee extensor strength, and kinesiophobia should be investigated alongside other psychological (e.g., self-efficacy, anxiety, depression) and social (e.g., social support, therapeutic alliance) health outcomes. Given that some psychological or social outcomes may be difficult to measure quantitatively, conducting qualitative research in active youth can provide a more comprehensive understanding of their HRQoL determinants. Regarding non-modifiable possible determinants of HRQoL, we were only able to examine injury type but not surgical management or time since surgery due to sample size limitations. Assessing these injury-related outcomes may point to subgroups of active youth who are at greatest risk of HRQoL deficits and may benefit the most from treatment strategies to boost HRQoL. Other variables to consider in future studies that may modify or confound the relationship between youth sport-related knee injuries and HRQoL include structural (e.g., socioeconomic status, healthcare accessibility) and demographic (e.g., gender) factors. Last, researchers should investigate if a relationship between generic and knee-specific HRQoL exists in this population.

6.3.2 Clinical Implications

Health-related quality of life provides an all-encompassing snapshot into one's overall health and knee health. Unfortunately, it is not traditionally used as an indicator of recovery following a knee injury with heavy emphasis placed on short-term rehabilitation goals such as RTS. However, clinicians should be aware of the lingering impact of youth sport-related knee injuries on short- and long-term HRQoL. Measuring generic and knee-specific HRQoL early and often after a knee injury can provide clinicians with a general sense of how a patient perceives their health. Responses from PROMs can be supplemented with responses from open-ended questions about overall health (e.g., "How do you feel about your overall health today?") and knee health (e.g., "How has your knee impacted your life in the last week?") to create tailored treatment strategies to optimize HRQoL.

Clinicians should note that a wide range of sport-related knee injuries lead to reduced short- and long-term knee-specific HRQoL in active youth. Although youth with an ACL rupture or meniscus injury may require closer monitoring as they tend to report greater deficits in knee-specific HRQoL, youth with any traumatic, sport-related knee injury are also at risk for these deficits. Our preliminary findings indicate that increasing MVPA and quadriceps strength while reducing intermittent knee pain and kinesiophobia are possible strategies to boost knee-specific HRQoL.

6.4 CONCLUSIONS

Following youth sport-related knee injuries, we must measure and monitor both generic and knee-specific HRQoL. This thesis revealed that youth who experience a wide range of sport-related knee injuries – including ACL ruptures and beyond – demonstrate significant and persistent deficits in knee-specific HRQoL compared to uninjured controls. It also provides preliminary evidence that intermittent knee pain, MVPA, knee extensor strength, kinesiophobia, and injury type are potential determinants of HRQoL. Equipped with this knowledge, our attention must now turn to identifying robust PROMs to measure HRQoL in this population and developing treatment strategies to minimize the lingering impact of youth sport-related knee injuries on HRQoL.

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Appendix A: Health Consequences in Youth with a Sport-Related Knee Injury (Chapter 1)

The following data extracted from studies examining youth (i.e., sample mean age between 15-24 years old) and comparing to uninjured controls or population norms.

		Time since Injury or Surgery		
Health Domain	**Consequence**	**Short-Term (0-2 Years)**	**Medium-Term (2-5 Years)**	**Long-Term (>5 Years)**
Physical	Pain	Casp et al. (2021)[1]: lower KOOS pain scores in individuals with ACLR (n=165, mean range 90.45-92.37) than controls (mean 98.58) at 6 months post-surgery (p<0.001) Fleming et al. (2013)[2]: lower KOOS pain scores in individuals with ACLR (n=85, mean range 88.3-90.21) than controls (mean 97.9) at 12 months post-surgery (p<0.01) Thorlund et al. (2012)[3]: lower KOOS pain scores in individuals with ACL rupture or ACLR (n=39, mean 79.8) than controls (mean 98.8) at 22 months post-injury (p<0.001) Antosh et al. (2018)[4]: lower KOOS pain scores in individuals with ACLR (n=30, mean 90.30) than controls (mean 98.86) at 24 months post-surgery (p<0.01)	Fleming et al. (2013)[2]: lower KOOS pain scores in individuals with ACLR (n=85, mean range 90.5-91.1) than controls (mean 96.2) at 3 years post-surgery (p<0.05) Myklebust et al. (2017)[5]: lower KOOS pain scores in individuals with ACL rupture or ACLR (n=80, mean 86.1) than controls (mean 96.1) at 3.5 years post-injury (between-group difference 10.0; 95%CI 6.7, 13.0) Miko et al. (2021)[6]: lower KOOS pain scores in individuals with ACLR (n=14, mean 84.6) than controls (mean 99.8) at 3.8 years post-surgery (p<0.001) Hoch et al. (2018)[7]: lower KOOS pain scores in individuals with ACLR (n=20, mean 91.7) than controls (mean 100.0) at 4.2 years post-surgery (p<0.05) Delahunt et al. (2012)[8]: lower KOOS pain scores in individuals with ACLR (n=14, mean 91.6) than controls	Lepley et al. (2019)[9]: lower KOOS pain scores in individuals with ACLR (n=11, mean 90.6) than controls (mean 100.0) at 5.8 years post-surgery (p<0.001) Akelman et al. (2016)[10]: lower KOOS pain scores in individuals with ACLR (n=36, mean 90.6) than controls (mean 96.0) at 7 years post-surgery (p<0.05) Lohmander et al. (2004)[11]: lower KOOS pain scores in individuals with ACL rupture or ACLR (n=84, mean 83) than reference group (mean 95) at 12 years post-injury (p<0.001) von Porat et al. (2004)[12]: lower KOOS pain scores in individuals with ACL rupture or ACLR (n=154, mean 85) than reference group (mean 96) at 14 years post-injury (p<0.05) Tengman et al. (2014)[13]: lower KOOS pain scores in individuals with ACL rupture or ACLR (n=70, mean range 78-85) than controls (mean 99) at 23 years post-injury (p<0.001)

		(mean 99.8) at 4.4 years post-surgery (p<0.05)	Whittaker et al. (2019)[14]: lower KOOS pain scores in individuals with *any traumatic knee injury* (n=100, mean 89) than controls (mean 100) at 6.9 years year post-injury (between-group difference -4.9; 95%CI -7.0, -2.7)
Knee symptoms	Casp et al. (2021)[1]: lower KOOS symptoms scores in ACLR groups (n=165, mean range 84.08-84.22) than controls (mean 96.11) at 6 months post-surgery (p<0.001) Fleming et al. (2013)[2]: lower KOOS symptoms scores in individuals with ACLR (n=85, mean range 79.6-85.1) than controls (mean 95.9) at 12 months post-surgery (p<0.01) Thorlund et al. (2012)[3]: lower KOOS symptoms scores in individuals with ACL rupture or ACLR (n=39, mean 72.6) than controls (mean 98.5) at 22 months post-injury (p<0.001) Antosh et al. (2018)[4]: lower KOOS symptoms scores in individuals with ACLR (n=30, mean 80.93) than controls (mean 95.63) at 24 months post-surgery (p<0.01)	Fleming et al. (2013)[2]: lower KOOS symptoms scores in in individuals with ACLR (n=85, mean range 82.3-86.21) than controls (mean 93.79) at 3 years post-surgery (p<0.01) Myklebust et al. (2017)[5]: lower KOOS symptoms scores in individuals with ACL rupture or ACLR (n=80, mean 75.0) than controls (mean 88.5) at 3.5 years post-injury (between-group difference 13.0; 95%CI 9.0, 18.0) Miko et al. (2021)[6]: lower KOOS symptoms scores in individuals ACLR (n=14, mean 73.5) than controls (mean 99.4) at 3.8 years post-surgery (p<0.001) Hoch et al. (2018)[7]: lower KOOS symptoms scores in individuals with ACLR (n=20, mean 78.6) than controls (mean 98.3) at 4.2 years post-surgery (p<0.05) Delahunt et al. (2012)[8]: lower KOOS symptoms scores in individuals with ACLR (n=14, mean 85.0) than controls (mean 98.4) at 4.4 years post-surgery (p<0.05)	Lepley et al. (2019)[9]: lower KOOS symptoms scores in individuals with ACLR (n=11, mean 83.4) than controls (mean 100.0) at 5.8 years post-surgery (p=0.001) Akelman et al. (2016)[10]: lower KOOS symptoms scores in individuals with ACLR (n=72, mean range 85.3-85.8) than controls (mean 93.0) at 5 years post-surgery (p<0.05); lower KOOS symptoms scores in individuals with ACLR (n=72, mean range 82.5-85.8) than controls (mean 92.4) at 7 years post-surgery (p<0.05) Lohmander et al. (2004)[11]: lower KOOS symptoms scores in individuals with ACL rupture or ACLR (n=84, mean 76) than reference group (mean 94) at 12 years post-injury (p<0.001) von Porat et al. (2004)[12]: lower KOOS symptoms scores in individuals with ACL rupture or ACLR (n=154, mean 76) than reference group (mean 46) at 14 years post-injury (p<0.05) Tengman et al. (2014)[13]: lower KOOS symptoms scores in individuals with ACL rupture or ACLR (n=70, mean

			range 72-79) than controls (mean 98) at 23 years post-injury (p<0.001) Whittaker et al. (2019)[14]: lower KOOS symptoms scores in individuals with *any traumatic knee injury* (n=100, mean 86) than controls (mean 96) at 6.9 years year post-injury (between-group difference -8.1; 95%CI -11.2, -5.0)
Knee muscle weakness	Casp et al. (2021)[1]: lower isokinetic knee extensor and flexor peak torque in individuals with ACLR (n=165, mean range 1.45-1.58 Nm/kg and 0.86-0.88 Nm/kg, respectively) than controls (mean 2.08 Nm/kg and 0.96 Nm/kg, respectively) at 6 months post-surgery (p<0.001) [a]Brown et al. (2021)[15]: weaker isometric or isokinetic knee extensor strength in individuals with ACLR (n=236) than controls at 5 months post-surgery (SMD -1.42; 95%CI -1.62, -1.23); weaker isometric or isokinetic knee extensor strength in individuals with ACLR (n=84) than controls at 9 months post-surgery (SMD -0.38; 95%CI -1.18, -0.66)	Hiemstra et al. (2007)[16]: lower isokinetic knee extensor and flexor strength in individuals with ACLR (n=12, mean 2.18 Nm/kg and 1.09 Nm/kg, respectively) than controls (mean 2.88 Nm/kg and 1.44 Nm/kg, respectively) at 3.3 years post-surgery (p<0.05)	Whittaker et al. (2019)[14]: lower isometric knee extensor and flexor strength in individuals with *any traumatic knee injury* (n=100, mean 1.8 Nm/kg and 0.9 Nm/kg, respectively) than controls (mean 1.8 Nm/kg and 1.1 Nm/kg, respectively) at 6.9 years year post-injury (between-group difference -0.18 Nm/kg; 95%CI -0.33, -0.02 and -0.21 Nm/kg; 95%CI -0.30, -0.11, respectively)
Physical inactivity	Zult et al. (2017)[17]: lower self-reported physical activity in individuals with ACL rupture (n=32, mean 2.6 hours/week) than controls (mean 6.6 hours/week) at 7 months post-injury (p<0.05) Ezzat et al. (2021)[18]: lower vigorous physical activity in individuals with	Bell et al. (2017)[19]: lower MVPA and step count in individuals with ACLR (n=33, mean 79.37 minutes/day and 8158 steps/day, respectively) than controls (mean 93.12 minutes/day and 9769 steps/day, respectively) at 2.3 years post-surgery (p=0.02)	Toomey et al. (2022)[21]: lower MVPA in individuals with *any traumatic knee injury* (n=42, mean 55.5 minutes/day) than controls (mean 67.3 minutes/day) at 8.1 years post-injury (between-group difference 13.5; 95%CI -25.6, -1.4)

		ACLR (n=51, mean 1.1 minutes/day) than controls (mean 2.6 minutes/day) at 1 year post-surgery (between-group difference -1.22 minutes/day; 95%CI -2.40, -0.04)	Kuenze et al. (2019)[20]: lower odds of meeting national physical activity guidelines (≥150 minutes of MVPA per week) in individuals with ACLR (n=59) than controls at 2.5 years post-surgery (OR 2.36; 95%CI 1.09, 5.08)	
	Obesity			Toomey et al. (2017)[22]: higher FMI, fat mass percentage, and abdominal fat in individuals with *any traumatic knee injury* (n=100, mean 5.6 kg/m^2, 22.2%, and 1479 g, respectively) than controls (mean 4.6 kg/m^2, 20.2%, and 1241 g, respectively) at 6.9 years year post-injury (between-group difference 1.05 kg/m^2; 95%CI 0.53, 1.57, 2.3%; 95%CI 0.97, 2.63, 461 g; 95%CI 228, 694, respectively)
Psychological	Kinesiophobia		Hoch et al. (2018)[7]: higher TSK-11 scores in individuals with ACLR (n=20, mean 17.0) than controls (mean 14.0) at 4.2 years post-surgery ($p<0.05$)	Lepley et al. (2019)[9]: higher TSK-17 scores in individuals with ACLR (n=11, mean 31.1) than controls (mean 20.9) at 5.8 years post-surgery ($p<0.001$)
Social	Social isolation			

[a]Data from a meta-analysis that also includes some adult cohorts.

ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction; FMI, fat mass index; kg, kilogram; KOOS, Knee injury and Osteoarthritis Outcome Score; MVPA, moderate-to-vigorous physical activity, n=number of participants; N, Newton; m, metre; OR, odds ratio; SMD, standardized mean difference; TSK, Tampa Scale for Kinesiophobia; 95%CI, 95% confidence interval

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Appendix B: Health Consequences in Adult with a Sport-Related Knee Injury (Chapter 1)

The following data extracted from studies examining adult (i.e., sample mean age between ≥25 years old) and comparing to uninjured controls or population norms.

		Time since Injury or Surgery		
Health Domain	**Consequence**	**Short-Term (0-2 Years)**	**Medium-Term (2-5 Years)**	**Long-Term (>5 Years)**
Physical	Pain	Ebrahimi et al. (2017)[1]: lower KOOS pain scores in individuals with *meniscus injury* (n=100, mean 52.08; 95%CI 48.23, 55.94) than controls (mean 86.39; 95%CI 82.17, 90.61) at 15 months post-injury	Tourville et al. (2013)[2]: lower KOOS pain scores in individuals with ACLR (n=31, mean range 89-95) than controls (mean 99) at 3.8 years post-surgery (p<0.0001) Alerskans et al. (2022)[3]: lower KOOS pain scores in individuals with *arthroscopic partial meniscectomy* (n=50, mean 82.8) than population norms (mean 92.1) at 4 years post-surgery (p<0.001) Varma et al. (2014)[4]: lower KOOS pain scores in individuals with ACLR (n=19, mean range 87.5-88.4) than controls (mean 99.1) at 4.5 years post-surgery (p<0.02) Kaur et al. (2021)[5]: lower KOOS pain scores in individuals with ACLR (n=25, mean 85.3) than controls (mean 98.8) at 5 years post-surgery (between-group difference 13.3; 95%CI 8.3, 18.4)	
	Knee symptoms	Ebrahimi et al. (2017)[1]: lower KOOS symptoms scores in individuals with *meniscus injury* (n=100, mean 56.39;	Tourville et al. (2013)[2]: lower KOOS symptoms scores in individuals with ACLR (n=31, mean range 84-88) than	[b]Kostogiannis et al. (2007)[6]: lower KOOS symptoms scores in individuals with ACL rupture (n=67) than

	95%CI 52.29, 60.49) than controls (mean 87.00; 95%CI 83.91, 90.09) at 15 months post-injury	controls (mean 98) at 3.8 years post-surgery (p<0.0001) Alerskans et al. (2022)[3]: lower KOOS pain scores in individuals with *arthroscopic partial meniscectomy* (n=50, mean 76.6) than population norms (mean 88.2) at 4 years post-surgery (p<0.001) Varma et al. (2014)[4]: lower KOOS symptoms scores in individuals with ACLR (n=24, mean range 80.7-85.1) than controls (mean 98.2) at 4.5 years post-surgery (p<0.05) Kaur et al. (2021)[5]: lower KOOS symptoms scores in individuals with ACLR (n=25, mean 77.2) than controls (mean 91.2) at 5 years post-surgery (between-group difference 13.9; 95%CI 7.8, 20.1)	controls at 15 years post-injury (p=0.001)
Knee muscle weakness	Chung et al. (2015)[7]: weaker isokinetic knee extensor and flexor peak torque in individuals with ACLR (n=75, mean 1.788 Nm/kg and 1.017 Nm/kg, respectively) than controls (mean 1.950 Nm/kg and 1.091 Nm/kg, respectively) at 3 months post-surgery (p<0.001); weaker isokinetic knee extensor and flexor peak torque in individuals with ACLR (n=75, mean 2.242 Nm/kg and 1.273 Nm/kg, respectively) than controls (mean 1.950 Nm/kg and 1.091 Nm/kg, respectively) at 6 months post-surgery (p<0.001); weaker isokinetic knee extensor and flexor peak torque in individuals with ACLR (n=75, mean	Landes et al. (2010)[12]: weaker isometric knee flexor in individuals with ACLR (n=20, mean 56.2 Nm) than controls (mean 70.7 Nm) at 2.3 years post-surgery (p<0.05)	

2.354 Nm/kg and 1.293 Nm/kg, respectively) than controls (mean 1.950 Nm/kg and 1.091 Nm/kg, respectively) at 12 months post-surgery (p<0.001); weaker isokinetic knee extensor and flexor peak torque in individuals with ACLR (n=75, mean 2.428 Nm/kg and 1.288 Nm/kg, respectively) than controls (mean 1.950 Nm/kg and 1.091 Nm/kg, respectively) at 24 months post-surgery (p<0.001)

Manchado et al. (2021)[8]: weaker isometric knee extensor strength in individuals with ACLR (n=194, mean 133.4 N) than controls (mean 174.8) at 4 months post-surgery (p<0.001)

Silva et al. (2012)[9]: lower isokinetic quads and hamstring LSI in individuals with ACLR (n=7, mean 66.4% and 83.8%, respectively) than controls (mean 94.1% and 91.5%, respectively) at 5 months post-surgery (p<0.001)

[a]Brown et al. (2021)[10]: weaker isometric or isokinetic knee extensor strength in individuals with ACLR (n=64) than controls at 9 months post-surgery (SMD -0.38; 95%CI -1.18, -0.66)

Patel et al. (2003)[11]: lower isokinetic knee extensor strength in individuals with ACL rupture (n=44, mean 9.6% body weight x height) than controls

		(mean 11.3% body weight x height) at 21 months post-injury (p<0.001)		
	Physical inactivity			
	Obesity			
Psychological	Kinesiophobia	Jamshidi et al. (2016)[13]: higher TSK-17 scores in individuals with ACL rupture (n=8) than controls at 13 months post-injury (between-group difference 7.750, p=0.035)	Balki et al. (2021)[14]: higher TSK-17 scores in individuals with ACLR (n=46, mean 39.56) than controls (mean 37.08) at 3 years post-surgery (p=0.043) Niederer et al. (2020)[15]: higher fear of re-injury VAS scores in individuals with ACLR (n=19, mean 38) than controls (mean 16) at 3.2 years post-surgery (p<0.05) Kaur et al. (2021)[5]: higher Fear of Re-injury Scale scores in individuals with ACLR (n=25, mean 44.0) than controls (mean 24.7) at 5 years post-surgery (between-group difference 19.7; 95%CI 11.5, 27.9)	
Social	Social isolation			

[a]Data from a meta-analysis that also includes some youth cohorts.
[b]KOOS subscale scores not reported.

ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction; kg, kilogram; KOOS, Knee injury and Osteoarthritis Outcome Score; MVPA, moderate-to-vigorous physical activity, n=number of participants; N, Newton; m, metre; TSK, Tampa Scale for Kinesiophobia; VAS, visual analogue scale; 95%CI, 95% confidence interval

Appendix B References

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Appendix C: Health-Related Quality of Life Outcomes in Youth with a Sport-Related Knee Injury (Chapter 1)

The following data extracted from studies examining youth (i.e., sample mean age between 15-24 years old) and comparing to uninjured controls or population norms.

	Time since Injury or Surgery		
HRQoL Construct	**Short-Term (0-2 Years)**	**Medium-Term (2-5 Years)**	**Long-Term (>5 Years)**
Generic			Domzalski et al. (2021)[1]: no difference in SF-36 PCS or MCS scores in individuals with ACLR (n=60) and controls at 5.9 years post-surgery Akelman et al. (2016)[2]: no differences in SF-36 domains in individuals with ACLR (n=72) and controls at 5 years post-surgery; no differences in SF-36 domains except for lower general health and social functioning scores in individuals with ACLR (n=36, mean 80.7 and 90.3, respectively) than controls (mean 86.9 and 97.2, respectively) at 7 years post-surgery ($p<0.05$) McAllister et al. (2003)[3]: no differences in SF-36 domains, PCS, or MCS in individuals with ACL or ACLR (n=33) than controls at 8.9 years post-injury von Porat et al. (2004)[4]: higher SF-36 social functioning and mental health scores in individuals with ACL rupture or ACLR (n=152, mean 93.6 and 86.4, respectively) than controls (mean 89.5 and 82.2, respectively) at 14 years post-injury ($p<0.05$); no differences in bodily pain, general health, vitality, and role emotional

			scores in individuals with ACL rupture or ACLR (n=154) and at 14 years post-injury; lower SF-36 physical functioning and role physical scores in individuals with ACL rupture or ACLR (n=154, mean 84.5 and 81.4, respectively) than controls (mean 93.1 and 88.5, respectively) at 14 years post-injury (p<0.05)
Knee-specific HRQoL	Casp et al. (2021)[5]: lower KOOS QOL scores in ACLR groups (n=165, mean range 66.20-70.07) than controls (mean 97.61) at 6 months post-surgery (p<0.001) Fleming et al. (2013)[6]: lower KOOS QOL scores in individuals with ACLR (n=85, mean range 67.8-74.1) than controls (mean 94.9) at 12 months post-surgery (p<0.01) Thorlund et al. (2012)[7]: lower KOOS QOL scores in individuals with ACL rupture or ACLR (n=39, mean 40.5) than controls (mean 95.9) at 22 months post-injury (p<0.001) Antosh et al. (2018)[8]: lower KOOS QOL scores in individuals with ACLR (n=30, mean 66.17) than controls (mean 94.34) at 24 months post-surgery (p<0.01)	Fleming et al. (2013)[6]: lower KOOS QOL scores in individuals with ACLR (n=85, mean range 76.9-78.9) than controls (mean 93.3) at 3 years post-surgery (p<0.01) Myklebust et al. (2017)[9]: lower KOOS QOL scores in individuals with ACL rupture or ACLR (n=80, mean 73.8) than controls (mean 91.6) at 3.5 years post-injury (between-group difference 18.0; 95%CI 13.0, 23.0) Miko et al. (2021)[10]: lower KOOS QOL scores in individuals with ACLR (n=14, mean 69.3) than controls (mean 100.0) at 3.8 years post-surgery (p<0.001) Hoch et al. (2018)[11]: lower KOOS QOL scores in individuals with ACLR (n=20, mean 75.0) than controls (mean 100.0) at 4.2 years post-surgery (p<0.05) Delahunt et al. (2012)[12]: lower KOOS QOL scores in individuals with ACLR (n=14, mean 73.4) than controls (mean 99.1) at 4.4 years post-surgery (p<0.05)	Lepley et al. (2019)[13]: lower KOOS QOL scores in individuals with ACLR (n=11, mean 83.5) than controls (mean 100.0) at 5.8 years post-surgery (p=0.001) Domzalski et al. (2021)[1]: no difference in KOOS QOL scores in individuals with ACLR (n=60) and controls at 5.9 years post-surgery Akelman et al. (2016)[2]: lower KOOS QOL scores in individuals with ACLR (n=36, mean range 74.6-75.3) than controls (mean 94.6) at 5 years post-surgery (p<0.05); lower KOOS QOL scores in individuals with ACLR (n=36, mean range 76.5-81.1) than controls (mean 92.3) at 7 years post-surgery (p<0.05) Lohmander et al. (2004)[14]: lower KOOS QOL scores in individuals with ACL rupture or ACLR (n=84, mean 54) than reference group (mean 89) at 12 years post-injury (p<0.001) von Porat et al. (2004)[4]: lower KOOS QOL scores in individuals with ACL rupture or ACLR (n=154, mean 60) than reference group (mean 92) at 14 years post-injury (p<0.05)

		Tengman et al. (2014)[15]: lower KOOS QOL scores in individuals with ACL rupture or ACLR (n=70, mean range 49-61) than controls (mean 98) at 23 years post-injury (p<0.001) Whittaker et al. (2019)[16]: lower KOOS QOL scores in individuals with *any traumatic knee injury* (n=100, mean 92) than controls (mean 100) at 6.9 years year post-injury (between-group difference -8.3; 95%CI -10.2, -6.0)

ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction; HRQoL, health-related quality of life; KOOS, Knee injury and Osteoarthritis Outcome Score; MCS, Mental Component Summary score; n=number of participants; QOL, quality of life; PCS, Physical Component Summary score; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; 95%CI, 95% confidence interval

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Appendix D: Health-Related Quality of Life Outcomes in Adult with a Sport-Related Knee Injury (Chapter 1)

The following data extracted from studies examining adult (i.e., sample mean age between ≥25 years old) and comparing to uninjured controls or population norms.

	Time since Injury or Surgery		
HRQoL Construct	**Short-Term (0-2 Years)**	**Medium-Term (2-5 Years)**	**Long-Term (>5 Years)**
Generic	Sripada et al. (2022)[1]: lower EQ-5D-5L index scores in individuals with ACL rupture (n=67, mean 0.557) than controls (mean 0.923) at 21 months post-injury (p<0.001); lower SF-36 domains (all) scores in individuals with ACL or ACLR (n=67) than controls at 21 months post-injury (all p<0.001)	McAllister et al. (2014)[2]: higher SF-36 physical functioning, role physical, bodily pain, social functioning, mental health, and PCS scores in individuals with ACLR (n=55, mean 90.9, 88.6, 82.9, 89.1, 79.5, and 53 respectively) than controls (mean 84.2, 80.9, 75.2, 83.3, 74.7, and 50, respectively) at 3.6 years post-surgery (p<0.01); no differences in general health, vitality, role emotional, or MCS scores in in individuals with ACLR (n=55) and controls at 3.6 years post-surgery Kaur et al. (2021)[3]: no difference in SF-12 MCS but lower SF-12 PCS scores in individuals with ACLR (n=25, mean 54.0) than controls (mean 56.9) at 5 years post-surgery (between-group difference 2.9; 95%CI 0.8, 5.1) Månsson et al. (2011)[4]: higher SF-36 general health, social functioning, role emotional, and mental health scores in individuals with ACLR (n=424, mean 82.7, 93.4, 90.7, and 84.2, respectively) than controls (mean 80.0, 89.9, 88.1, and 81.1, respectively) at 2-7 years post-surgery (p<0.05); no differences in bodily pain and vitality scores in individuals with	

		ACLR (n=424) and at 2-7 years post-surgery; lower SF-36 physical functioning and role physical scores in individuals with ACLR (n=424, mean 87.1 and 85.1, respectively) than controls (mean 94.1 and 89.6, respectively) at 2-7 years post-surgery (p<0.05)	
Knee-specific HRQoL	Ebrahimi et al. (2017)[5]: lower KOOS QOL scores in individuals with *meniscus injury* (n=100, mean 28.94; 95%CI 25.03, 32.84) than controls (mean 76.75; 95%CI 71.30, 82.20) at 15 months post-injury	Tourville et al. (2013)[6]: lower KOOS QOL scores in individuals with ACLR (n=31, mean range 76-88) than controls (mean 99) at 3.8 years post-surgery (p<0.0001) Alerskans et al. (2022)[7]: lower KOOS QOL scores in individuals with *arthroscopic partial meniscectomy* (n=50, mean 62.9) than population norms (mean 84.4) at 4 years post-surgery (p<0.001) Varma et al. (2014)[8]: lower KOOS QOL scores in individuals with ACLR (n=24, mean range 64.5-70.0) than controls (mean 100.0) at 4.5 years post-surgery (p<0.05) Kaur et al. (2021)[3]: lower KOOS QOL scores in individuals with ACLR (n=25, mean 47.0) than controls (mean 80.4) at 5 years post-surgery (between-group difference 33.4; 95%CI 24.6, 42.2)	[a]Kostogiannis et al. (2007)[9]: lower KOOS QOL scores in individuals with ACL rupture (n=67) than controls at 15 years post-injury (p=0.001)

[a]KOOS subscale scores not reported.

ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction; HRQoL, health-related quality of life; KOOS, Knee injury and Osteoarthritis Outcome Score; MCS, Mental Component Summary score; n=number of participants; QOL, quality of life; PCS, Physical Component Summary score; SF-12, Medical Outcomes Study 12-Item Short-Form Health Survey; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; 95%CI, 95% confidence interval

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Appendix E: Chapter 2 Original Publication – Journal of Orthopaedic & Sports Physical Therapy

[LITERATURE REVIEW]

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Searching for the Holy Grail: A Systematic Review of Health-Related Quality of Life Measures for Active Youth

Health-related quality of life (HRQoL) encompasses the physical, psychological, and social domains of health. It is influenced by an individual's perceptions, experiences, expectations, beliefs,[11] and environment.[8] Determinants of HRQoL that may be most relevant to youth include supportive parents,[12] quality of education,[12] and participating in sports.[47] Youth athletes report higher HRQoL compared to nonathletes.[24,47] Youths who participate in sports and recreational activities may experience greater physical (eg, increased fitness), psychological (eg, increased autonomy), and social (eg, established feelings of community) health benefits than those who do not.[9,31,32] Active youth may also report higher HRQoL, given the association between socioeconomic status and sports participation.[13]

OBJECTIVE: To identify the most suitable existing generic and condition-specific health-related quality of life (HRQoL) patient-reported outcome measures (PROMs) for active youth with and without a musculoskeletal injury, based on measurement properties, interpretability, and feasibility.

DESIGN: Systematic review of clinimetrics.

LITERATURE SEARCH: We searched MEDLINE, Embase, CINAHL, SPORTDiscus, PsycINFO, and Scopus from inception to April 30, 2020.

STUDY SELECTION CRITERIA: Records with original data describing the evaluation of a PROM or PROM subscale in active youth (15-24 years old) with or without a musculoskeletal injury were included. Non-English studies and those including individuals with a cognitive, developmental, or systemic condition were excluded.

DATA SYNTHESIS: This review was conducted according to the COSMIN user manual for systematic reviews of PROMs and the PRISMA guidelines. The COSMIN user manual guided our measurement property evaluation and interpretability and feasibility description.

RESULTS: Of 6931 potential records, 21 studies were included. Eleven generic and 7 condition-specific PROMs were identified. No PROM received a final COSMIN recommendation of "A" because all lacked sufficient content validity. The 8-item Disablement in the Physically Active scale-mental summary component Short Form (DPA-MSC SF-8), Quality of Life Survey, and Functional Arm Scale for Throwers (FAST) were the most suitable existing PROMs, given their high-quality evidence for sufficient structural validity and internal consistency.

CONCLUSION: No definitively robust PROM for measuring generic or condition-specific HRQoL of active youth was identified. Until one exists, we recommend the DPA-MSC SF-8, the Quality of Life Survey, or the FAST and applying mixed methods to best characterize the HRQoL of active youth. *J Orthop Sports Phys Ther 2021;51(10):478-491. doi:10.2519/jospt.2021.10412*

KEY WORDS: *athlete, questionnaire, reliability, validity, well-being*

Despite the many benefits of sports participation,[3,4,49,57] active youth (15-24 years old)[39,45,53] face an increased risk of musculoskeletal injury.[15,16] Sport-related injuries are associated with long-term consequences and negatively impact HRQoL.[1,14,28,30] Youth athletes who suffer a sport-related injury report lower HRQoL compared to uninjured peers,[24,54] even after returning to sport.[25] A better understanding of how youth HRQoL changes after a sport-related injury may identify which health domains

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are most affected and guide patient-centered care.

Patient-reported outcome measures (PROMs) provide the patient's perspective of the patient's health and can inform individual care.[7] Both generic and condition-specific PROMs are needed to build a complete picture of the HRQoL of active youth.[19] To accurately measure and monitor changes in HRQoL and evaluate an intervention's effectiveness following injury, a PROM must demonstrate acceptable content validity (ie, relevant, comprehensive, and comprehensible to active youths).[41,51] A PROM should be psychometrically robust (ie, valid, reliable, and responsive), easy to interpret, and feasible to use in clinical and research settings.

Previous research aimed at understanding the HRQoL of active youth has relied heavily on PROMs developed in adult populations. Important information about the HRQoL of active youth and its determinants may have been missed or misunderstood. The objective of our systematic review was to identify the most suitable existing generic and condition-specific HRQoL PROMs for active youth with or without a musculoskeletal injury, based on measurement properties, interpretability, and feasibility.

METHODS

This review was registered in the PROSPERO database (CRD42019123282), conducted according to the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) manual for systematic reviews of PROMs (Version 1.0),[36,37,41,51] and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[33] guidelines. The COSMIN user manual[37] is an internationally accepted guideline designed for systematic reviews examining PROMs.[36,41,51] It provides steps to rigorously evaluate measurement properties of PROMs, which leads to identifying the most robust PROM(s) for a specific purpose.[41]

Information Sources and Search

Eligible records were identified by searching 6 online databases—MEDLINE (Ovid), Embase (Ovid), CINAHL Plus with Full Text (EBSCOhost), SPORTDiscus (EBSCOhost), PsycINFO (Ovid), and Scopus—from inception to April 30, 2020. Medical subject headings and key words were selected to capture the constructs of youth, physical activity, HRQoL, PROMs, and measurement properties. The final search strategy was determined in collaboration with a health sciences librarian scientist (L.D.) (supplemental file 1). Reference lists of included studies were hand searched for relevant records.

Eligibility Criteria

Records reporting original data about the HRQoL of active youth with or without a musculoskeletal injury and describing the development of a PROM or evaluation of at least 1 measurement property of a generic or condition-specific HRQoL PROM or PROM subscale were included. Generic HRQoL PROMs assessing overall HRQoL may be used to compare groups who differ in demographics, medical condition, or health care intervention received. Condition-specific HRQoL PROMs pertain to a particular patient population or health condition.

The term *active youth* indicated a sample of individuals with a mean or median age of 15 to 24 years[53] who were identified as recreational, competitive, or elite athletes or individuals who regularly participated in light to vigorous physical activity. For the latter, authors had to report on minutes of physical activity per week or enrollment in physical education or fitness classes.

Non-English records and those including nonhuman participants or individuals with a cognitive (eg, brain injury), developmental (eg, developmental delay), or systemic (eg, diabetes, cancer) condition were excluded. Conference abstracts, editorials, commentaries, reviews, case series, case studies, and gray literature were also excluded.

Study Selection

Records were organized using reference management software (EndNote X8.2; Clarivate Analytics, Philadelphia, PA). After removing duplicates, titles and corresponding abstracts were independently reviewed by pairs of 2 reviewers (C.L. and L.T., C.H., S.F., Wasim Labban, or J.W.) blinded to the record author(s) and journal title, using an Excel (Microsoft Corporation, Redmond, WA) workbook designed specifically for screening.[56]

Prior to title/abstract screening, all reviewers independently screened a random sample of 120 records to assess the applicability of the exclusion criteria. The agreement between reviewers and the senior author (J.W.) on these 120 records ranged between 69% and 83% (Cohen's κ = 0.28-0.66). Discrepancies were discussed and exclusion criteria clarified before title/abstract screening began in full.

If a record title of interest was found but the abstract was unavailable, the full text was retrieved to ensure potentially relevant studies were not missed. The full texts of relevant records were independently reviewed by 2 reviewers to determine final study selection. The senior author (J.W.) mediated any disagreements at all stages when primary reviewers could not reach consensus. If multiple records reported on the same measurement property from the same study, we included the first published record.

Data Extraction

Data extraction followed recommendations from the COSMIN user manual[36,37,41,51] and included study characteristics (eg, sample size, mean or median age, sex), PROM characteristics (eg, target population, number of subscales and items, scoring), and information about measurement properties, interpretability, and feasibility (as described below). Initial data extraction was completed by the lead author (C.L.), then independently verified by a second reviewer. Disagreements were resolved by consensus or by the senior author (J.W.). Study authors were contacted for missing data or clarification as needed.

Measurement Property Evaluation

As per the COSMIN user manual,[36,37,41,51] the evaluation of each measurement property (see **TABLE 1** for definitions) of included PROMs involved the 4 steps outlined below (**FIGURE 1**). A hypothetical example of the evaluation process can be found in supplemental file 2.

Evaluate the Methodological Quality of Measurement Properties by Individual Study First, we evaluated the methodological quality of individual studies that assessed a measurement property, using the COSMIN risk-of-bias checklist.[36,37,41,51] Checklist items were graded as "very good," "adequate," "doubtful," and "inadequate," and the final rating for the methodological quality of a measurement property was determined by taking the lowest rating of any item assessing that property (ie, "the worst score counts"[36,37,41,51]).

Rate the Results of Measurement Properties by Individual Study Second, we rated the result of individual studies that estimated a measurement property by applying the criteria for good measurement properties (supplemental file 3).[42,51] A rating of "sufficient," "insufficient," "inconsistent," or "indeterminate" was assigned to each measurement property.

Summarize the Evidence for Measurement Properties by PROM Third, we qualitatively summarized the evidence for a measurement property of a PROM across studies (as appropriate) and rated the summarized results by applying the criteria for good measurement properties. An overall rating of sufficient was assigned if at least 75% of the results were sufficient.[36,37,41,51] In the case of inconsistent results across studies, we re-examined each study for sample heterogeneity. If sample heterogeneity existed, we provided an overall rating for each subgroup (ie, sex, sport type, competition level). If no heterogeneity was found, the measurement property received an overall rating of inconsistent.

Grade the Quality of Evidence for Measurement Properties by PROM Fourth, we graded the quality of the evidence for each PROM measurement property as "high," "moderate," "low," or "very low," using a modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (supplemental file 4).[36,37,41,51] The quality of evidence referred to the confidence that the overall results and ratings for each measurement property were trustworthy. As per the GRADE approach, the evidence was assumed to be of high quality until possibly downgraded, based on 4 factors: (1) risk of bias (methodological quality of the studies), (2) inconsistency (inconsistency of summarized results), (3) imprecision (total sample size across studies), and (4) indirectness (inclusion of individuals beyond the target population, for example, participants aged older than 24 years despite a sample mean age of 18 years).[36,37,41,51]

TABLE 1 DEFINITIONS OF MEASUREMENT PROPERTIES, ADAPTED FROM THE COSMIN USER MANUAL[36,37,41,51]

Domain/Measurement Property	Definition
Validity	The degree to which a PROM assesses the construct(s) it intends to measure
Content validity	The degree to which the content of a PROM reflects the construct to be measured (ie, is relevant, comprehensive, and comprehensible)
Structural validity	The degree to which the scores of a PROM adequately reflect the dimensionality of the construct to be measured
Cross-cultural validity	The degree to which the performance of items on a translated or culturally adapted PROM adequately reflects the performance of items on the original version
Construct validity	The degree to which the scores of a PROM are consistent with hypotheses, based on the assumption that the PROM validly measures the construct to be measured (eg, scores of a generic HRQoL PROM hypothesized to have a high positive correlation with scores of another generic HRQoL PROM)
Criterion validity	The degree to which scores of a PROM adequately reflect a gold standard
Reliability	The degree to which a PROM is free from measurement error
Internal consistency	The degree of interrelatedness among items of a PROM
Reliability (test-retest)	The proportion of total variance in measurements that is due to "true" differences between individuals
Measurement error	The systematic and random error of an individual's score that is not attributed to true chance in the construct to be measured
Responsiveness	The ability of a PROM to detect change over time in the construct to be measured
Interpretability[a]	The degree to which one can assign qualitative meaning (ie, clinical or commonly understood connotations) to a PROM's scores or change in scores
Feasibility[a]	The ease of application of a PROM in its intended setting given various constraints (eg, time, money)

Abbreviations: HRQoL, health-related quality of life; PROM, patient-reported outcome measure.
[a]This is not considered a measurement property but is still an important characteristic of a PROM.

HRQoL PROM Selection

Description of Interpretability and Feasibility As no scoring scales exist for rating PROM interpretability or feasibility, we described characteristics of interpretability (distribution of scores, percentage of missing items, floor and ceiling effects, minimal important change, and response shift) and feasibility (patient and/or clinician comprehensibility, completion time, and cost of use) as outlined in the COSMIN user manual.[36,37,41,51] Instruments containing information that would help clinicians and researchers interpret scores and minimize barriers to use in real-world settings were considered ideal.

Final Recommendation All identified HRQoL PROMs were given a final recommendation of "A" (evidence for sufficient content validity and at least low-quality evidence for sufficient internal consistency), "B" (neither "A" nor "C"), or "C" (high-quality evidence for any insufficient measurement property), as per the COSMIN user manual.[36,37,41,51] The emphasis on content validity and internal consistency in the final recommendation reflects the importance of a PROM's relevance, comprehensiveness, and comprehensibility to a target population as well as its internal structure, respectively.[36,37,41,51]

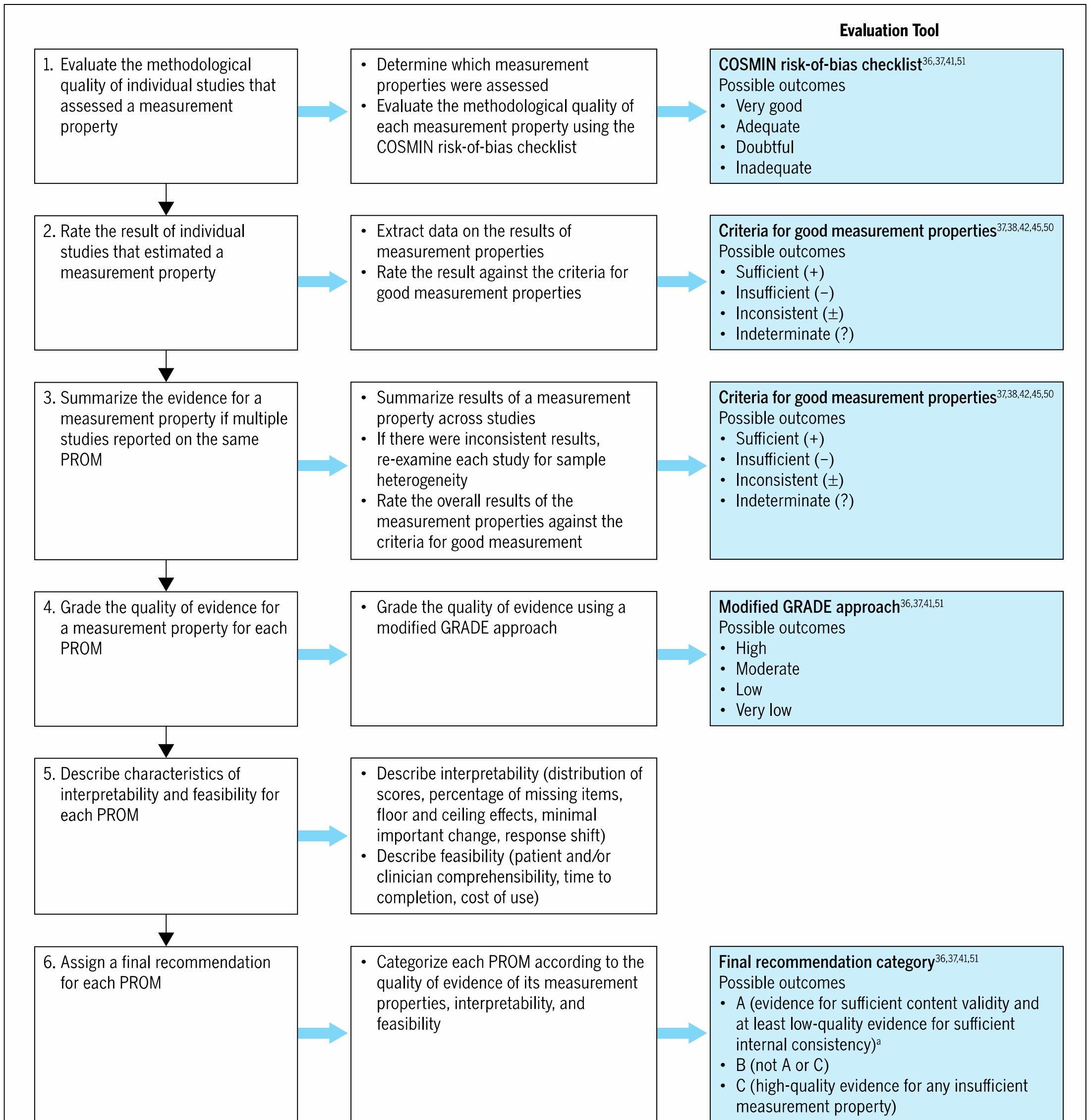

FIGURE 1. Patient-reported outcome measure evaluation and selection process, as recommended by and adapted from the COSMIN user manual.[36,37,41,51] [a]The instruments with a final recommendation of "A" and acceptable interpretability and feasibility were deemed the most suitable PROMs. Abbreviations: COSMIN, COnsensus-based Standards for the selection of health Measurement INstruments; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PROM, patient-reported outcome measure.

Instruments categorized as "A" that had acceptable interpretability and feasibility were deemed the most suitable HRQoL PROMs.

RESULTS

Study Selection

Of 6931 records, 1834 duplicates were removed, 5097 unique records underwent title/abstract screening, 635 records were reviewed in full, and 21 studies were included in the analysis (**FIGURE 2**). We attempted to contact the authors of 9 studies via e-mail to clarify sample characteristics and determine eligibility. Of the 9 studies, 1 was included and 8 were excluded (3 authors provided information proving that their study was ineligible due to the age or activity level of the participants and 5 authors failed to respond after 2 attempts to contact them over 30 days).

We identified 18 HRQoL PROMs across 21 included studies, including 11 generic[2,5,17,18,22,23,25,29,40,46,55,59,60] and 7 condition-specific[6,10,11,20,21,26,43,44] PROMs. Eight generic and 5 condition-specific HRQoL PROMs were assessed in only 1 study. An overview of the studies, including the HRQoL PROM(s) evaluated and study sample characteristics, can be found in **TABLE 2**. Studies were published between 2007 and 2020 and included participants from 5 countries (United States,[2,6,11,17,18,21,22,23,25,26,40,43,44,55,59,60] Australia,[10,20] Brazil,[5] Croatia,[29] and Norway[46]). Competitive athletes (professional, collegiate, or high school athletes) were assessed in 7 studies,[6,10,17,21,23,25,44] recreational athletes in 9 studies,[5,11,18,20,29,40,46,59,60] or both competitive and recreational athletes in 5 studies.[2,22,26,43,55] Ten studies examined uninjured active youth,[5,17,18,21,25,29,43,44,46,60] 7 studies examined active youth with a musculoskeletal injury,[6,11,20,22,23,40,55] and 4 studies examined both.[2,10,24,59]

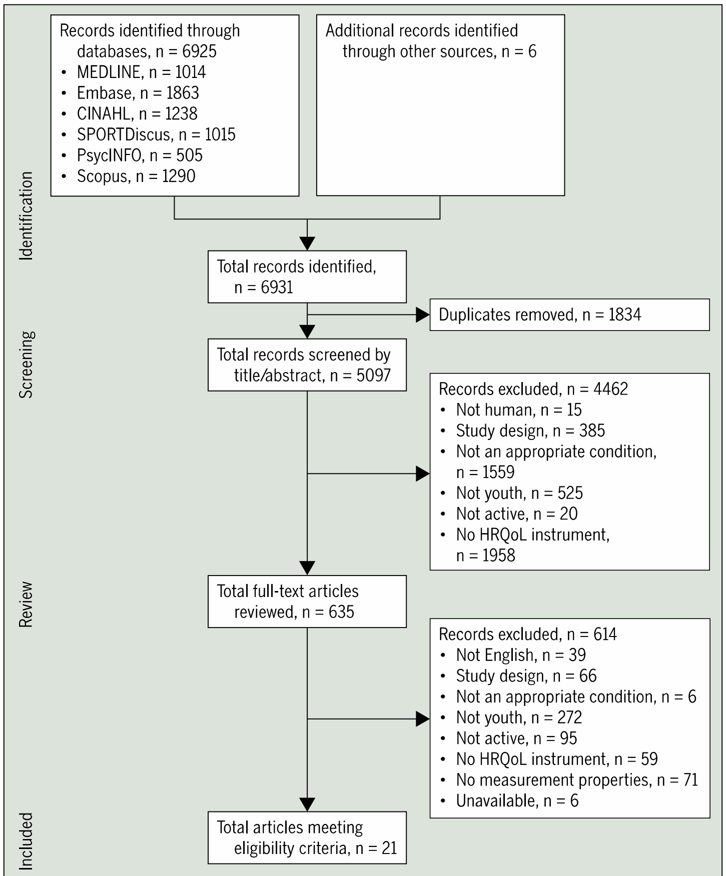

FIGURE 2. PRISMA flow chart. Abbreviation: HRQoL, health-related quality of life.

Generic HRQoL Instruments

Eleven generic HRQoL PROMs were evaluated in 13 of 21 included studies (62%).[2,5,17,18,22,23,25,29,40,46,55,59,60] These included the Athlete Life Quality Scale (ALQS),[17] Disablement in the Physically Active scale-mental summary component (DPA-MSC),[2,22,23,40,55,59] 10-item Disablement in the Physically Active scale-mental summary component Short Form (DPA-MSC SF-10),[2] 8-item Disablement in the Physically Active scale-mental summary component Short Form (DPA-MSC SF-8),[2] 52-item KIDSCREEN questionnaire (KIDSCREEN-52),[29] 10-item KIDSCREEN index (KIDSCREEN-10),[46] Pediatric Quality of Life Inventory (PedsQL),[60] Quality of Life (QoL) Survey,[18] Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36),[18,25] Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12),[22] and World Health Organization Quality of Life instrument-abbreviated version (WHOQOL-BREF).[5,18] An overview of these generic HRQoL instruments is found in supplemental file 5. Three generic HRQoL PROMs were a subscale of a larger instrument, whereas 8 generic HRQoL PROMs were multidimensional, consisting of subscales that encompassed various health domains. Higher scores indicated better outcomes on all PROMs except for the DPA-MSC and its short forms. All studies used self-completed administration (ie, no proxy).

TABLE 2 Characteristics of Included Studies

Study, Country	HRQoL PROM	Language of PROM	Primary Objective	Sample[a]	Physical Activity Description	HRQoL Definition	Measurement Properties Evaluated
Gentner et al[17] United States	ALQS	English	Develop a PROM for assessing the QoL of athletes	n = 159 NCAA Division I college athletes; age, 18-22 y; 50% women	Participated in collegiate sports	"Mental, emotional, physical, and spiritual health and the possession of socially desirable attributes, life satisfaction, and positive feelings"	Content validity, structural validity, internal consistency, feasibility
Vela and Denegar[55] United States	DPA-MSC	English	Establish standard values and evaluate measurement properties of the DPA	n = 368 competitive and recreational athletes with and without an acute or persistent musculoskeletal injury; age, 20.1 ± 3.8 y; 55% women	Engaged in athletic, recreational, or occupational activities ≥3 times per week	"The psychosocial effects of injury"	Content validity, structural validity, internal consistency, test-retest reliability, criterion validity, responsiveness, interpretability
Houston et al[23] United States	DPA-MSC	English	Evaluate the structural validity of the DPA	n = 467 NCAA Division I and III athletes; age, 19.5 ± 1.3 y; 57% women	Participated in collegiate sports	"The physical, psychological and social components of health"	Structural validity, internal consistency, criterion validity, feasibility
Baker et al[2] United States	DPA-MSC, DPA-MSC SF-10, DPA-MSC SF-8	English	Re-evaluate the structural validity and establish a short-form version of the DPA	n = 1592 physically active individuals with and without an acute, subacute, or persistent musculoskeletal injury; age, 23 ± 9 y; 49% women	Participated in athletic, recreational, or occupational activities ≥3 times per week	"Patients' perceptions of physical, psychological, and social subconstructs of their health status and recovery"	Structural validity, internal consistency
White et al[59] United States	DPA-MSC	English	Evaluate the internal consistency of the DPA	n = 31 university students enrolled in a dance course, with or without a history of a musculoskeletal injury; age, 20.8 ± 2.6 y; 100% women	Reported being physically active for ≥30 min 3 times per week	NR	Internal consistency
Powden et al[40] United States	DPA-MSC	English	Evaluate the response shift phenomenon in individuals with chronic ankle instability	n = 22 individuals with self-reported chronic ankle instability; age, 24.91 ± 7.33 y; 75% women	Scored >24 on the GLTEQ	NR	Internal consistency, interpretability, feasibility
Lorger et al[29] Croatia	KIDSCREEN-52	Croatian	Identify factors that contribute to the QoL of young athletes	n = 343 young athletes; age, 15.1 y; 56% female	Participated in organized individual and team sports	NR	Structural validity, internal consistency, feasibility
Sigvartsen et al[46] Norway	KIDSCREEN-10	Norwegian	Describe QoL and physical activity across different physical education programs	n = 156 high school students; age, 16.1 ± 0.8 y; 79% female	Reported being physically active for a mean of 2.0 hours/day 2.4 times per week	NR	Internal consistency, feasibility
Zhang et al[60] United States	PedsQL	English	Evaluate the relationship between HRQoL, individual factors, environmental factors, and physical activity	n = 235 undergraduate women; age, 21.0 ± 1.7 y; 100% women	Reported a mean of 460.54 minutes/week of MVPA	"Comprehensive construct including physical and psychosocial health functioning"	Internal consistency, construct validity, feasibility

Table continues on page 484.

TABLE 2 Characteristics of Included Studies (continued)

Study, Country	HRQoL PROM	Language of PROM	Primary Objective	Sample[a]	Physical Activity Description	HRQoL Definition	Measurement Properties Evaluated
Gill et al[18] United States	QoL Survey, SF-36, WHOQOL-BREF	English	Evaluate the measurement properties of the QoL Survey and compare them to those of the SF-36	n = 446 university students enrolled in Fitness for Life classes; age, 20.4 ± 4.02; 67% women	Enrolled in a Fitness for Life class	"A subjective, multidimensional, integrative construct that reflects optimal well-being and positive health"	Structural validity, internal consistency, test-retest reliability, construct validity
Huffman et al[25] United States	SF-36	English	Compare SF-36 scores of competitive athletes with those of an age-matched general population sample	n = 696 NCAA Division I and II college athletes; age, 20.4 y (17-23 y); 41% female	Participated in collegiate sports	NR	Internal consistency
Hoch et al[22] United States	SF-12, DPA-MSC	English	Determine the relationship between the SF-12, DPA, and PROMIS-PF	n = 100 collegiate or recreational athletes with a lower extremity musculoskeletal injury; age, 20.40 ± 2.19 y; sex NR	Reported being physically active >90 minutes/week	NR	Construct validity, interpretability, feasibility
Cielask et al[5] Brazil	WHOQOL-BREF	NR	Describe HRQoL and physical activity	n = 85 physical education students; age, 20.74 ± 2.79 y; 46% women	Classified as very active or active on the IQPA	"The individual's perception of his position in life in the context of culture and system of values and in relation to his objectives, expectations, patterns, and worries"	Internal consistency
Sauers et al[43] United States	FAST	English	Develop an upper extremity, region-specific and population-specific PROM to measure HRQoL in throwing athletes	n = 830 baseball and softball athletes, with and without a throwing injury; age, 16.5 ± 0.9 y (baseball) and 19.5 ± 1.1 y (softball); 0% (baseball) and 28% (softball) female	Participated in baseball or softball	"The physical, psychological, and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations, and perceptions"	Content validity, structural validity, internal consistency
Sauers et al[44] United States	FAST	English	Evaluate relationships between upper extremity injury history, current pain rating, and HRQoL in softball pitchers	n = 25 competitive high school and college softball pitchers without a current musculoskeletal injury; age, 18.3 ± 2.0 y; 100% female	Participated in softball	"The physical, psychological, and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations, and perceptions"	Construct validity
Huxel Bliven et al[26] United States	FAST	English	Evaluate the measurement properties of the FAST	n = 557 baseball and softball players, with and without a current musculoskeletal upper extremity injury; age, 17.9 ± 2.3 y; 18.2 ± 2.1 y; 18.8 ± 2.2 y; 20.0 ± 2.2 y; 0%-27% women	Participated in baseball or softball	NR	Test-retest reliability, measurement error, construct validity, responsiveness, interpretability

Table continues on page 485.

TABLE 2 Characteristics of Included Studies (continued)

Study, Country	HRQoL PROM	Language of PROM	Primary Objective	Sample[a]	Physical Activity Description	HRQoL Definition	Measurement Properties Evaluated
Drew et al[10] Australia	HAGOS-QoL	English	Establish normative HAGOS scores in Australian football	n = 75 professional and semi-professional Australian football players, with and without current groin pain; age, 23.1 ± 3.1 y; 0% women	Participated in Australian football	NR	Structural validity, interpretability
Hinman et al[20] Australia	HAGOS-QoL, HOOS-QoL, iHOT-33	English	Evaluate the test-retest reliability of hip-related PROMs in active youth with FAI	n = 30 young adults with hip and/or groin pain; age, 24 ± 4 y; 50% women	Reported being physically active for a mean of 6 hours/week	NR	Test-retest reliability, measurement error, feasibility
Clapp et al[6] United States	iHOT-12	English	Compare 2-y iHOT-12 scores of competitive athletes and nonathletes undergoing hip arthroscopy	n = 59 professional, semi-professional, or college athletes who underwent hip arthroscopy for FAI; age, 22.0 ± 4.8 y; 63% women	Participated in competitive sports	NR	Interpretability
Hoch et al[21] United States	KOOS-QoL	English	Evaluate the test-retest reliability and estimate the MDC of the DPA, FAAM-S, and KOOS	n = 16 NCAA Division I soccer players without a current musculoskeletal injury; age, 19.7 ± 1.0 y (women) and 19.9 ± 0.9 y (men); 56% women	Participated in soccer	"A person's function in everyday life and an evaluation of his or her physical, psychological, and social aspects of health derived from personal beliefs, preferences, experiences, and expectations"	Test-retest reliability, measurement error, feasibility
Edmonds et al[11] United States	PASS	English	Evaluate the reliability and validity of the PASS	n = 132 individuals with a shoulder injury; age, 16 ± 2 y; 30% female	Participated in a sport, including overhead throwing sports	NR	Construct validity, responsiveness, interpretability, feasibility

Abbreviations: ALQS, Athlete Life Quality Scale; DPA, Disablement in the Physically Active scale; DPA-MSC, Disablement in the Physically Active scale-mental summary component; DPA-MSC SF-8, 8-item Disablement in the Physically Active scale-mental summary component Short Form; DPA-MSC SF-10, 10-item Disablement in the Physically Active scale-mental summary component Short Form; FAAM-S, Foot and Ankle Ability Measure sports subscale; FAI, femoroacetabular impingement; FAST, Functional Arm Scale for Throwers; GLTEQ, Godin Leisure-Time Exercise Questionnaire; HAGOS-QoL, Copenhagen Hip and Groin Outcome Score hip-related quality of life subscale; HOOS-QoL, Hip dysfunction and Osteoarthritis Outcome Score hip-related quality of life subscale; HRQoL, health-related quality of life; iHOT-12, 12-item International Hip Outcome Tool; iHOT-33, 33-item International Hip Outcome Tool; IQPA, International Questionnaire of Physical Activity; KIDSCREEN-10, 10-item KIDSCREEN index; KIDSCREEN-52, 52-item KIDSCREEN questionnaire; KOOS-QoL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; MDC, minimal detectable change; MVPA, moderate-to-vigorous physical activity; NCAA, National Collegiate Athletic Association; NR, not reported; PASS, Pediatric/Adolescent Shoulder Survey; PedsQL, Pediatric Quality of Life Inventory; PROM, patient-reported outcome measure; PROMIS-PF, Patient-Reported Outcomes Measurement Information System physical functioning domain; QoL, quality of life; SF-12, Medical Outcomes Study 12-Item Short-Form Health Survey; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; WHOQOL-BREF, World Health Organization Quality of Life instrument-abbreviated version.
[a]Age values are mean, mean ± SD, mean (range), or range.

Content Validity Two studies[17,55] described the development of the ALQS and DPA-MSC (supplemental file 6). The ALQS[17] had very low–quality evidence for insufficient content validity because it did not address relevance, comprehensiveness, or comprehensibility in a sample of uninjured collegiate athletes (supplemental file 7). The development of the DPA-MSC[55] included qualitative interviews with injured competitive and recreational youth athletes, but it was unclear whether the athletes were asked about comprehensiveness or comprehensibility; therefore, it was rated as low-quality evidence due to inconsistent content validity.

Structural Validity Six studies[2,17,18,23,29,55] assessed the structural validity of 6 PROMs. The DPA-MSC was investigated across 3 studies.[2,23,55] In 1 study including injured active youth,[55] the DPA-MSC possessed high-quality evidence for insufficient structural validity; however, in studies with uninjured active youth[23] or both injured and uninjured active youth,[2] its structural validity was indeterminate. The DPA-MSC SF-10,[2] DPA-MSC SF-8,[2] KIDSCREEN-52,[29] and QoL Survey[18] demonstrated moderate- or high-quality evidence for sufficient structural validity. The ALQS[17] demonstrated indeterminate structural validity.

Internal Consistency Twelve studies[2,5,17,18,23,25,29,40,46,55,59,60] investigated the internal consistency of 10 PROMs. The DPA-MSC SF-10,[2] DPA-MSC SF-8,[2] KIDSCREEN-52,[29] and QoL Survey[18] had high-quality evidence for sufficient internal consistency. The ALQS,[17] PedsQL,[60] SF-36,[18,25] and WHOQOL-BREF[18] had indeterminate ratings, as they lacked sufficient structural validity in active youth. The DPA-MSC had very low–quality evidence for insufficient internal consistency in injured active youth[40,55] but indeterminate findings in uninjured active youth[23] and in both injured and uninjured active youth.[59] The WHOQOL-BREF findings from 1 study[5] were not included in the qualitative summary due to poor overall study quality.

TABLE 3 Overall Rating and Quality of Evidence for HRQoL PROMs[a]

	Content Validity		Structural Validity		Internal Consistency		Test-Retest Reliability		Measurement Error		Construct Validity		Criterion Validity		Responsiveness		
	Rating[b]	QE[c]	Rating[b]	QE[c]	Rating[b]	QE[c]	Rating[b]	QE[c]	Rating[b]	QE[c]	Rating[b]	QE[c]	Rating[b]	QE[c]	Rating[b]	QE[c]	FR[d]
Generic PROMs																	
ALQS	–	VL	?	M	?	L											B
DPA-MSC	±	L	–, ?	H, M	–, ?	VL, H	+	VL			?	VL	+, –	VL, H	+	L	C
DPA-MSC SF-10[e]			+	H	+	H											B
DPA-MSC SF-8[e]			+	H	+	H											B
KIDSCREEN-52			+	M	+	H											B
KIDSCREEN-10					+	VL											B
PedsQL					?	H					?	H					B
QoL Survey[e]			+	H	+	H	+	M			?	M					B
SF-36					?	H	?	M									B
SF-12											?	VL					B
WHOQOL-BREF					?	H											B
Condition-specific PROMs																	
FAST[e]	±	L	+	H	+	H	+	L	?	L	?, +	VL			+	L	B
HAGOS-QoL			?	VL			+	VL	?	VL							B
HOOS-QoL							+	VL	?	VL							B
iHOT-33							+	VL	?	VL							B
iHOT-12																	B
KOOS-QoL							+	VL	?	VL							B
PASS	–	VL									?	VL			?	VL	B

Abbreviations: –, insufficient; +, sufficient; ±, inconsistent; ?, indeterminate; ALQS, Athlete Life Quality Scale; DPA-MSC, Disablement in the Physically Active scale-mental summary component; DPA-MSC SF-8, 8-item Disablement in the Physically Active scale-mental summary component Short Form; DPA-MSC SF-10, 10-item Disablement in the Physically Active scale-mental summary component Short Form; FAST, Functional Arm Scale for Throwers; FR, final recommendation; H, high; HAGOS-QoL, Copenhagen Hip and Groin Outcome Score hip-related quality of life subscale; HOOS-QoL, Hip dysfunction and Osteoarthritis Outcome Score hip-related quality of life subscale; HRQoL, health-related quality of life; iHOT-12, 12-item International Hip Outcome Tool; iHOT-33, 33-item International Hip Outcome Tool; KIDSCREEN-10, 10-item KIDSCREEN index; KIDSCREEN-52, 52-item KIDSCREEN questionnaire; KOOS-QoL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; L, low; M, moderate; PASS, Pediatric/Adolescent Shoulder Survey; PedsQL, Pediatric Quality of Life Inventory; PROM, patient-reported outcome measure; QE, quality of evidence; QoL, quality of life; SF-12, Medical Outcomes Study 12-Item Short-Form Health Survey; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; VL, very low; WHOQOL-BREF, World Health Organization Quality of Life instrument-abbreviated version.

[a]*Blank cells indicate that no identified study evaluated the measurement property. Each measurement property could have more than 1 overall rating and/or QE rating.*

[b]*The overall rating of summarized results by PROM, rated as sufficient, indeterminate, inconsistent, or insufficient, as per the COnsensus-based Standards for the selection of health Measurement INstruments criteria for good measurement properties.*[45,53]

[c]*The QE by PROM, graded as high, moderate, low, or very low, as per the modified Grading of Recommendations Assessment, Development and Evaluation approach.*[36,37,41,51]

[d]*The FR for a PROM was categorized as "A" (evidence for sufficient content validity and at least low-quality evidence for sufficient internal consistency), "B" (neither "A" nor "C"), or "C" (high-quality evidence for any insufficient measurement property).*[36,37,41,51]

[e]*The most suitable existing HRQoL PROMs, after evaluating measurement properties, interpretability, and feasibility.*

Test-Retest Reliability Two studies[18,55] examined the test-retest reliability of 3 PROMs. The DPA-MSC[55] demonstrated very low–quality evidence for sufficient reliability due to imprecision (ie, sample size fewer than 50), the QoL Survey[18] had moderate-quality evidence for sufficient reliability, and the SF-36[18] had indeterminate reliability.

Construct Validity Four studies evaluated the construct (convergent) validity of the DPA-MSC,[59] PedsQL,[60] QoL Survey,[18] and SF-12[22] compared to generic HRQoL, life satisfaction, physical functioning, physical activity, self-efficacy, and/or social support. All studies had indeterminate results because no a priori hypotheses were provided.

Criterion Validity Two studies[23,55] evaluated the criterion validity of the DPA-MSC. The DPA-MSC demonstrated very low–quality evidence for sufficient criterion validity with a single global functioning item in injured active youth,[55] and high-quality evidence for insufficient criterion validity with the DPA total score in uninjured active youth.[24]

Responsiveness One study[55] assessed the responsiveness of the DPA-MSC. The DPA-MSC[55] possessed low-quality evidence for sufficient responsiveness in active youth with an acute or persistent musculoskeletal injury.

Other Measurement Properties No included studies assessed the measurement error or cross-cultural validity (ie, validity across ethnicities, languages, sexes, ages, or patient groups) of generic HRQoL PROMs.

Interpretability and Feasibility Interpretability and feasibility characteristics for generic HRQoL PROMs are outlined in supplemental files 8 and 9. The minimal important change (MIC) for the DPA-MSC[55] was estimated to be 9 points for youth with an acute musculoskeletal injury and 6 points for youth with a persistent musculoskeletal injury, using anchor-based methods. The SF-36[25,58] was reported to have a MIC of 10 points for domain scores and 5 points for summary component scores. The KIDSCREEN questionnaires (for commercial use), PedsQL, and SF-12 had a user fee.

Final Recommendation All generic HRQoL PROMs except the DPA-MSC were given a final recommendation of "B," as none provided evidence for sufficient content validity in active youth (**TABLE 3**). The DPA-MSC was assigned a final recommendation of "C" due to high-quality evidence for insufficient structural validity[55] and criterion validity.[23] The DPA-MSC SF-10, DPA-MSC SF-8, and QoL Survey had high-quality evidence for sufficient structural validity and internal consistency, and the QoL Survey also had moderate-quality evidence for sufficient test-retest reliability. With other generic instruments having indeterminate or inconsistent measurement properties, the DPA-MSC SF-10, DPA-MSC SF-8, and QoL Survey were considered the most suitable existing generic HRQoL PROMs for active youth.

Condition-Specific HRQoL Instruments

Seven condition-specific HRQoL PROMs were evaluated in 8 of 21 studies (38%).[6,10,11,20,21,26,43,44] An overview of these instruments is found in supplemental file 5. Two PROMs were specific to the upper extremity (the Functional Arm Scale for Throwers [FAST][26,43,44] and Pediatric/Adolescent Shoulder Survey [PASS][11]), 4 to the hip (Copenhagen Hip and Groin Outcome Score hip-related quality of life [HAGOS-QoL] subscale,[10,20] Hip dysfunction and Osteoarthritis Outcome Score hip-related quality of life [HOOS-QoL] subscale,[20] 33-item International Hip Outcome Tool [iHOT-33],[20] and 12-item International Hip Outcome Tool [iHOT-12][6]), and 1 to the knee (Knee injury and Osteoarthritis Outcome Score knee-related quality of life [KOOS-QoL] subscale[21]). Three condition-specific instruments were a subscale of a larger PROM. Higher scores reflected better HRQoL outcomes in all PROMs except for the FAST. All studies used self-completed administration.

Content Validity Two studies[11,43] described the content validity of the FAST and PASS (supplemental file 6). The FAST had low-quality evidence for inconsistent content validity, as relevance, comprehensiveness, and comprehensibility were not established in uninjured competitive and recreational throwing athletes (supplemental file 7).[43] The PASS demonstrated very low–quality evidence for insufficient content validity because the study did not conduct interviews or focus groups in active youth with a shoulder injury.[11]

Structural Validity Two studies[10,43] examined the structural validity of 2 PROMs. The FAST[43] had high-quality evidence for sufficient structural validity, whereas the HAGOS-QoL subscale[10] had indeterminate structural validity.

Internal Consistency One study[43] evaluated internal consistency. The FAST[43] demonstrated high-quality evidence for sufficient internal consistency.

Test-Retest Reliability Three studies[20,21,26] investigated the test-retest reliability of 5 PROMs. The HAGOS-QoL subscale,[20] HOOS-QoL subscale,[20] iHOT-33,[20] and KOOS-QoL subscale[21] possessed very low–quality evidence for sufficient reliability due to imprecision. The FAST[26] had low-quality evidence for sufficient reliability due to a short test-retest interval (mean, 4.5 days).

Measurement Error Three studies[20,21,26] examined the measurement error of 5 PROMs. The FAST,[26] HAGOS-QoL subscale,[20] HOOS-QoL subscale,[20] iHOT-33,[20] and KOOS-QoL[21] subscale all had indeterminate results, as a MIC was not defined.

Construct Validity Three studies[11,26,44] assessed the convergent validity of 2 PROMs. The FAST[26,44] and PASS[11] had indeterminate results because no a priori hypotheses were stated. The FAST[26] demonstrated low-quality evidence for sufficient known-groups validity between injured and uninjured active youth.

Responsiveness Two studies[11,26] assessed the responsiveness of 2 PROMs. The FAST[26] had low-quality evidence for sufficient responsiveness, whereas the PASS had indeterminate responsiveness.[11]

Other Measurement Properties No included studies assessed the criterion or cross-cultural validity of condition-specific HRQoL instruments.

Interpretability and Feasibility Interpretability and feasibility characteristics for condition-specific HRQoL PROMs are described in supplemental files 8 and 9. There were missing data for the KOOS-QoL subscale (11%)[21] and PASS (20.5%).[11] The MIC for the iHOT-12 was estimated to be 12.1 points[6] using distribution-based methods. The MIC for both the HAGOS-QoL subscale and iHOT-33 was stated to be 10 to 15 points.[35,52] All condition-specific HRQoL instruments were free to use.

Final Recommendation All condition-specific HRQoL PROMs were given a final recommendation of "B" due to a lack of sufficient content validity in active youth (**TABLE 3**). The FAST was the only instrument with high-quality evidence for sufficient structural validity and internal consistency. We judged the FAST to be the most suitable existing condition-specific HRQoL PROM for active youth.

Comparison of HRQoL PROMs Between Injured and Uninjured Active Youth

Of the 18 HRQoL PROMs identified, 5 were only evaluated in injured active youth (the SF-12,[22] HOOS-QoL subscale,[20] iHOT-33,[20] iHOT-12,[6] and PASS[11]), 8 were only evaluated in uninjured active youth (the ALQS,[17] KIDSCREEN-52,[29] KIDSCREEN-10,[46] PedsQL,[60] QoL Survey,[18] SF-36,[18,25] WHOQOL-BREF,[5,18] and KOOS-QoL subscale[21]), and 5 were evaluated in both injured and uninjured active youth (the DPA-MSC,[2,22,23,40,55,59] DPA-MSC SF-10,[2] DPA-MSC SF-8,[2] FAST,[26,43,44] and HAGOS-QoL subscale[10,20]). Of the instruments evaluated in both injured and uninjured active youth, there was limited overlap in the measurement properties assessed. Only the DPA-MSC had the same measurement properties assessed across multiple studies involving different samples.[2,22,23,40,55,59] The structural validity and internal consistency of the DPA-MSC demonstrated insufficient results in injured active youth but indeterminate results otherwise (supplemental file 7).

DISCUSSION

We identified and evaluated 11 generic and 7 condition-specific HRQoL PROMs for active youth. The methodological quality, overall results ratings, and quality of evidence for measurement properties across different instruments were highly variable. Only 2 generic and 2 condition-specific HRQoL PROMs assessed content validity, and all demonstrated low or very low evidence for inconsistent or insufficient content validity. There was little information about interpretability and feasibility. Ultimately, no identified PROMs warranted a final recommendation of "A," suggesting that there is no suitable generic or condition-specific HRQoL PROM for active youth.

Lacking sufficient content validity undermines the methodological quality of a study and reduces confidence in its results.[51] The absence of sufficient content validity across PROMs used to assess the HRQoL of active youth is a serious limitation. We note that all PROM development studies[11,17,43,55] identified in our review were published before the 2018 COSMIN risk-of-bias checklist[36,41,51] and would not have benefited from this resource to assess content validity.

Structural validity, internal consistency, and cross-cultural validity of a PROM describe how individual items within an instrument are related and organized into subscales.[36] The DPA-MSC SF-10,[2] DPA-MSC SF-8,[2] QoL Survey,[18] and FAST[43,44] were the only PROMs with high-quality evidence for sufficient structural validity and internal consistency, and are therefore considered the most suitable existing HRQoL PROMs for active youth. Given that there is no difference in the items of the 2 DPA-MSC short forms (ie, the discrepancy in items lies in the physical summary component), we recommend the DPA-MSC SF-8, as it requires less time to complete and score.

The absence of evidence of other measurement properties limits the ability of PROMs to monitor HRQoL over time. Establishing test-retest reliability, measurement error, and responsiveness allows clinicians and researchers to understand whether a change in PROM score truly reflects patients' perceived change of their HRQoL (ie, not due to random error). Estimating a MIC is also important for determining whether change scores are meaningful to patients.

This systematic review is the first to examine the quality of existing HRQoL instruments used in active youth. Although not specifically focused on active youth or musculoskeletal conditions, 1 previous review in 2008[48] identified 94 instruments, with the KIDSCREEN and PedsQL demonstrating acceptable validity and reliability. In contrast, we found that the KIDSCREEN-52 had moderate- or high-quality evidence for sufficient structural validity and internal consistency, while the PedsQL showed indeterminate ratings for internal consistency and construct validity, suggesting that both instruments should be further examined to determine whether they are suitable for active youth populations.

Research Recommendations

The ideal HRQoL PROM for active youth is psychometrically robust, easy to interpret, and applicable in clinical and research settings. Without an ideal instrument, researchers must re-evaluate existing HRQoL PROMs or develop a new HRQoL PROM for active youth. As instrument development requires immense time, effort, and resources, it may be prudent to first re-evaluate existing HRQoL PROMs.

Future studies examining measurement properties of HRQoL instruments should follow the COSMIN risk-of-bias checklist.[36,41,51] Content validity must be well established by seeking input from members of the target population who represent different manifestations of HRQoL (eg, high and low HRQoL) and demographics (eg, varying age, sex, and ethnicity). Then, other measurement properties can be assessed, starting with structural validity and internal consistency, to understand a PROM's internal structure. To address interpretability and feasibility, investigators should report missing item data, floor and ceiling effects, a MIC, time to complete and score, and costs.

Until a suitable HRQoL PROM is available, we propose using a mixed-methods approach[27] in which generic and condition-specific PROMs are used alongside qualitative methods to study the HRQoL of active youth. When possible, we recommend the DPA-MSC SF-8, QoL Survey, and FAST to measure HRQoL. Additionally, conducting interviews with young people from varying sports or activities, competition levels, and health statuses may provide a more in-depth understanding of what HRQoL means to active youth and which determinants are important to them.

Clinical Implications

Clinicians who wish to learn how to select a suitable PROM are encouraged to review the COSMIN risk-of-bias checklist[36,41,51] and explore the COSMIN website resources. The most suitable PROM for clinical use is one that is easy to understand, requires minimal time to complete and score, and is free to use. To assess the HRQoL of active youth with musculoskeletal injuries, we recommend collating findings from generic and condition-specific PROMs and selecting the DPA-MSC SF-8, QoL Survey, and FAST when appropriate. Clinicians may also review responses to individual items to spark conversations regarding a patient's perception of injury, facilitators of and barriers to rehabilitation, and strategies to improve recovery. Information from overall PROM scores and individual item responses can help clinicians tailor treatment plans to the individual athlete.

Strengths and Limitations

Adhering to the COSMIN user manual[36,37,41,51] provided a standardized approach to evaluating measurement properties, interpretability, and feasibility and providing a final recommendation. As the COSMIN user manual[36,37,41,51] is a universal resource, the findings of this review can be compared to past and future research.

A limitation of using the COSMIN user manual,[36,37,41,51] including the 2018 COSMIN risk-of-bias checklist, is that many studies (71%) were judged on more rigorous criteria that did not exist at the time of their design. This may have resulted in stricter ratings and final recommendations for PROMs developed or evaluated before 2018. Despite a comprehensive search strategy, our stringent inclusion criteria likely excluded some relevant PROMs. For example, using sample mean or median age excluded the Anterior Cruciate Ligament-Quality of Life (ACL-QoL) questionnaire, a commonly used condition-specific PROM for young athletes with an anterior cruciate ligament injury, because it was developed in a sample with a mean age of 27.6 years.[34] It is worth assessing other HRQoL PROMs like the ACL-QoL questionnaire to determine their measurement properties, interpretability, and feasibility for active youth. We also acknowledge the heterogeneity of the included studies, with few studies assessing the same PROM. Finally, there is likely a difference in variability of PROM scores between injured and uninjured youth (ie, injured youth tend to demonstrate greater variability) across studies, which may limit the generalizability of measurement properties evaluated between the 2 groups.

CONCLUSION

No HRQoL PROM had sufficient content validity. The DPA-MSC SF-8 (generic), QoL Survey (generic), and FAST (condition-specific) demonstrated high-quality evidence for sufficient structural validity and internal consistency and were the most suitable existing HRQoL PROMs for active youth. Until a definitively robust instrument is available, we recommend selecting the DPA-MSC SF-8, QoL Survey, and FAST; using multiple PROMs; and applying mixed methods to gain a holistic understanding of the HRQoL of active youth. ◉

KEY POINTS

FINDINGS: No definitively robust patient-reported outcome measure (PROM) to measure the health-related quality of life (HRQoL) of active youth currently exists, due to the lack of sufficient content validity. The 8-item Disablement in the Physically Active scale-mental summary component Short Form (DPA-MSC SF-8), Quality of Life (QoL) Survey, and Functional Arm Scale for Throwers (FAST) are the most suitable existing HRQoL PROMs, as they demonstrated sufficient structural validity and internal consistency.

IMPLICATIONS: Until a robust PROM is available, we recommend selecting the DPA-MSC SF-8, QoL Survey, or FAST to assess the HRQoL of active youth when possible. Researchers may also consider using mixed methods, combining quantitative and qualitative approaches, to best capture active youth HRQoL.

CAUTION: Low to very low quality of evidence or indeterminate results for some measurement properties of the identified HRQoL PROMs indicate that these instruments need to be re-examined for use in active youth, not that they should be abandoned altogether.

STUDY DETAILS

AUTHOR CONTRIBUTIONS: Christina Y. Le and Dr Whittaker were responsible for the conception of the research question and study design. Christina Y. Le, Liz Dennett, and Dr Whittaker developed the search strategy, and Christina Y. Le executed the search strategy. Christina Y. Le, Linda K. Truong, Christopher J. Holt, and Drs Filbay and Whittaker independently reviewed records, and all authors contributed to the patient-reported outcome measure evaluation

process, including data extraction and interpretation of findings. Christina Y. Le was responsible for the first draft of the manuscript. All authors contributed to the critical revision of the manuscript and reviewed the document prior to submission.

DATA SHARING: All data sets not included in the online supplemental files are available from the corresponding author on reasonable request.

PATIENT AND PUBLIC INVOLVEMENT: No patients or public partners were involved in this research.

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Appendix F: Search Strategy (Chapter 2)

1. Search strategy for MEDLINE (OVID)

No.	Search
1	adolescent/ or young adult/ or child/
2	(youth* or adolescen* or teen* or child* or pediatr* or paediatr* or school* or pubescen* or young adult* or high school or senior high or university* or colleg* or post secondary* or student* or varsity).mp.
3	1 or 2
4	exp Sports/
5	Athletes/
6	(sport* or athlet* or phys ed or physical education or gym* or aerobic* or exercise* or physical* activ* or fitness or archery or badminton or baseball or basketball or bandy or biathlon or bobsleigh* or body building or bowling or boxing or boxer* or bull fight* or canoe* or cheerlead* or cricket* or cross country ski* or curling or curler* or cycling or danc* or decathlon or diving or equestrian* or fencing or fencer* or field hockey or figure skat* or football* or gridiron or golf* or gymnast* or handball or hockey or ice hockey or judo or jogging or jogger* or ju jitsu or karate or kayak* or kung fu or lacrosse or lawn bowl* or luge* or martial art* or mountain bik* or marathon or mountaineering or netball or nordic combined or pentathlon or plyometric* or polo or racing or racquetball or rock climb* or rodeo or rowing or rugby or running or runner* or sailing or shooting* or ski or skiing or skier* or skat* or skeleton or soccer or softball or snowboard* or squash or surfer* or surfing or swim* or taewkondo or tennis or (track and field) or trampolin* or triathlon or ultimate frisbee or volleyball or walker or walking or water polo or weight lift* or workouts or work* out* or wrestl* or yoga).mp.
7	4 or 5 or 6
8	(quality of life or QOL* or health-related quality of life or HRQoL or HRQL or wellbeing or well-being or wellness or life satisfaction).mp.
9	exp "surveys and questionnaires"/ or exp health care surveys/
10	(questionnaire or survey or scale or scale* or survey* or questionnaire* or index or checklist or tool or tools or test or tests or instrument or instruments or score* or inventory or self report* or self-rated or SF* or short-form 36 or short-form 12 or short-form 8 or EQ-5D* or EQ-VAS or health utilities index* or Sickness Impact Profile or Nottingham Health Profile or RAND or Quality of Well Being Scale or QWB or Athlete Life Quality Scale or ALQS or Flourishing Scale or Trojan Lifetime Champions or (Knee injury and Osteoarthritis Outcome Score) or KOOS or (Disabilities of the Arm Shoulder and Hand) or Pediatric Quality of Life Inventory or PedsQL or Pediatric Outcomes Data Collection Instrument or PODCI).mp.
11	9 or 10
12	Psychometrics/
13	validation studies/
14	exp "REPRODUCIBILITY OF RESULTS"/
15	(valid* or responsive* or reproduca* or reproduci* or generali?ab* or reliability or sensitivity or specificity or correlation* or psychometric or clinimetric* or accuracy or interpretability or minimal clinical* important difference or MCID or minimal important difference or MID or minimal clinical* important change or MCIC or minimal clinical* important improvement or MCII or standard error of measurement or SEM or COSMIN or internal consistency or measurement propert* or measurement error or hypotheses test* or cross cultural validity or criterion validity or construct validity or content validity or face validity).mp.
16	12 or 13 or 14 or 15
17	3 and 7 and 8 and 11 and 16
18	17 not (elder* or geriatric* or older adult* or infant* or preschool* or pre-school* or ADHD or amput* or aneurysm or angina or arthrit* or asthm* or autis* or bowel disease* or bowel syndrome* or brain injur* or cancer* or cardiac or cardiomyopath* or cerebral palsy or CP or cleft or

	concussion* or COPD or cystic fibrosis or dental or depression or diabet* or down* syndrome or eczema or epilep* or fibromyalg* or heart disease* or CHD or heart failure or CHF or hemophili* or haemophili* or HIV or hypertension or HTN or incontinence or infection* or kidney disease* or CKD or leukaemia or leukemia or lung disease* or menopaus* or multiple scleros* or muscular dystrophy or oral health* or obes* or osteoarthriti* or OA or overweight or parkinson* or post natal or post-natal or post stroke or post-stroke or post traumatic stress or post-traumatic stress or pregnan* or psychiatric or psychotic* or pulmonary disease or scolio* or schizophr* or sexual* abus* or spina bifida or spinal cord injur* or SCI or stenosis or stroke or transplant* or tumor* or tumour* or vestibular).ti.
19	limit 18 to English language

2. Search strategy for EMBASE (OVID)

No.	Search
1	adolescent/ or young adult/ or child/
2	(youth* or adolescen* or teen* or child* or pediatr* or paediatr* or school* or pubescen* or young adult* or high school or senior high or university* or colleg* or post secondary* or student* or varsity).mp.
3	1 or 2
4	exp sports/
5	exp athlete/
6	(sport* or athlet* or phys ed or physical education or gym* or aerobic* or exercise* or physical* activ* or fitness or archery or badminton or baseball or basketball or bandy or biathlon or bobsleigh* or body building or bowling or boxing or boxer* or bull fight* or canoe* or cheerlead* or cricket* or cross country ski* or curling or curler* or cycling or danc* or decathlon or diving or equestrian* or fencing or fencer* or field hockey or figure skat* or football* or gridiron or golf* or gymnast* or handball or hockey or ice hockey or judo or jogging or jogger* or ju jitsu or karate or kayak* or kung fu or lacrosse or lawn bowl* or luge* or martial art* or mountain bik* or marathon or mountaineering or netball or nordic combined or pentathlon or plyometric* or polo or racing or racquetball or rock climb* or rodeo or rowing or rugby or running or runner* or sailing or shooting* or ski or skiing or skier* or skat* or skeleton or soccer or softball or snowboard* or squash or surfer* or surfing or swim* or taewkondo or tennis or (track and field) or trampolin* or triathlon or ultimate frisbee or volleyball or walker or walking or water polo or weight lift* or workouts or work* out* or wrestl* or yoga).mp.
7	4 or 5 or 6
8	(quality of life or QOL* or health-related quality of life or HRQoL or HRQL or wellbeing or well-being or wellness or life satisfaction).mp.
9	exp questionnaires/ or exp health care surveys/
10	(questionnaire or survey or scale or scale* or survey* or questionnaire* or index or checklist or tool or tools or test or tests or instrument or instruments or score* or inventory or self report* or self-rated or SF* or short-form 36 or short-form 12 or short-form 8 or EQ-5D* or EQ-VAS or health utilities index* or Sickness Impact Profile or Nottingham Health Profile or RAND or Quality of Well Being Scale or QWB or Athlete Life Quality Scale or ALQS or Flourishing Scale or Trojan Lifetime Champions or (Knee injury and Osteoarthritis Outcome Score) or KOOS or (Disabilities of the Arm Shoulder and Hand) or Pediatric Quality of Life Inventory or PedsQL or Pediatric Outcomes Data Collection Instrument or PODCI).mp.
11	9 or 10
12	psychometry/
13	validation study/
14	reproducibility/

15	(valid* or responsive* or reproduca* or reproduci* or generali?ab* or reliability or sensitivity or specificity or correlation* or psychometric or clinimetric* or accuracy or interpretability or minimal clinical* important difference or MCID or minimal important difference or MID or minimal clinical* important change or MCIC or minimal clinical* important improvement or MCII or standard error of measurement or SEM or COSMIN or internal consistency or measurement propert* or measurement error or hypotheses test* or cross cultural validity or criterion validity or construct validity or content validity or face validity).mp.
16	12 or 13 or 14 or 15
17	3 and 7 and 8 and 11 and 16
18	17 not (elder* or geriatric* or older adult* or infant* or preschool* or pre-school* or ADHD or amput* or aneurysm or angina or arthrit* or asthm* or autis* or bowel disease* or bowel syndrome* or brain injur* or cancer* or cardiac or cardiomyopath* or cerebral palsy or CP or cleft or concussion* or COPD or cystic fibrosis or dental or depression or diabet* or down* syndrome or eczema or epilep* or fibromyalg* or heart disease* or CHD or heart failure or CHF or hemophili* or haemophili* or HIV or hypertension or HTN or incontinence or infection* or kidney disease* or CKD or leukaemia or leukemia or lung disease* or menopaus* or multiple scleros* or muscular dystrophy or oral health* or obes* or osteoarthriti* or OA or overweight or parkinson* or post natal or post-natal or post stroke or post-stroke or post traumatic stress or post-traumatic stress or pregnan* or psychiatric or psychotic* or pulmonary disease or scolio* or schizophr* or sexual* abus* or spina bifida or spinal cord injur* or SCI or stenosis or stroke or transplant* or tumor* or tumour* or vestibular).ti.
19	limit 19 to English language

3. Search strategy for CINAHL (EBSCOhost)

No.	Search
S1	(MH "Adolescence")
S2	(MH "Young Adult")
S3	(MH "Child")
S4	youth* or adolescen* or teen* or child* or pediatr* or paediatr* or school* or pubescen* or young adult* or high school or senior high or university* or colleg* or post secondary* or student* or varsity
S5	S1 OR S2 OR S3 OR S4
S6	(MH "Sports+")
S7	(MH "Athletes")
S8	sport* or athlet* or phys ed or physical education or gym* or aerobic* or exercise* or physical* activ* or fitness or archery or badminton or baseball or basketball or bandy or biathlon or bobsleigh* or body building or bowling or boxing or boxer* or bull fight* or canoe* or cheerlead* or cricket* or cross country ski* or curling or curler* or cycling or danc* or decathlon or diving or equestrian* or fencing or fencer* or field hockey or figure skat* or football* or gridiron or golf* or gymnast* or handball or hockey or ice hockey or judo or jogging or jogger* or ju jitsu or karate or kayak* or kung fu or lacrosse or lawn bowl* or luge* or martial art* or mountain bik* or marathon or mountaineering or netball or nordic combined or pentathlon or plyometric* or polo or racing or racquetball or rock climb* or rodeo or rowing or rugby or running or runner* or sailing or shooting* or ski or skiing or skier* or skat* or skeleton or soccer or softball or snowboard* or squash or surfer* or surfing or swim* or taewkondo or tennis or (track and field) or trampolin* or triathlon or ultimate frisbee or volleyball or walker or walking or water polo or weight lift* or workouts or work* out* or wrestl* or yoga
S9	S6 OR S7 OR S8
S10	quality of life or QOL* or health-related quality of life or HRQoL or HRQL or wellbeing or well-being or wellness or life satisfaction

S11	(MH "Surveys") OR (MH "Questionnaires")
S12	questionnaire or survey or scale or scale* or survey* or questionnaire* or index or checklist or tool or tools or test or tests or instrument or instruments or score* or inventory or self report* or self-rated or SF* or short-form 36 or short-form 12 or short-form 8 or EQ-5D* or EQ-VAS or health utilities index* or Sickness Impact Profile or Nottingham Health Profile or RAND or Quality of Well Being Scale or QWB or Athlete Life Quality Scale or ALQS or Flourishing Scale or Trojan Lifetime Champions or (Knee injury and Osteoarthritis Outcome Score) or KOOS or (Disabilities of the Arm Shoulder and Hand) or Pediatric Quality of Life Inventory or PedsQL or Pediatric Outcomes Data Collection Instrument or PODCI
S13	S11 OR S12
S14	(MH "Psychometrics")
S15	(MH "Validation Studies")
S16	(MH "Reproducibility of Results")
S17	valid* or responsive* or reproduca* or reproduci* or generali?ab* or reliability or sensitivity or specificity or correlation* or psychometric or clinimetric* or accuracy or interpretability or minimal clinical* important difference or MCID or minimal important difference or MID or minimal clinical* important change or MCIC or minimal clinical* important improvement or MCII or standard error of measurement or SEM or COSMIN or internal consistency or measurement propert* or measurement error or hypotheses test* or cross cultural validity or criterion validity or construct validity or content validity or face validity
S18	S14 OR S15 OR S16 OR S17
S19	S5 AND S9 AND S10 AND S13 AND S18
S20	S19 NOT (elder* or geriatric* or older adult* or infant* or preschool* or pre-school* or ADHD or amput* or aneurysm or angina or arthrit* or asthm* or autis* or bowel disease* or bowel syndrome* or brain injur* or cancer* or cardiac or cardiomyopath* or cerebral palsy or CP or cleft or concussion* or COPD or cystic fibrosis or dental or depression or diabet* or down* syndrome or eczema or epilep* or fibromyalg* or heart disease* or CHD or heart failure or CHF or hemophili* or haemophili* or HIV or hypertension or HTN or incontinence or infection* or kidney disease* or CKD or leukaemia or leukemia or lung disease* or menopaus* or multiple scleros* or muscular dystrophy or oral health* or obes* or osteoarthriti* or OA or overweight or parkinson* or post natal or post-natal or post stroke or post-stroke or post traumatic stress or post-traumatic stress or pregnan* or psychiatric or psychotic* or pulmonary disease or scolio* or schizophr* or sexual* abus* or spina bifida or spinal cord injur* or SCI or stenosis or stroke or transplant* or tumor* or tumour* or vestibular)
S21	Limiters – English language

4. Search strategy for SPORTDIscus (EBSCOhost)

No.	Search
S1	adolescen* or young adult* or child* or youth* or teen* or child* or pediatr* or paediatr* or school* or pubescen* or high school or senior high or university* or colleg* or post secondary* or student* or varsity
S2	sport* or athlet* or phys ed or physical education or gym* or aerobic* or exercise* or physical* activ* or fitness or archery or badminton or baseball or basketball or bandy or biathlon or bobsleigh* or body building or bowling or boxing or boxer* or bull fight* or canoe* or cheerlead* or cricket* or cross country ski* or curling or curler* or cycling or danc* or decathlon or diving or equestrian* or fencing or fencer* or field hockey or figure skat* or football* or gridiron or golf* or gymnast* or handball or hockey or ice hockey or judo or jogging or jogger* or ju jitsu or karate or kayak* or kung fu or lacrosse or lawn bowl* or luge* or martial art* or mountain bik* or marathon or mountaineering or netball or nordic combined or pentathlon or plyometric* or polo or racing or racquetball or rock climb* or rodeo or rowing or rugby or running or runner* or sailing or shooting* or ski or skiing or

	skier* or skat* or skeleton or soccer or softball or snowboard* or squash or surfer* or surfing or swim* or taewkondo or tennis or (track and field) or trampolin* or triathlon or ultimate frisbee or volleyball or walker or walking or water polo or weight lift* or workouts or work* out* or wrestl* or yoga
S3	quality of life or QOL* or health-related quality of life or HRQoL or HRQL or wellbeing or well-being or wellness or life satisfaction
S4	questionnaire* or survey* or scale* or survey* or questionnaire* or index or checklist or tool or tools or test or tests or instrument or instruments or score* or inventory or self report* or self-rated or SF* or short-form 36 or short-form 12 or short-form 8 or EQ-5D* or EQ-VAS or health utilities index* or Sickness Impact Profile or Nottingham Health Profile or RAND or Quality of Well Being Scale or QWB or Athlete Life Quality Scale or ALQS or Flourishing Scale or Trojan Lifetime Champions or (Knee injury and Osteoarthritis Outcome Score) or KOOS or (Disabilities of the Arm Shoulder and Hand) or Pediatric Quality of Life Inventory or PedsQL or Pediatric Outcomes Data Collection Instrument or PODCI
S5	psychometric* or validation stud* or reproducibility of results or valid* or responsive* or reproduca* or reproduci* or generali?ab* or reliability or sensitivity or specificity or correlation* or psychometric or clinimetric* or accuracy or interpretability or minimal clinical* important difference or MCID or minimal important difference or MID or minimal clinical* important change or MCIC or minimal clinical* important improvement or MCII or standard error of measurement or SEM or COSMIN or internal consistency or measurement propert* or measurement error or hypotheses test* or cross cultural validity or criterion validity or construct validity or content validity or face validity
S6	S1 AND S2 AND S3 AND S4 AND S5
S7	S6 NOT (elder* or geriatric* or older adult* or infant* or preschool* or pre-school* or ADHD or amput* or aneurysm or angina or arthrit* or asthm* or autis* or bowel disease* or bowel syndrome* or brain injur* or cancer* or cardiac or cardiomyopath* or cerebral palsy or CP or cleft or concussion* or COPD or cystic fibrosis or dental or depression or diabet* or down* syndrome or eczema or epilep* or fibromyalg* or heart disease* or CHD or heart failure or CHF or hemophili* or haemophili* or HIV or hypertension or HTN or incontinence or infection* or kidney disease* or CKD or leukaemia or leukemia or lung disease* or menopaus* or multiple scleros* or muscular dystrophy or oral health* or obes* or osteoarthriti* or OA or overweight or parkinson* or post natal or post-natal or post stroke or post-stroke or post traumatic stress or post-traumatic stress or pregnan* or psychiatric or psychotic* or pulmonary disease or scolio* or schizophr* or sexual* abus* or spina bifida or spinal cord injur* or SCI or stenosis or stroke or transplant* or tumor* or tumour* or vestibular)
S8	Limiters – English language

5. Search strategy for PsycINFO (OVID)

No.	Search
1	(youth* or adolescen* or teen* or child* or pediatr* or paediatr* or school* or pubescen* or young adult* or high school or senior high or university* or colleg* or post secondary* or student* or varsity).mp.
2	exp sports/
3	exp athletes/
4	(sport* or athlet* or phys ed or physical education or gym* or aerobic* or exercise* or physical* activ* or fitness or archery or badminton or baseball or basketball or bandy or biathlon or bobsleigh* or body building or bowling or boxing or boxer* or bull fight* or canoe* or cheerlead* or cricket* or cross country ski* or curling or curler* or cycling or danc* or decathlon or diving or equestrian* or fencing or fencer* or field hockey or figure skat* or football* or gridiron or golf* or gymnast* or handball or hockey or ice hockey or judo or jogging or jogger* or ju jitsu or karate or kayak* or kung fu or lacrosse or lawn bowl* or luge* or martial art* or mountain bik* or marathon or mountaineering

	or netball or nordic combined or pentathlon or plyometric* or polo or racing or racquetball or rock climb* or rodeo or rowing or rugby or running or runner* or sailing or shooting* or ski or skiing or skier* or skat* or skeleton or soccer or softball or snowboard* or squash or surfer* or surfing or swim* or taewkondo or tennis or (track and field) or trampolin* or triathlon or ultimate frisbee or volleyball or walker or walking or water polo or weight lift* or workouts or work* out* or wrestl* or yoga).mp.
5	2 or 3 or 4
6	(quality of life or QOL* or health-related quality of life or HRQoL or HRQL or wellbeing or well-being or wellness or life satisfaction).mp.
7	exp questionnaires/ or exp surveys/
8	(questionnaire or survey or scale or scale* or survey* or questionnaire* or index or checklist or tool or tools or test or tests or instrument or instruments or score* or inventory or self report* or self-rated or SF* or short-form 36 or short-form 12 or short-form 8 or EQ-5D* or EQ-VAS or health utilities index* or Sickness Impact Profile or Nottingham Health Profile or RAND or Quality of Well Being Scale or QWB or Athlete Life Quality Scale or ALQS or Flourishing Scale or Trojan Lifetime Champions or (Knee injury and Osteoarthritis Outcome Score) or KOOS or (Disabilities of the Arm Shoulder and Hand) or Pediatric Quality of Life Inventory or PedsQL or Pediatric Outcomes Data Collection Instrument or PODCI).mp.
9	7 or 8
10	Psychometrics
11	test reliability/ or exp test validity/
12	(valid* or responsive* or reproduca* or reproduci* or generali?ab* or reliability or sensitivity or specificity or correlation* or psychometric or clinimetric* or accuracy or interpretability or minimal clinical* important difference or MCID or minimal important difference or MID or minimal clinical* important change or MCIC or minimal clinical* important improvement or MCII or standard error of measurement or SEM or COSMIN or internal consistency or measurement propert* or measurement error or hypotheses test* or cross cultural validity or criterion validity or construct validity or content validity or face validity).mp.
13	10 or 11 or 12
14	1 and 5 and 6 and 9 and 13
15	14 not (elder* or geriatric* or older adult* or infant* or preschool* or pre-school* or ADHD or amput* or aneurysm or angina or arthrit* or asthm* or autis* or bowel disease* or bowel syndrome* or brain injur* or cancer* or cardiac or cardiomyopath* or cerebral palsy or CP or cleft or concussion* or COPD or cystic fibrosis or dental or depression or diabet* or down* syndrome or eczema or epilep* or fibromyalg* or heart disease* or CHD or heart failure or CHF or hemophili* or haemophili* or HIV or hypertension or HTN or incontinence or infection* or kidney disease* or CKD or leukaemia or leukemia or lung disease* or menopaus* or multiple scleros* or muscular dystrophy or oral health* or obes* or osteoarthriti* or OA or overweight or parkinson* or post natal or post-natal or post stroke or post-stroke or post traumatic stress or post-traumatic stress or pregnan* or psychiatric or psychotic* or pulmonary disease or scolio* or schizophr* or sexual* abus* or spina bifida or spinal cord injur* or SCI or stenosis or stroke or transplant* or tumor* or tumour* or vestibular).ti.
16	limit 15 to English language

6. Search strategy for Scopus

No.	Search
1	TITLE-ABS (youth* OR adolescen* OR teen* OR child* OR pediatr* OR paediatr* OR school* OR pubescen* OR "young adult" OR "high school" OR "senior high" OR university* OR colleg* OR "post secondary" OR student* OR varsity)

2	TITLE-ABS (sport* or athlete* or "phys ed" OR "physical education" OR gym OR aerobic OR exercise OR "physical activity" OR fitness OR archery OR badminton OR baseball OR basketball OR bandy OR biathlon OR bobsleigh OR "body building" OR bowling OR bowler OR boxing OR boxer OR "bull fight" OR "bull fighter" OR canoe OR cheerlead* OR cricket* OR "cross country ski*" OR curling OR curler OR cycling OR cyclist OR danc* OR decathlon OR diving OR diver OR equestrian OR fencing OR fencer OR "field hockey" OR "figure skat*" OR football* OR gridiron OR golf* OR gymnast* OR handball OR hockey OR "ice hockey" OR judo OR jog* OR "ju jitsu" OR karate OR kayak* OR "kung fu" OR lacrosse OR "lawn bowl*" OR luge* OR "martial art" OR "mountain bik*" OR marathon OR mountaineer* OR netball OR "nordic combined" OR pentathlon OR plyometric* OR polo OR racing OR racquetball OR "rock climb*" OR rodeo OR rowing OR rugby OR running OR runner* OR sailing OR shooting* OR skiing OR skier OR ski OR skat* OR skeleton OR soccer OR softball OR snowboard* OR squash OR surfing OR surfer OR swim* OR taekwondo OR tennis OR "track and field" OR trampolin* OR triathlon OR "ultimate frisbee" OR volleyball OR walker OR walking OR "water polo" OR "weight lift*" OR workout* OR "work out*" OR wrestl* OR yoga)
3	TITLE-ABS ("quality of life" OR qol* OR "health-related quality of life" OR hrqol OR hrql OR "well being" OR wellbeing OR wellness OR "life satisfaction")
4	TITLE-ABS (survey OR questionnaire OR scale OR index OR checklist OR tool OR test OR instrument OR score OR inventory OR "self report" OR "self reported" OR "self rated" OR sf-* OR "short-form 36" OR "short-form 12" OR "short-form 8" OR eq-5d* OR eq-vas OR "health utilities index" OR "Sickness Impact Profile" OR "Nottingham Health Profile" OR rand OR "Quality of Well Being Scale" OR qwb OR "Athlete Life Quality Scale" OR alqs OR "Flourishing Scale" OR "Trojan Lifetime Champions" OR "Knee injury and Osteoarthritis Outcome Score" OR koos OR "Disabilities of the Arm Shoulder and Hand" OR "Pediatric Quality of Life Inventory" OR pedsql OR "Pediatric Outcomes Data Collection Instrument" OR podci)
5	TITLE-ABS (psychometrics OR "validation stud*" OR "reproducibility of results" OR valid* OR responsive* OR reproduca* OR reproduci* OR generali?ab* OR reliability OR sensitivity OR specificity OR correlation* OR psychometric OR clinimetric* OR accuracy OR interpretability OR "minimal clinical* important difference" OR mcid OR "minimal important difference" OR mid OR "minimal clinical* important change" OR mcic OR "minimal clinical* important improvement" OR mcii OR "standard error of measurement" OR sem OR cosmin OR "internal consistency" OR "measurement property" OR "measurement error" OR "hypotheses test" OR "cross cultural validity" OR "criterion validity" OR "construct validity" OR "content validity" OR "face validity")
6	#1 AND #2 AND #3 AND #4 AND #5
7	TITLE-ABS (elder or geriatric or "older adult" or infant* or preschool or ADHD or amputee or aneurysm or angina or arthrit* or asthm* or autis* or "bowel disease*" or "bowel syndrome*" or brain injur* or cancer* or cardiac or cardiomyopath* or "cerebral palsy" or CP or cleft or concussion* or COPD or "cystic fibrosis" or dental or depression or diabet* or "down syndrome" or eczema or epilep* or fibromyalg* or "heart disease*" or CHD or "heart failure" or CHF or hemophili* or haemophili* or HIV or hypertension or HTN or incontinence or infection* or "kidney disease*" or CKD or leukaemia or leukemia or "lung disease*" or menopaus* or "multiple scleros*" or "muscular dystrophy" or "oral health*" or obes* or osteoarthriti* or OA or overweight or parkinson* or "post natal" or "post stroke" or "post traumatic stress" or pregnan* or psychiatric or psychotic* or "pulmonary disease" or scolio* or schizophr* or "sexual abuse" or "spina bifida" or "spinal cord injury" or stenosis or stroke or transplant* or tumor* or tumour* or vestibular)
8	#6 AND NOT #7
9	Limit to English

Appendix G: Example of Evaluating Test-Retest Reliability (Chapter 2)

The following represents a hypothetical example of the evaluation process outlined by the COSMIN User Manual[1-4] to evaluate test-retest reliability of the SF-36.

Evaluation Process	Data Extraction	Rating or Result

1. Evaluate the methodological quality of individual studies using the **COSMIN Risk of Bias checklist**.	• Evaluate the methodological quality of Study A:
	  • Evidence that patients were stable during the interim period (very good)
	  • Time interval was two weeks which is considered appropriate (very good)
	  • Evidence that test conditions were similar for measurements (very good)
	  • ICC was calculated (very good)
	• Evaluate the methodological quality of Study B:
	  • Assumable that patients were stable during the interim period (adequate)
	  • Time interval was two days which may not be long enough to prevent recall bias (doubtful)
	  • Evidence that test conditions were similar for measurements (very good)
	  • ICC was calculated (very good)
		Quality of Study A: Very good
		Quality of Study B: Doubtful

2. Rate the result of individual studies using the **criteria for good measurement properties**	• Evaluate the results of Study A:
	  • ICC=0.85 (sufficient)
	• Evaluate the results of Study B:
	  • ICC=0.90 (sufficient)
		Result of Study A: Sufficient
		Result of Study B: Sufficient

3. Summarize the results across studies using the **criteria for good measurement properties**	• Summarize the results of Study A and B: • ICC≥0.70 for both studies (sufficient)	**Summarized result for SF-36:** Sufficient

4. Grade the quality of evidence across studies using the **modified GRADE approach**	• Evaluate the methodological quality of Study A and B:
	  • One study of very good quality available (no downgrading for risk of bias)
	  • No inconsistency across studies (no downgrading for inconsistency)
	  • Pooled sample size is 80 (downgrade -1 for imprecision)
	  • Population of included studies align with interests of the review (no downgrading for indirectness)
		Quality of evidence for SF-36: Moderate

Overall finding: The SF-36 has moderate quality of evidence for sufficient test-retest reliability

Appendix G References

1. Mokkink LB, de Vet HCW, Prinsen CAC, Patrick DL, Alonso J, Bouter LM, et al. COSMIN Risk of Bias checklist for systematic reviews of patient-reported outcome measures. Qual Life Res. 2018;27(5):1171-9. 10.1007/s11136-017-1765-4
2. Prinsen CAC, Mokkink LB, Bouter LM, Alonso J, Patrick DL, de Vet HCW, et al. COSMIN guideline for systematic reviews of patient-reported outcome measures. Qual Life Res. 2018;27(5):1147-57. 10.1007/s11136-018-1798-3
3. Terwee CB, Prinsen CAC, Chiarotto A, Westerman MJ, Patrick DL, Alonso J, et al. COSMIN methodology for evaluating the content validity of patient-reported outcome measures: a Delphi study. Qual Life Res. 2018;27(5):1159-70. 10.1007/s11136-018-1829-0
4. Mokkink LB, Prinsen CAC, Patrick DL, Alonso J, Bouter LM, de Vet HCW, et al. COSMIN Methodology for Systematic Reviews of Patient-Reported Outcome Measures (PROMs) – User Manual. Amsterdam, Netherlands: COSMIN Initative; 2018.

Appendix H: Criteria for Good Measurement Properties (Chapter 2)

Adapted from the COSMIN User Manual,[1-4] Prinsen et al. (2016),[5] and Terwee et al. (2007).[6]

Measurement Property	Rating	Criteria
Structural validity[a]	+	CFA: CFI or TLI or comparable measure >0.95 *OR* RMSEA <0.06 *OR* SRMR <0.082 EFA: First factor accounts for at least 20% of the variability *AND* ratio of the variance explained by the first to the second factor greater than 4[b]
	?	Not all information for ‘+’ reported
	–	Criteria for ‘+’ not met
Internal consistency	+	At least low evidence for sufficient structural validity *AND* Cronbach's alpha(s) ≥ 0.70 for each unidimensional scale or subscale
	?	Criteria for “at least low evidence for sufficient structural validity” not met
	–	At least low evidence for sufficient structural validity *AND* Cronbach’s alpha(s) < 0.70 for each unidimensional scale or subscale
Test-retest reliability	+	ICC or weighted Kappa ≥ 0.70
	?	ICC or weighted Kappa not reported
	–	ICC or weighted Kappa < 0.70
Measurement error	+	SDC or LoA < MIC
	?	MIC not defined
	–	SDC or LoA > MIC
Cross-cultural validity	+	No important differences found between group factors (such as age, gender, language) in multiple group factor analysis
	?	No multiple group factor analysis
	–	Important differences between group factors
Hypotheses testing for construct validity	+	The result is in accordance with a-priori hypotheses
	?	No a-priori hypotheses were defined
	–	The result is not in accordance with the hypotheses
Criterion validity	+	Correlation with gold standard ≥0.70 *OR* AUC ≥0.70
	?	Not all information for ‘+’ reported
	–	Correlation with gold standard <0.70 *OR* AUC <0.70
Responsiveness	+	The result is in accordance with a-priori hypotheses *OR* AUC ≥0.70
	?	No a-priori hypotheses were defined
	–	The result is not in accordance with a-priori hypotheses *OR* AUC <0.70

Rating legend: sufficient (+), indeterminate (?), or insufficient (–)
[a]Only criteria for classical test theory listed as no item response theory instruments were identified
[b]Criteria for exploratory factor analysis taken from Prinsen et al. (2016)[5]

AUC, area under the curve; CFA, confirmatory factor analysis; CFI, comparative fit index; EFA, exploratory factor analysis; ICC, intraclass correlation coefficient; LoA, limits of agreement; MIC, minimal important change; RMSEA, root mean square error of approximation; SDC, smallest detectable change; SRMR, standardized root mean square residual; TLI, Tucker-Lewis Index

Appendix H References

1. Mokkink LB, de Vet HCW, Prinsen CAC, Patrick DL, Alonso J, Bouter LM, et al. COSMIN Risk of Bias checklist for systematic reviews of patient-reported outcome measures. Qual Life Res. 2018;27(5):1171-9. 10.1007/s11136-017-1765-4
2. Prinsen CAC, Mokkink LB, Bouter LM, Alonso J, Patrick DL, de Vet HCW, et al. COSMIN guideline for systematic reviews of patient-reported outcome measures. Qual Life Res. 2018;27(5):1147-57. 10.1007/s11136-018-1798-3
3. Terwee CB, Prinsen CAC, Chiarotto A, Westerman MJ, Patrick DL, Alonso J, et al. COSMIN methodology for evaluating the content validity of patient-reported outcome measures: a Delphi study. Qual Life Res. 2018;27(5):1159-70. 10.1007/s11136-018-1829-0
4. Mokkink LB, Prinsen CAC, Patrick DL, Alonso J, Bouter LM, de Vet HCW, et al. COSMIN Methodology for Systematic Reviews of Patient-Reported Outcome Measures (PROMs) – User Manual. Amsterdam, Netherlands: COSMIN Initative; 2018.
5. Prinsen CAC, Vohra S, Rose MR, Boers M, Tugwell P, Clarke M, et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline. Trials. 2016;17(1):449. 10.1186/s13063-016-1555-2
6. Terwee CB, Bot SDM, de Boer MR, van der Windt DAWM, Knol DL, Dekker J, et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol. 2007;60(1):34-42. 10.1016/j.jclinepi.2006.03.012

Appendix I: Modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Approach (Chapter 2)

We assume that the starting point for the quality of evidence for each measurement property is high. The quality is subsequently downgraded based on ratings for risk of bias, inconsistency, imprecision, or indirectness.[1-4]

Quality Level	Definition
High	High confidence in the summarized results of the measurement property. The true measurement property lies close to the estimate.
Moderate	Moderate confidence in the summarized results of the measurement property. The true measurement property is likely to be close to the estimate but it is possible that it is substantially different.
Low	Limited confidence in the summarized results of the measurement property. The true measurement property may be substantially different from the estimate.
Very low	Very low confidence in the summarized results of the measurement property. The true measurement property is likely substantially different from the estimate.

GRADE Factor	Rating	Downgrading for Risk of Bias
Risk of bias *Occurs if the quality of the study is doubtful or inadequate as assessed with the COSMIN Risk of Bias checklist*	No	Multiple studies of at least adequate quality or only 1 study of very good quality available.
	Serious (-1)	Multiple studies of doubtful quality or only 1 study of adequate quality available.
	Very serious (-2)	Multiple studies of inadequate quality or only 1 study of doubtful quality available.
	Extremely serious (-3)	Only 1 study of inadequate quality available.
Inconsistency *Occurs when there is no explanation for inconsistent results between multiple studies examining the same HRQoL instrument*	No	Any inconsistency is solved by pooling or summarizing results in subgroups of studies with similar results.
	Serious (-1)	Majority but not all results could be pooled or summarized as sufficient or insufficient.
	Very serious (-2)	Only some but not the majority of the results could be pooled or summarized as sufficient or insufficient.
Imprecision *Refers to the total sample of the pooled or summarized studies*	No	Sample size of pooled/summarized studies is ≥100.
	Serious (-1)	Sample size of pooled/summarized studies is between 50-99.
	Very serious (-2)	Sample size of pooled/summarized studies is <50.
Indirectness *Occurs if studies included were performed in a population not of interest in the systematic review*	No	Population of included studies aligns with the interests of the review.
	Serious (-1)	Population of the majority but not all of included studies align with the interests of the review.
	Very serious (-2)	Population of only some but not the majority of the included studies align with the interests of the review.

Appendix J: Overview of Identified HRQoL PROMS (Chapter 2)

HRQoL PROM	Target Population	Mode of Administration	Subscales or Domains	Number of Items	Response Options	Scoring	Original Reference
Generic PROMs							
ALQS	Athletes	Self-report	General Life Satisfaction Physical Satisfaction Team/Sport Satisfaction Primary Social Satisfaction Recovery/ Social Satisfaction	4 2 4 2 3	7-point Likert	Subscale scores: Range from 2-14 to 4-28, depending on the subscale Total score: None Higher scores indicate better outcomes	Gentner et al. (2011)[1]
DPA-MSC[a]	Physically active individuals	Self-report	Mental Summary Component	4	4-point Likert	Subscale score: 0-16 Lower scores indicate better outcomes	Vela & Denegar (2010),[2] Houston et al. (2015)[3]
DPA SF-8 MSC[a]	Physically active individuals	Self-report	Mental Summary Component	4	4-point Likert	Subscale score: 0-16 Lower scores indicate better outcomes	Baker et al. (2019)[4]
DPA SF-10 MSC[a]	Physically active individuals	Self-report	Mental Summary Component	4	4-point Likert	Subscale score: 0-16 Lower scores indicate better outcomes	Baker et al. (2019)[4]
KIDSCREEN-52	Healthy and ill children and adolescents	Self-report	Physical Well-Being Psychological Well-Being Moods & Emotions Self-Perception Autonomy Parent Relations and Home Life Social Support and Peers School Environment Bullying Financial Resources	5 6 7 5 5 6 6 6 3 3	5-point Likert	Subscale scores: Standardized scores using T-score transformation with a mean of 50 and SD of 10 Total score: None Higher scores indicate better outcomes	The KIDSCREEN Group Europe (2006)[5]
KIDSCREEN-10	Healthy and ill children and adolescents	Self-report	N/A, only total score	10	5-point Likert	Subscale scores: None Total score: Standardized scores using T-score transformation with a mean of 50 and SD of 10 Higher scores indicate better outcomes	Ravens-Sieberer et al. (2010)[6]
PedsQL	Children, adolescents, and young adults	Self-report and proxy	Physical Functioning Social Functioning School Functioning Emotional Functioning Physical Health Summary Psychosocial Health Summary	8 5 5 5 8 15	5-point Likert	Subscale scores: 0-100 Total score: Physical Health Summary summarizes the Physical Functioning subscale. Psychosocial Health Summary summarizes the Social Functioning, School Functioning, and Emotional Functioning subscales	Varni et al. (1999)[7]

						Higher scores indicate better outcomes	
QoL survey	General population	Self-report	Social Emotional Cognitive Spiritual Physical Activities of Daily Living Integrated	5 5 5 5 5 3 4	5-point Likert	Subscale scores: Range from 1-15 to 1-25 depending on the subscale Total score: None Higher scores indicate better outcomes	Gill et al. (2011)[8]
SF-36	General population	Self-report	Physical Functioning Role-Physical Pain General Health Vitality Social Functioning Role-Emotional Mental Health	10 4 2 5 4 2 3 5	Yes/no, 3-, 5-, and 6-point Likert	Domain scores: Standardized scores using T-score transformation with a mean of 50 and SD of 10 Total score: Physical Component Score summarizes the Physical Functioning, Role-Physical, Pain, and General Health domains. Mental Component Score summarizes the Vitality, Social Functioning, Role-Emotional, and Mental Health domains Higher scores indicate better outcomes	Ware & Sherbourne (1992)[9]
SF-12	General population	Self-report	Physical Functioning Role-Physical Pain General Health Vitality Social Functioning Role-Emotional Mental Health	2 2 1 1 1 1 2 2	Yes/no, 3-, 5-, and 6-point Likert	Domain scores: Standardized scores using T-score transformation with a mean of 50 and SD of 10 Total score: Physical Component Score summarizes the Physical Functioning, Role-Physical, Pain, and General Health domains. Mental Component Score summarizes the Vitality, Social Functioning, Role-Emotional, and Mental Health domains Higher scores indicate better outcomes	Ware et al. (1996)[10]
WHOQOL-BREF	General population	Self-report	Physical Psychological Social Environmental "How would you rate your quality of life?" "How satisfied are you with your health?"	7 6 3 8 1 1	5-point Likert	Subscale scores: Range from 1-5 to 8-40 depending on the subscale Total score: None Higher scores indicate better outcomes	The WHOQOL Group (1998)[11]

Condition-Specific PROMs							
FAST	Throwing athletes	Self-report	Throwing Activities of Daily Living Psychological Impact Advancement Pain (cross subscale) Pitcher Module	10 5 4 3 6 9	5-point Likert	Subscale scores: 0-100 Total score: 0-100 Lower scores indicate better outcomes	Sauers et al. (2017)[12]
HAGOS QOL subscale[a]	Physically active youth and middle-aged adults with hip and/or groin pain	Self-report	Hip- and/or Groin-Related QOL	5	5-point Likert	Subscale score: 0-100 Higher scores indicate better outcomes	Thorborg et al. (2011)[13]
HOOS QOL subscale[a]	Middle-aged and older adults with hip osteoarthritis	Self-report	Hip-related QOL	4	5-point Likert	Subscale score: 0-100 Higher scores indicate better outcomes	Klässbo et al. (2003)[14]
iHOT-33	Young-to-middle aged active individuals with hip disorders	Self-report	Symptoms and Functional Limitations Sports and Recreational Activities Limitations Job-Related Concerns Social, Emotional, and Lifestyle Concerns	16 6 4 7	100-mm VAS	Subscale scores: None Total score: 0-100 Higher scores indicate better outcomes	Mohtadi et al. (2012)[15]
iHOT-12	Young-to-middle aged active individuals with hip disorders	Self-report	N/A, only total score	12	100-mm VAS	Subscale scores: None Total score: 0-100 Higher scores indicate better outcomes	Griffin et al. (2012)[16]
KOOS QOL subscale[a]	Individuals with knee injuries and conditions	Self-report	Knee-specific HRQoL	4	5-point Likert	Subscale score: 0-100 Higher scores indicate better outcomes	Roos et al. (1998)[17]
PASS	Children and adolescents with shoulder pain or injury	Self-report	Compensatory Mechanism/Function Domain Symptoms/Emotion Domain	6 7	5- and 10-point Likert	Subscale scores: 0-100 Total score: 0-100 Higher scores indicate better outcomes	Edmonds et al. (2017)[18]

[a]Subscale within a PROM.

ALQS, Athlete Life Quality Scale; DPA, Disablement of the Physically Active; DPA-MSC, DPA-Mental Summary Component; DPA-MSC SF-10, DPA-MSC Short-Form 10; DPA-MSC SF-8, DPA-MSC Short-Form 8; FAST, Functional Arm Scale for Throwers; HAGOS QOL, Copenhagen Hip and Groin Outcome Score Quality of Life subscale; HOOS QOL, Hip dysfunction and Osteoarthritis Outcome Score Quality of Life subscale; HRQoL, health-related quality of life; iHOT-33, International Hip Outcome Tool-33; iHOT-12, International Hip Outcome Tool-12; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; mm, millimetre; N/A, not applicable; QoL survey, Quality of Life survey; PASS, Pediatric/Adolescent Shoulder Survey; PedsQL, Pediatric Quality of Life Inventory; PROM, patient-reported outcome measure; SD, standard deviation; SF-36, Short-Form 36; SF-12, Short-Form 12; VAS, visual analogue scale; WHOQOL-BREF, World Health Organization Quality of Life abbreviated instrument

Appendix K: Summary of Measurement Properties for Generic HRQoL PROMs (Chapter 2)

HRQoL PROM	Reference & Country	I. Structural Validity			II. Internal Consistency			III. Test-Retest Reliability			IV. Measurement Error		
		n	Quality[a]	Result[b]	n	Quality	Result	n	Quality	Result	n	Quality	Result
ALQS	Gentner et al. (2011), USA[1]	159	Adequate	5-factor model (factor 1=30.205%, factor 2=11.167%, factor 3=9.580%, factor 4=7.541%, and factor 5=6.841% of total variance) (?)	159	Doubtful	Cronbach's alpha=0.54-0.83; item-total correlation=0.267-0.580 (?)						
Overall Rating[c]		*Indeterminate (?)*			*Indeterminate (?)*								
DPA-MSC	Vela & Denegar (2010), USA[2]	125	Very good	2-factor model (CFI=0.937, TLI=0.924, RMSEA=0.085) (–)	28	Doubtful	Cronbach alpha's=0.881-0.908; item-total correlation=0.421-0.744 (–)	31	Inadequate	ICC=0.943 (+)			
	Houston et al. (2015), USA[3]	456	Adequate	2-factor model (factors explained 65.1% of total variance) (?)	456	Very good	Cronbach's alpha=0.878 (?)						
	Baker et al. (2019), USA[4]	796	Very good	2-factor model (CFI=0.962, TLI=0.947, RMSEA=0.060) (?)									
	White et al. (2018), USA[5]				31	Very good	Cronbach's alpha=0.91 (?)						
	Powden et al. (2019), USA[6]				20	Very good	Cronbach's alpha=0.667 (–)						
	Hoch et al. (2019), USA[7]												
Overall Rating		*Indeterminate (?)*			*Indeterminate (?)*			*Sufficient (+)*					
DPA-MSC SF-10	Baker et al. (2019), USA[4]	796	Very good	2-factor model (CFI=0.981-0.996, TLI=0.968-0.990,	690	Very good	Cronbach alpha's=0.850 (+)						

				RMSEA=0.028-0.050) (+)						
Overall Rating			*Sufficient (+)*			*Sufficient (+)*				
DPA-MSC SF-8	Baker et al. (2019), USA[4]	796	Very good	2-factor model (CFI=0.996-0.997, TLI=0.993-0.994, RMSEA=0.023-0.025) (+)	690	Very good	Cronbach's alpha=0.852 (+)			
Overall Rating			*Sufficient (+)*			*Sufficient (+)*				
KIDSCREEN-52	Lorger et al. (2012), Croatia[8]	343	Adequate	11-factor model (factor 1>20% of total variance, ratio of variance explained by first to second factor >4) (+)	343	Very good	Cronbach's alpha=0.71-0.88 (+)			
Overall Rating			*Sufficient (+)*			*Sufficient (+)*				
KIDSCREEN-10	Sigvartsen et al. (2016), Norway[9]				156	Inadequate	Cronbach's alpha=0.74 (+)			
Overall Rating						*Sufficient (+)*				
PedsQL	Zhang et al. (2018), USA[10]				235	Very good	Cronbach's alpha=0.79-0.87 (+)			
Overall Rating						*Sufficient (+)*				
QoL Survey	Gill et al. (2015), USA[11]	446	Very good	7-factor model (CFI=0.98, RMSEA=0.077, SRMR=0.055) (+)	446	Very good	Cronbach's alpha=0.793-0.950 (+)	340	Adequate	ICC=0.676-0.809 (±)
Overall Rating			*Sufficient (+)*			*Sufficient (+)*			*Sufficient (+)*	
SF-36	Gill et al. (2015), USA[11]				446	Very good	Cronbach's alpha=0.610-0.932 (?)	340	Adequate	ICC=0.505-0.756 (?)
	Huffman et al. (2008), USA[12]				696	Very good	Cronbach's alpha=0.83-1.00 (?)			
Overall Rating						*Indeterminate (?)*			*Indeterminate (?)*	
SF-12	Hoch et al. (2019), USA[7]									
Overall Rating										
WHOQOL-BREF	Gill et al. (2015), USA[11]				446	Very good	Cronbach's alpha=0.698-0.831 (?)			

	Cieslak et al. (2007), Brazil[13]				46	Inadequate	Cronbach's alpha=0.77-0.80 (?)						
	Overall Rating					*Indeterminate (?)*							

HRQoL PROM	Reference & Country	V. Content Validity			VI. Hypothesis Testing for Construct Validity			VII. Criterion Validity			VIII. Responsiveness		
		n	Quality	Result	n	Quality	Result	n	Quality	Result	n	Quality	Result
ALQS	Gentner et al. (2011), USA[1]	31	Inadequate	Insufficient (–)									
	Overall Rating		*Insufficient (–)*										
DPA-MSC	Vela & Denegar (2010), USA[2]	31	Doubtful	Inconsistent (±)				82	Adequate	Correlation with global functioning item=-0.714- -751 (+)	33	Very good	AUC=0.895-0.911 (acute injury over 1 week and to RTS) and 0.702-0.902 (persistent injury over 6 weeks) (+)
	Houston et al. (2015), USA[3]							456	Very good	Correlation with original DPA=0.691 (–)			
	Baker et al. (2019), USA[4]												
	White et al. (2018), USA[5]				100	Inadequate	No hypotheses stated for correlation with SF-12 or PROMIS-PF (?)						
	Powden et al. (2019), USA[6]												
	Hoch et al. (2019), USA[7]												
	Overall Rating		*Inconsistent (±)*			*Indeterminate (?)*			*Sufficient (+) with global functioning item* *Insufficient (–) with original DPA*			*Sufficient (+)*	
DPA-MSC SF-10	Baker et al. (2019), USA[4]												
	Overall Rating												
DPA-MSC SF-8	Baker et al. (2019), USA[4]												

Overall Rating						
KIDSCREEN-52	Lorger et al. (2012), Croatia[8]					
Overall Rating						
KIDSCREEN-10	Sigvartsen et al. (2016), Norway[9]					
Overall Rating						
PedsQL	Zhang et al. (2018), USA[10]		235	Very good	No hypotheses stated for correlation with SEEB, PACES, SSES, PANES, or physical activity (?)	
Overall Rating				*Indeterminate (?)*		
QoL Survey	Gill et al. (2015), USA[11]		446	Adequate	No hypotheses stated for correlation with SF-36, WHOQOL-BREF, SWLS, or GLTEQ (?)	
Overall Rating				*Indeterminate (?)*		
SF-36	Gill et al. (2015), USA[11]					
	Huffman et al. (2008), USA[12]					
Overall Rating						
SF-12	Hoch et al. (2019), USA[7]		100	Inadequate	No hypotheses stated for correlation with DPA or PROMIS-PF (?)	
Overall Rating				*Indeterminate (?)*		
WHOQOL-BREF	Gill et al. (2015), USA[11]					
	Cieslak et al. (2007), Brazil[13]					
Overall Rating						

[a]Study methodological quality scored as ‘very good,’ ‘adequate,’ ‘doubtful,’ or ‘inadequate’ as per the COSMIN Risk of Bias checklist[14-17]
[b]Study results rated as ‘sufficient (+),’ ‘indeterminate (?),’ ‘inconsistent (±),’ or ‘insufficient (–)‘ as per the COSMIN criteria for good measurement properties[14-19]

[c]Overall PROM rating across studies summarized as ‘sufficient (+),’ ‘indeterminate (?),’ ‘inconsistent (±),’ or ‘insufficient (–)‘ as per the COSMIN criteria for good measurement properties[14-19]
Grey shading indicates no identified study evaluated the measurement property

ALQS, Athlete Life Quality Scale; AUC, area under the curve; CFI, comparative fit index; DPA, Disablement of the Physically Active; DPA-MSC, DPA-Mental Summary Component; DPA-MSC SF-10, DPA-MSC Short-Form 10; DPA-MSC SF-8, DPA-MSC Short-Form 8; GLTEQ, Godin Leisure Time Exercise Questionnaire; HRQoL, health-related quality of life; ICC, intraclass correlation coefficient; n, sample size; QoL survey, Quality of Life survey; PACES, Physical Activity Enjoyment Scale; PANES, Physical Activity Neighborhood Environment Scale; PedsQL, Pediatric Quality of Life Inventory; PROM, patient-reported outcome measure; PROMIS-PF, Patient-Reported Outcomes Measurement Information System Physical Functioning subscale; RMSEA, root mean square error of approximation; RTS, return to sport; SEEB, Self-Efficacy for Exercise Behaviors questionnaire; SF-36, Short-Form 36; SF-12, Short-Form 12; SRMR, standardized root mean square residual; SSES, Social Support and Exercise Survey; SWLS, Satisfaction With Life Scale; TLI, Tucker-Lewis Index; WHOQOL-BREF, World Health Organization Quality of Life abbreviated instrument

Appendix L: Summary of Measurement Properties for Condition-Specific HRQoL PROMs (Chapter 2)

HRQoL PROM	Reference & Country	I. Structural Validity			II. Internal Consistency			III. Test-Retest Reliability			IV. Measurement Error		
		n	Quality†	Result‡	n	Quality	Result	n	Quality	Result	n	Quality	Result
FAST	Sauers et al. (2017), USA[1]	557	Very good	4-factor model (GFI=0.991, SRMR=0.043) (+)	557	Very good	Cronbach's alpha=0.84-0.95 (+)						
	Sauers et al. (2011), USA[2]												
	Huxel Blivin et al. (2017), USA[3]							154	Doubtful	ICC=0.91-0.98 (+)	154	Doubtful	SEM=3.8-6.1, MDC=10.5-17.0 (?)
Overall Rating§			*Sufficient (+)*			*Sufficient (+)*			*Sufficient (+)*			*Indeterminate (?)*	
HAGOS QOL subscale	Drew et al. (2017), Australia[4]	73	Inadequate	8-factor model (factor 1=49% of total variance) (?)									
	Hinman et al. (2014), Australia[5]							23	Adequate	ICC=0.85 (+)	23	Adequate	SEM=6.5, individual MDC_{95}=18.1, group MDC_{95}=3.8 (?)
Overall Rating			*Indeterminate (?)*						*Sufficient (+)*			*Indeterminate (?)*	
HOOS QOL subscale	Hinman et al. (2014), Australia[5]							30	Adequate	ICC=0.92 (+)	30	Adequate	SEM=5.9, individual MDC_{95}=16.4, group MDC_{95}=3.0 (?)
Overall Rating									*Sufficient (+)*			*Indeterminate (?) – MIC not defined*	
iHOT-33	Hinman et al. (2014), Australia[5]							30	Adequate	ICC=0.93 (+)	30	Adequate	SEM=5.6, individual MDC_{95}=15.6, group MDC_{95}=2.9 (?)
Overall Rating									*Sufficient (+)*			*Indeterminate (?)*	
iHOT-12	Clapp et al. (2019), USA[6]												
Overall Rating													
KOOS QOL subscale	Hoch et al. (2015), USA[7]							16	Doubtful	ICC=0.894 (+)	16	Doubtful	SEM=6.2; MDC=17.29 (?)
Overall Rating									*Sufficient (+)*			*Indeterminate (?)*	
PASS	Edmonds et al. (2017), USA[8]												

HRQoL PROM	Reference & Country	V. Content Validity			VI. Hypothesis Testing for Construct Validity			VII. Criterion Validity			VIII. Responsiveness		
	Overall Rating												
		n	Quality	Result	n	Quality	Result	n	Quality	Result	n	Quality	Result
FAST	Sauers et al. (2017), USA[1]	51	Doubtful	Inconsistent (±)									
	Sauers et al. (2011), USA[2]				25	Adequate	No hypotheses stated for correlation with DASH (?)						
	Huxel Blivin et al. (2017), USA[3]				106	Doubtful	No hypotheses stated for correlation with DASH or KJOC; no hypothesis stated for discriminating between injured and uninjured individuals (?)				18	Very good	AUC=0.946 between improved vs not improved (+)
	Overall Rating	*Inconsistent (±)*			*Indeterminate (?)*						*Sufficient (+)*		
HAGOS QOL subscale	Drew et al. (2017), Australia[4]												
	Hinman et al. (2014), Australia[5]												
	Overall Rating												
HOOS QOL subscale	Hinman et al. (2014), Australia[5]												
	Overall Rating												
iHOT-33	Hinman et al. (2014), Australia[5]												
	Overall Rating												
iHOT-12	Clapp et al. (2019), USA[6]												
	Overall Rating												
KOOS QOL subscale	Hoch et al. (2015), USA[7]												
	Overall Rating												

PASS	Edmonds et al. (2017), USA[8]	132	Inadequate	Inconsistent (±)	132	Inadequate	No hypotheses stated for correlation with duration of symptoms (?)				25	Inadequate	No hypothesis stated for change in mean score (?)
Overall Rating			*Inconsistent (±)*			*Indeterminate (?)*						*Indeterminate (?)*	

[a]Study methodological quality scored as 'very good,' 'adequate,' 'doubtful,' or 'inadequate' as per the COSMIN Risk of Bias checklist[9-12]
[b]Study results rated as 'sufficient (+),' 'indeterminate (?),' 'inconsistent (±),' or 'insufficient (–)' as per the COSMIN criteria for good measurement properties[9-14]
[c]Overall PROM rating across studies summarized as 'sufficient (+),' 'indeterminate (?),' 'inconsistent (±),' or 'insufficient (–)' as per the COSMIN criteria for good measurement properties[9-14]
Grey shading indicates no identified study evaluated the measurement property

AUC, area under the curve; DASH, Disabilities of the Arm, Shoulder, and Hand questionnaire; FAST, Functional Arm Scale for Throwers; GFI, goodness of fit index; HAGOS QOL, Copenhagen Hip and Groin Outcome Score Quality of Life subscale; HOOS QOL, Hip dysfunction and Osteoarthritis Outcome Score Quality of Life subscale; HRQoL, health-related quality of life; ICC, intraclass correlation coefficient; iHOT-33, International Hip Outcome Tool-33; iHOT-12, International Hip Outcome Tool-12; KJOC, Kerlan-Jobe Orthopaedic Clinic questionnaire; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; MDC, minimal detectable change; n, sample size; PASS, Pediatric/Adolescent Shoulder Survey; PROM, patient-reported outcome measure; SEM, standard error of measurement; SRMR, standardized root mean square residual

Appendix M: Overall Rating and Quality of Evidence for Identified HRQoL PROMs (Chapter 2)

HRQoL PROM	Methodological Quality	Summarized Result	Sample Size[a]	Overall Rating	Quality of Evidence[b]
Content validity					
Generic PROMs					
ALQS	1 inadequate study	*Uninjured collegiate athletes:* Insufficient relevance, insufficient comprehensiveness, insufficient comprehensibility	31	Insufficient	Very low
DPA-MSC	1 doubtful study	*Injured competitive and recreational youth athletes:* Inconsistent relevance, insufficient comprehensiveness, insufficient comprehensibility	31	Inconsistent	Low
DPA-MSC SF-10					
DPA-MSC SF-8					
KIDSCREEN-52					
KIDSCREEN-10					
PedsQL					
QoL survey					
SF-36					
SF-12					
WHOQOL-BREF					
Condition-Specific PROMs					
FAST	1 doubtful study	*Uninjured competitive and recreational throwing athletes:* Inconsistent relevance, insufficient comprehensiveness, inconsistent comprehensibility	63	Inconsistent	Low
HAGOS QOL					
HOOS QOL					
iHOT-33					
iHOT-12					
KOOS QOL					
PASS	1 inadequate study	*Injured active youth:* Inconsistent relevance, insufficient comprehensiveness, insufficient comprehensibility	NR	Insufficient	Very low

Structural validity					
Generic PROMs					
ALQS	1 adequate study	Multidimensional score EFA: Factor 1=30.205%, factor 2=11.167%, factor 3=9.580%, factor 4=7.541%, and factor 5=6.841% of total variance	159	Indeterminate	Moderate
DPA-MSC	1 very good study	*Injured active youth:* Multidimensional score CFA: CFI=0.937, TLI=0.924, RMSEA=0.085	125	Insufficient	High
	1 adequate study	*Uninjured active youth:* Multidimensional score EFA: 2 factors explain 65.1% of total variance	456	Indeterminate	Moderate
	1 very good study	*Injured and uninjured active youth:* Multidimensional score CFA: CFI=0.962, TLI=0.947, RMSEA=0.060	796	Indeterminate	High
DPA-MSC SF-10	1 very good study	Multidimensional score CFA: CFI=0.981-0.996, TLI=0.968-0.990, RMSEA=0.028-0.050	796	Sufficient	High
DPA-MSC SF-8	1 very good study	Multidimensional score CFA: CFI=0.996-0.997, TLI=0.993-0.994, RMSEA=0.023-0.025	796	Sufficient	High
KIDSCREEN-52	1 inadequate study	Multidimensional score EFA: Factor 1=26.71%, factor 2=6.37%, factor 3=5.23%, factor 4=5.09%, factor 5=4.22%, factor 6=3.79%, factor 7=3.50%, factor 8=1.53%, factor 9=1.43%, factor 10=1.23%, and factor 11=1.04% of total variance	343	Sufficient	Moderate
KIDSCREEN-10					
PedsQL					
QoL survey	1 very good study	Multidimensional score CFA: CFI=0.98, RMSEA=0.077, SRMR=0.055	446	Sufficient	High

SF-36					
SF-12					
WHOQOL-BREF					
Condition-Specific PROMs					
FAST	1 very good study	Multidimensional score CFA: GFI=0.991, SRMR=0.043	557	Sufficient	High
HAGOS QOL	1 inadequate study	Multidimensional score EFA: Factor 1=49% of total variance	73	Indeterminate	Very low
HOOS QOL					
iHOT-33					
iHOT-12					
KOOS QOL					
PASS					
Internal consistency					
Generic PROMs					
ALQS	1 doubtful study	Cronbach's alpha=0.54-0.83, item-total correlation=0.267-0.580	159	Indeterminate (Lack of sufficient structural validity in an active youth population)	Low
DPA-MSC	1 very high and 1 doubtful study	*Injured active youth:* Cronbach's alpha=0.667, item-total correlation=0.421-0.744	48	Insufficient	Very low
	1 very good study	*Uninjured active youth:* Cronbach's alpha=0.878	456	Indeterminate (Lack of sufficient structural validity in an active youth population)	High
	1 very good study	*Injured and uninjured active youth:* Cronbach's alpha=0.91	31	Indeterminate (Lack of sufficient structural validity in an active youth population)	High
DPA-MSC SF-10	1 very good study	Cronbach's alpha=0.850	690	Sufficient	High
DPA-MSC SF-8	1 very good study	Cronbach's alpha=0.852	690	Sufficient	High
KIDSCREEN-52	1 very good study	Cronbach's alpha=0.71-0.88	343	Sufficient	High
KIDSCREEN-10	1 inadequate study	Cronbach's alpha=0.74	156	Sufficient	Very low
PedsQL	1 very good study	Cronbach's alpha=0.79-0.87	235	Indeterminate	High

				(Lack of sufficient structural validity in an active youth population)	
QoL survey	1 very good study	Cronbach's alpha=0.793-0.950	446	Sufficient	High
SF-36	Multiple studies of at least adequate quality	Summarized Cronbach's alpha=0.610-1.00	1142	Indeterminate (Lack of sufficient structural validity in an active youth population)	High
SF-12					
WHOQOL-BREF	1 very good study[c]	Cronbach's alpha=0.698-0.831	531	Indeterminate (Lack of sufficient structural validity in an active youth population)	High
Condition-Specific PROMs					
FAST	1 very good study	Cronbach's alpha=0.84-0.95	557	Sufficient	High
HAGOS QOL					
HOOS QOL					
iHOT-33					
iHOT-12					
KOOS QOL					
PASS					
Test-retest reliability					
Generic PROMs					
ALQS					
DPA-MSC	1 inadequate study	*Injured active youth:* ICC=0.943	31	Sufficient	Very low
DPA-MSC SF-10					
DPA-MSC SF-8					
KIDSCREEN-52					
KIDSCREEN-10					
PedsQL					
QoL survey	1 adequate study	ICC=0.676-0.809	340	Sufficient	Moderate
SF-36	1 adequate study	ICC=0.505-0.756	340	Indeterminate	Moderate
SF-12					
WHOQOL-BREF					
Condition-Specific PROMs					
FAST	1 doubtful study	ICC=0.91-0.98	154	Sufficient	Low
HAGOS QOL	1 adequate study	ICC=0.85	23	Sufficient	Very Low
HOOS QOL	1 adequate study	ICC=0.92	30	Sufficient	Very Low

iHOT-33	1 adequate study	ICC=0.93	30	Sufficient	Very Low
iHOT-12					
KOOS QOL	1 doubtful study	ICC=0.894	16	Sufficient	Very low
PASS					
Measurement error					
Generic PROMs					
ALQS					
DPA-MSC					
DPA-MSC SF-10					
DPA-MSC SF-8					
KIDSCREEN-52					
KIDSCREEN-10					
PedsQL					
QoL survey					
SF-36					
SF-12					
WHOQOL-BREF					
Condition-Specific PROMs					
FAST	1 doubtful study	SEM=3.8-6.1, MDC=10.5-17.0	154	Indeterminate (MIC is not defined)	Low
HAGOS QOL	1 adequate study	SEM=6.5, individual MDC_{95}=18.1, group MDC_{95}=3.8	23	Indeterminate (MIC is not defined)	Very Low
HOOS QOL	1 adequate study	SEM=5.9, individual MDC_{95}=16.4, group MDC_{95}=3.0	30	Indeterminate (MIC is not defined)	Very Low
iHOT-33	1 adequate study	SEM=5.6, individual MDC_{95}=15.6, group MDC_{95}=2.9	30	Indeterminate (MIC is not defined)	Very Low
iHOT-12					
KOOS QOL	1 doubtful study	SEM=6.2, MDC=17.29	16	Indeterminate (MIC is not defined)	Very low
PASS					
Hypothesis testing for construct validity					
Generic PROMs					
ALQS					
DPA-MSC	1 inadequate study	*Injured active youth:* Correlation with SF-12 PCS=-0.43, SF-12 MCS=-0.53, PROMIS-PF=-0.40	100	Indeterminate (No hypothesis defined)	Very low
DPA-MSC SF-10					
DPA-MSC SF-8					

KIDSCREEN-52					
KIDSCREEN-10					
PedsQL	1 very good study	*Physical Health Summary Score:* Correlation with SEEB=0.38, PACES=0.48, SSES=0.17-0.18, PANES=-0.05-0.08, physical activity=0.19 *Psychosocial Health Summary Score:* Correlation with SEEB=0.23, PACES=0.26, SSES=0.09-0.12, PANES=-0.03-0.12, physical activity=0.02	235	Indeterminate (No hypothesis defined) Indeterminate (No hypothesis defined)	High
QoL survey	1 adequate study	*Social subscale:* Correlation with SF-36=0.226-0.386, WHOQOL Social=0.688, SWLS=0.606, GLTEQ METS=0.186-0.203 *Emotional subscale:* Correlation with SF-36=0.311-0.622, WHOQOL Psychological=0.668, SWLS=0.606, GLTEQ METS=0.197-0.224 *Cognitive subscale:* Correlation with SF-36=0.325-0.499, WHOQOL Psychological=0.588, SWLS=0.497, GLTEQ METS=0.165-0.175 *Spiritual subscale:* Correlation with SF-36=0.082-242, SWLS=0.435, GLTEQ METS=0.130-0.132 *Physical subscale:* Correlation with SF-36=0.164-0.437, WHOQOL Physical=0.435,	446	Indeterminate (No hypothesis defined) Indeterminate (No hypothesis defined) Indeterminate (No hypothesis defined) Indeterminate (No hypothesis defined) Indeterminate (No hypothesis defined) Indeterminate (No hypothesis defined)	Moderate

		SWLS=0.458, GLTEQ METS=0.393-0.423 *Activities of daily living subscale:* Correlation with SF-36=0.182-0.437, WHOQOL Physical=0.527, SWLS=0.511, GLTEQ METS=0.211-0.213 *Integrated subscale:* Correlation with SF-36=0.331-0.569, SWLS=0.698, GLTEQ METS=0.224-0.235		Indeterminate (No hypothesis defined)	
SF-36					
SF-12	1 inadequate study	*Physical Component Score:* Correlation with DPA Total=-0.65, DPA-PSC=-0.64, DPA-MSC=-0.43, PROMIS-PF=0.65 *Mental Component Score:* Correlation with DPA Total=-0.21, DPA-PSC=-0.10, DPA-MSC=-0.53, PROMIS-PF=0.20	100	Indeterminate (No hypothesis defined) Indeterminate (No hypothesis defined)	Very low
WHOQOL-BREF					
Condition-Specific PROMs					
FAST	1 adequate study	Correlation with DASH Total=0.54-0.84, DASH Sport=0.46-0.78, KJOC=0.62-0.81	25	Indeterminate (No hypothesis defined)	Very low
	1 doubtful study	AUC=0.91 for detecting presence of an upper extremity injury	106	Sufficient	Low
HAGOS QOL					
HOOS QOL					
iHOT-33					
iHOT-12					
KOOS QOL					
PASS	1 inadequate study	Correlation with duration of symptoms=0.15-0.28	132	Indeterminate (No hypothesis defined)	Very low
Criterion validity					

Generic PROMs					
ALQS					
DPA-MSC	1 adequate study	*Injured active youth:* Correlation with global functioning item=-0.714- -0.751	28	Sufficient	Very low
	1 very good study	*Uninjured active youth:* Correlation coefficient with total DPA=0.691	456	Insufficient	High
DPA-MSC SF-10					
DPA-MSC SF-8					
KIDSCREEN-52					
KIDSCREEN-10					
PedsQL					
QoL survey					
SF-36					
SF-12					
WHOQOL-BREF					
Condition-Specific PROMs					
FAST					
HAGOS QOL					
HOOS QOL					
iHOT-33					
iHOT-12					
KOOS QOL					
PASS					
Responsiveness					
Generic PROMs					
ALQS					
DPA-MSC	1 very good study	*Active youth with an acute injury:* AUC=0.895-0.911 over 1 week and to return to sport	33	Sufficient	Low
	1 very good study	*Active youth with a persistent injury:* AUC=0.702-0.902 over 6 weeks	40	Sufficient	Low
DPA-MSC SF-10					
DPA-MSC SF-8					
KIDSCREEN-52					
KIDSCREEN-10					

PedsQL					
QoL survey					
SF-36					
SF-12					
WHOQOL-BREF					
Condition-Specific PROMs					
FAST	1 very good study	AUC=0.946	18	Sufficient	Low
HAGOS QOL					
HOOS QOL					
iHOT-33					
iHOT-12					
KOOS QOL					
PASS	1 inadequate study	No correlation or AUC calculated	25	Indeterminate	Very low

[a]Sample size of pooled or summarized studies
[b]Quality of evidence by PROM graded as 'high,' 'moderate,' 'low,' or 'very low' as per the modified GRADE approach[1-4]
[c]Ignored results from Cieslak et al. (2007)[5] due to poor study quality
Grey shading indicates no identified study evaluated the measurement property

ALQS, Athlete Life Quality Scale; AUC, area under the curve; CFA, confirmatory factor analysis; CFI, comparative fit index; DASH, Disabilities of the Arm, Shoulder, and Hand questionnaire; DPA, Disablement of the Physically Active; DPA-MSC, DPA-Mental Summary Component; DPA-MSC SF-10, DPA-MSC Short-Form 10; DPA-MSC SF-8, DPA-MSC Short-Form 8; EFA, exploratory factor analysis; FAAM-S, Foot and Ankle Ability Measure-Sport; FAI, femoroacetabular impingement; FAST, Functional Arm Scale for Throwers; GFI, goodness of fit index; GLTEQ, Godin Leisure Time Exercise Questionnaire; HAGOS QOL, Copenhagen Hip and Groin Outcome Score Quality of Life subscale; HOOS QOL, Hip dysfunction and Osteoarthritis Outcome Score Quality of Life subscale; HRQoL, health-related quality of life; ICC, intraclass correlation coefficient; iHOT-33, International Hip Outcome Tool-33; iHOT-12, International Hip Outcome Tool-12; IQPA, International Questionnaire of Physical Activity; KJOC, Kerlan-Jobe Orthopaedic Clinic questionnaire; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; MDC, minimal detectable change; METS, metabolic equivalents; MIC, minimal important change; MVPA, moderate-to-vigorous physical activity; n, sample size; NCAA, National Collegiate Athletic Association; NR, not reported; QoL survey, Quality of Life survey; PACES, Physical Activity Enjoyment Scale; PANES, Physical Activity Neighborhood Environment Scale; PASS, Pediatric/Adolescent Shoulder Survey; PedsQL, Pediatric Quality of Life Inventory; PROM, patient-reported outcome measure; PROMIS-PF, Patient-Reported Outcomes Measurement Information System Physical Functioning subscale; RMSEA, root mean square error of approximation; SCB, substantial clinical benefit; SD, standard deviation; SEEB, Self-Efficacy for Exercise Behaviors questionnaire; SEM, standard error of measurement; SF-36, Short-Form 36; SF-12, Short-Form 12; SRMR, standardized root mean square residual; SSES, Social Support and Exercise Survey; SWLS, Satisfaction With Life Scale; TLI, Tucker-Lewis Index; WHOQOL-BREF, World Health Organization Quality of Life abbreviated instrument

Appendix N: Interpretability and Feasibility for Identified HRQoL PROMs (Chapter 2)

HRQoL PROM	Percentage of Missing Items	Floor and Ceiling Effects	Minimal Important Change	Response Shift	Comprehens-ibility	Time to Complete	Cost
Generic PROMs							
ALQS						15 minutes[1]	Free
DPA-MSC	<1% missing[2]	No floor effects[3, 4] but ceiling effects exist for injured athletes[3]	9 points for individuals with an acute injury and 6 points for individuals with a persistent injury[4]	No evidence of a response shift in individuals with chronic ankle instability following a rehabilitation intervention[5]	MDC=2.74 in individuals with chronic ankle instability[5]		Free
DPA SF-10 MSC							Free
DPA SF-8 MSC							Free
KIDSCREEN-52							Free for academic and non-commercial research; €500 for commercial studies
KIDSCREEN-10							Free for academic and non-commercial research; €500 for commercial studies
PedsQL							Fee varies >$1000 USD
QoL survey							Free
SF-36			10 points for domain scores and 5 points for summary scores[a]				Free
SF-12							$150 USD for professional, clinical, or research use
WHOQOL-BREF							Free
Condition-Specific PROMs							
FAST		Floor effects exist for the Psychological Impact and Advancement subscales for injured and uninjured baseball players and ceiling effects exist for the Pitcher Module for injured					Free

		and uninjured pitchers[6]					
HAGOS QOL subscale	<1% missing[7]	No floor effects but ceiling effects may exist for professional and semi-professional Australian football players[8]	10-15 points[a]				Free
HOOS QOL subscale	<1% missing[7]						Free
iHOT-33	<1% missing[7]		10-15 points[a]				Free
iHOT-12			12.1 points[9]		Substantial clinical benefit score=84.7[9]		Free
KOOS QOL subscale	<11% missing[10]						Free
PASS	20.5% missing[11]	No floor or ceiling effects[11]					Free

[a]Estimate of MIC was not performed in active youth. The MIC for the SF-36 is from Ware et al. (1994),[12] HAGOS QOL subscale is referenced from Thorborg et al. (2011),[13] and iHOT-33 from Mohtadi et al. (2012)[14]
Grey shading indicates no identified study reported the characteristic

ALQS, Athlete Life Quality Scale; DPA, Disablement of the Physically Active; DPA-MSC, DPA-Mental Summary Component; DPA-MSC SF-10, DPA-MSC Short-Form 10; DPA-MSC SF-8, DPA-MSC Short-Form 8; FAST, Functional Arm Scale for Throwers; HAGOS QOL, Copenhagen Hip and Groin Outcome Score Quality of Life subscale; HOOS QOL, Hip dysfunction and Osteoarthritis Outcome Score Quality of Life subscale; iHOT-33, International Hip Outcome Tool-33; iHOT-12, International Hip Outcome Tool-12; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; MDC, minimal detectable change; MIC, minimal important change; QoL survey, Quality of Life survey; PASS, Pediatric/Adolescent Shoulder Survey; PedsQL, Pediatric Quality of Life Inventory; PROM, patient-reported outcome measure; SF-36, Short-Form 36; SF-12, Short-Form 12; USD, US dollars; WHOQOL-BREF, World Health Organization Quality of Life abbreviated instrument

Appendix O: Distribution of Identified HRQoL PROM Scoring for Interpretability (Chapter 2)

HRQoL PROM	Reference & Country	Subscales or Domains	Distribution of Scores Mean±SD	Scoring Range
Generic PROMs				
ALQS	Gentner et al. (2011), USA[1]	General Life Satisfaction	NR	4-28
		Physical Satisfaction	NR	2-14
		Team/Sport Satisfaction	NR	4-28
		Primary Social Satisfaction	NR	2-14
		Recovery/ Social Satisfaction	NR	3-21
DPA-MSC	Vela & Denegar (2010), USA[2]	Mental Summary Component	NR	0-16
	Houston et al. (2015), USA[3]	Mental Summary Component	3.00±3.70	0-16
	Baker et al. (2019), USA[4]	Mental Summary Component	NR	0-16
	White et al. (2018), USA[5]	Mental Summary Component	4.1±4.3	0-16
	Hoch et al. (2019), USA[6]	Mental Summary Component	2.00±5	0-16
	Powden et al. (2019), USA[7]	Mental Summary Component	2.30±2.62	0-16
DPA MSC SF-8	Baker et al. (2019), USA[4]	Mental Summary Component	NR	0-16
DPA MSC SF-8	Baker et al. (2019), USA[4]	Mental Summary Component	NR	0-16
KIDSCREEN-52	Lorger et al. (2012), Croatia[8]	Physical Well-Being	N/A	Standardized scores with a mean of 50 and SD of 10
		Psychological Well-Being	N/A	
		Moods & Emotions	N/A	
		Self-Perception	N/A	
		Autonomy	N/A	
		Parent Relations and Home Life	N/A	
		Social Support and Peers	N/A	
		School Environment	N/A	
		Bullying	N/A	
		Financial Resources	N/A	
KIDSCREEN-10	Sigvartsen et al. (2016), Norway[9]	*Overall Score*	*62.1±17.1*	Standardized scores with a mean of 50 and SD of 10
PedsQL	Zhang et al. (2018), USA[10]	Physical Functioning	NR	0-100 for all scores
		Social Functioning	NR	
		School Functioning	NR	
		Emotional Functioning	NR	
		Physical Health Summary	NR	
		Psychosocial Health Summary	NR	

QoL survey	Gill et al. (2015), USA[11]	Social	18.7±3.75	1-25
		Emotional	17.7±3.89	1-25
		Cognitive	18.5±3.19	1-25
		Spiritual	17.5±4.88	1-25
		Physical	18.0±3.90	1-25
		Activities of Daily Living	12.6±2.05	1-15
		Integrated	15.7±3.02	1-20
SF-36	Gill et al. (2015), USA[11]	Physical Functioning	28.5±3.35	Standardized scores with a mean of 50 and SD of 10
		Role-Physical	17.7±3.17	
		Pain	8.3±1.56	
		General Health	19.5±3.58	
		Vitality	13.2±2.60	
		Social Functioning	8.4±1.68	
		Role-Emotional	12.5±2.76	
		Mental Health	19.0±3.33	
		Physical Component Score	*74.0±8.17*	
		Mental Component Score	*53.2±8.68*	
	Huffman et al. (2008), USA[12]	Physical Functioning	97.7±8.0	Standardized scores with a mean of 50 and SD of 10
		Role-Physical	94.5±17.8	
		Pain	83.9±17.9	
		General Health	84.5±13.4	
		Vitality	69.1±13.7	
		Social Functioning	94.5±11.9	
		Role-Emotional	96.8±14.2	
		Mental Health	82.6±10.7	
SF-12	Hoch et al. (2019), USA[6]	*Physical Component Score*	*45.58±13*	Standardized scores with a mean of 50 and SD of 10
		Mental Component Score	*56.53±10*	
WHOQOL-BREF	Gill et al. (2015), USA[11]	Physical	29.0±3.75	7-35
		Psychological	23.4±3.68	6-30
		Social	11.6±2.28	3-15
		Environmental	30.7±4.93	8-40
		"How would you rate your quality of life?"	4.20±0.73	1-5
		"How satisfied are you with your health?"	3.79±0.94	1-5
	Cieslak et al. (2007), Brazil[13a]	Physical	N/A	
		Psychological	N/A	
		Social	N/A	
		Environmental	N/A	
		"How would you rate your quality of life?"	N/A	
		"How satisfied are you with your health?"	N/A	
Condition-Specific PROMs				
FAST	Sauers et al. (2017), USA[14]	*Overall Score*	*NR*	0-100
	Sauers et al. (2011), USA[15]	*Overall Score*	*9.9±10.3*	0-100
	Huxel Blivin et al. (2017), USA[16]	Throwing	Uninjured throwing athletes: 10.2±10.4	0-100

		Activities of Daily Living Psychological Impact Advancement Pain Pitcher Module *Overall Score*	5.3±9.6 3.4±9.9 5.8±14.5 6.1±9.9 17.2±14.2 *7.3±10.4*	
		Throwing Activities of Daily Living Psychological Impact Advancement Pain Pitcher Module *Overall Score*	Injured throwing athletes: 42.0±23.4 21.8±17.8 16.5±17.7 44.3±35.5 29.0±19.0 52.8±35.0 *33.5±18.5*	0-100
HAGOS QOL subscale	Drew et al. (2017), Australia[17]	Hip- and/or Groin-Related QOL Subscale	Median 95, range 75-100	0-100
	Hinman et al. (2014), Australia[18]	Hip- and/or Groin-Related QOL Subscale	34.8±16.7	0-100
HOOS QOL subscale	Hinman et al. (2014), Australia[18]	Hip-related QOL Subscale	36.4±20.3	0-100
iHOT-33	Hinman et al. (2014), Australia[18]	Symptoms and Functional Limitations Sports and Recreational Activities Limitations Job-Related Concerns Social, Emotional, and Lifestyle Concerns *Overall Score*	60.9±22.3 29.3±23.0 60.1±30.7 45.9±24.2 *51.8±21.5*	0-100
iHOT-12	Clapp et al. (2019), USA[19]	*Overall Score*	*42.6±18.2*	0-100
KOOS QOL subscale	Hoch et al. (2015), USA[20]	Knee-related QOL Subscale	84.4±22.5	0-100
PASS	Edmonds et al. (2017), USA[21]	Compensatory Mechanism/Function Domain Symptoms/Emotion Domain *Overall Score*	55±21 63±19 *57±17*	0-100

[a]Study did not describe scores that corresponding with the PROM scoring and were subsequently omitted
Italicized scores indicate summary scores or overall scores

ALQS, Athlete Life Quality Scale; DPA, Disablement of the Physically Active; DPA-MSC, DPA-Mental Summary Component; DPA-MSC SF-10, DPA-MSC Short-Form 10; DPA-MSC SF-8, DPA-MSC Short-Form 8; FAST, Functional Arm Scale for Throwers; HAGOS QOL, Copenhagen Hip and Groin Outcome Score Quality of Life subscale; HOOS QOL, Hip dysfunction and Osteoarthritis Outcome Score Quality of Life subscale; iHOT-33, International Hip Outcome Tool-33; iHOT-12, International Hip Outcome Tool-12; KOOS QOL, Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale; N/A, not applicable; NR, not reported; QoL survey, Quality of Life survey; PASS, Pediatric/Adolescent Shoulder Survey; PedsQL, Pediatric Quality of Life Inventory; PROM, patient-reported outcome measure; SD, standard deviation; SF-36, Short-Form 36; SF-12, Short-Form 12; WHOQOL-BREF, World Health Organization Quality of Life abbreviated instrument

Appendix P: Chapter 3 Original Publication – International Journal of Public Health and Environmental Research

International Journal of *Environmental Research and Public Health*

MDPI

Article

What Does the Future Hold? Health-Related Quality of Life 3–12 Years Following a Youth Sport-Related Knee Injury

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Abstract: Knee trauma can lead to poor health-related quality of life (HRQoL) and osteoarthritis. We aimed to assess HRQoL 3–12 years following youth sport-related knee injury considering HRQoL and osteoarthritis determinants. Generic (EQ-5D-5L index, EQ-VAS) and condition-specific (Knee injury and Osteoarthritis Outcome Score quality of life subscale, KOOS QOL) HRQoL were assessed in 124 individuals 3–12 years following youth sport-related knee injury and 129 uninjured controls of similar age, sex, and sport. Linear regression examined differences in HRQoL outcomes by injury group. Multivariable linear regression explored the influence of sex, time-since-injury, injury type, body mass index, knee muscle strength, Intermittent and Constant Osteoarthritis Pain (ICOAP) score, and Godin Leisure-Time Exercise Questionnaire (GLTEQ) moderate-to-strenuous physical activity. Participant median (range) age was 23 years (14–29) and 55% were female. Injury history was associated with poorer KOOS QOL (−8.41; 95%CI −10.76, −6.06) but not EQ-5D-5L (−0.0074; −0.0238, 0.0089) or EQ-VAS (−3.82; −8.77, 1.14). Injury history (−5.14; −6.90, −3.38), worse ICOAP score (−0.40; −0.45, −0.36), and anterior cruciate ligament tear (−1.41; −2.77, −0.06) contributed to poorer KOOS QOL. Worse ICOAP score contributed to poorer EQ-5D-5L (−0.0024; −0.0034, −0.0015) and higher GLTEQ moderate-to-strenuous physical activity to better EQ-VAS (0.10; 0.03, 0.17). Knee trauma is associated with poorer condition-specific but not generic HRQoL 3–12 years post-injury.

Keywords: osteoarthritis; pain; physical activity; prevention

1. Introduction

Traditionally, osteoarthritis has been considered a disease, largely defined by structural findings seen on imaging. However, there is an inconsistent relationship between imaging findings and outcomes associated with the personal (e.g., disability [1], obesity [2], reduced health-related quality of life, HRQoL [3]) and societal burden (e.g., rising health-care costs, workforce productivity loss [4,5]) of osteoarthritis. We must distinguish between osteoarthritis disease (i.e., pathophysiology) and illness (i.e., a person's lived experience of a condition) because the features of osteoarthritis illness, rather than osteoarthritis disease, are what drives people to seek healthcare.

Knee joint trauma is highly prevalent [6] and an established risk factor for osteoarthritis disease [7–9], but it is unclear if it is also associated with features of osteoarthritis illness, including reduced HRQoL. Health-related quality of life is a multifactorial construct that encompasses the physical, psychological, and social domains of health and is influenced by an individual's perceptions, experiences, expectations, and beliefs [10]. Following a traumatic knee injury, HRQoL may serve as a valuable indicator of osteoarthritis illness because it represents one's health across multiple domains. To gain a thorough understanding of HRQoL, we must assess both generic and condition-specific HRQoL. Generic instruments are best for capturing overall HRQoL and allow for comparisons across different demographic groups or medical conditions. On the other hand, condition-specific HRQoL instruments offer a more nuanced understanding of a particular patient group or condition. Previous research has revealed that individuals with osteoarthritis (injury history not specified) report worse generic and condition-specific HRQoL compared to healthy individuals [11,12]. Similarly, there is evidence of poor generic and condition-specific HRQoL of individuals who have experienced an anterior cruciate ligament (ACL) tear at various timepoints [13–15].

How and to what extent knee joint trauma contributes to changes in HRQoL is unknown. Female sex [16], older age [17], increased pain [18], less physical activity [19], and obesity [20] are associated with reduced generic HRQoL in healthy populations. Similarly, not returning to sport at the same or higher level and higher body mass index (BMI) are linked to poorer generic HRQoL (Assessment of Quality of Life 8D Utility Instrument; r^2 0.19), whereas not returning to sport, higher BMI, and subsequent surgery are linked to poorer condition-specific HRQoL (Knee injury and Osteoarthritis Outcome Score quality of life subscale, KOOS QOL; r^2 0.24) in adults experiencing knee difficulties (e.g., pain, symptoms, functional limitations) 5–20 years post-ACL reconstruction [21]. Notably, many of these characteristics are also established risk factors for structural features of osteoarthritis disease, including female sex [7], older age [7,8], obesity [22,23], and knee extensor muscle weakness [24].

Despite preliminary evidence that HRQoL is impacted following an ACL tear, there is a lack of knowledge about generic and condition-specific HRQoL, and potential osteoarthritis illness, of individuals who have experienced a broader range of knee injuries compared to individuals of similar age, sex, and sport exposure. A better understanding of what factors influence HRQoL of youth and young adults with a history of knee joint trauma is needed to inform future interventions. Therefore, the objective of this study was to assess generic (EQ-5D five-level index score, EQ-5D-5L and EQ-visual analogue scale, EQ-VAS) or condition-specific (KOOS QOL) HRQoL in individuals with a 3–12 year history of a youth sport-related knee injury compared to uninjured controls. To further understand what factors may influence the relationship between injury history and HRQoL, general determinants of HRQoL and osteoarthritis disease (i.e., sex, time since injury, type of injury, BMI, knee extensor strength, knee flexor strength, intermittent knee pain, and self-reported physical activity) were also examined.

2. Materials and Methods

2.1. Study Design

This study was a cross-sectional analysis of data from the first follow-up (3–12 years post-injury) of the Alberta Youth Prevention of Early Osteoarthritis (PrE-OA) historical cohort study.

2.2. Ethics

Ethics approval was granted by the Conjoint Health Research Ethics Board at the University of Calgary, Canada (Ethics ID E-25075). Before testing, all participants provided informed consent/assent and completed a Physical Activity Readiness Questionnaire (PAR-Q, 2002).

2.3. Participants

The PrE-OA cohort consists of a convenience sample of individuals who sustained a youth (≤18 years old) sport-related knee injury 3–12 years previously and uninjured controls of similar age (within 12 months), sex, and sport at the time of injury. Information about cohort recruitment, injury diagnosis, and inclusion and exclusion criteria has been described previously [22,25,26]. Briefly, injured and uninjured participants were recruited after being identified from previous cohort studies examining risk factors for sport injury, a university-based sport medicine centre database, or through collaborators and participants. Injured participants sustained a youth sport-related knee injury (clinical diagnosis of a ligament, meniscus, or other intra-articular tibiofemoral or patellofemoral injury) that required medical attention (e.g., physician, physiotherapist) and disrupted sport participation 3–12 years previously. Uninjured controls were included if they reported no previous knee injury resulting in time-loss from sport. Individuals were excluded if they were pregnant; reported non-steroidal anti-inflammatory use, cortisone injection, or other musculoskeletal injury that disrupted sport, school, or work participation within three months prior to testing; or had a diagnosis of other arthritides or any medical conditions that prevented study participation (e.g., neurological conditions).

2.4. Procedures

These analyses examined data from the first follow-up (3–12 years post-injury) collected during one testing session at the University of Calgary between 2013–2017 [22,25]. Participants completed a battery of questionnaires (study questionnaire, EQ-5D, KOOS, Intermittent and Constant Osteoarthritis Pain Score, ICOAP, and Godin Leisure-Time Exercise Questionnaire score, GLTEQ) then rotated through testing stations that measured their height, weight, and isometric knee strength. A secure, online database was used to store and manage data (REDCap 8.6.5, Vanderbilt University, Nashville, TN, USA).

A study questionnaire gathered participant information (i.e., age, sex), sport information (i.e., pre-injury main sport, sport participation in the last 12 months), and knee injury details as applicable (i.e., type of injury, injury date, subsequent injury or surgery).

2.5. Outcomes

2.5.1. Generic Health-Related Quality of Life

The EQ-5D is a self-reported instrument that measures generic HRQoL [23,27,28]. The EQ-5D is a widely used health utility instrument that consists of two components: the EQ-5D-5L index and EQ-VAS scores. The EQ-5D-5L describes one's health state and is measured in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Participants indicated their health state by selecting one of five levels of responses ranging from no problems to extreme problems for each dimension. Using the Canadian value set [26], health states were converted into EQ-5D-5L index scores which range from −0.148 (worst health status) to 0.949 (best health status). The EQ-VAS evaluates health on a 20 cm vertical visual analog scale with anchors of 0 (worst health you can imagine) and 100 (best health you can imagine). The EQ-5D has been shown to have acceptable reliability [27] and validity [27,28] across musculoskeletal conditions. Although the EQ-5D has not been validated for individuals following a knee injury, it has been previously applied to individuals following ACL reconstruction [29]. The minimal important change (MIC) for Canadian EQ-5D-5L index scores is 0.056 [30] but no MIC for the EQ-VAS in a comparable sample has been established. However, it should be noted that our analyses did not measure change in scores over time.

2.5.2. Condition-Specific Health-Related Quality of Life

The KOOS QOL is one of five subscales of the KOOS [31,32] and assesses knee-specific HRQoL. It consists of four items (awareness of knee problem, lifestyle modification, knee confidence, and overall knee difficulty) scored on a 5-point Likert scale. Subscale scores are converted into a score ranging from 0–100 with higher scores indicating better outcomes. The KOOS demonstrates sufficient internal consistency (pooled Cronbach's alpha 0.79), test-retest reliability (pooled intraclass correlation coefficient 0.88), and measurement error (pooled standard error of measurement 5.9, pooled smallest detectable change 16.3) in ACL injured samples [31,33]. The MIC for the KOOS QOL subscale is 18.3 in individuals who have undergone ACL reconstruction [34].

2.5.3. Body Mass Index

Body mass index (kg/m^2) was calculated from weight (to the nearest 0.1 kg) and height (to the nearest 0.1 cm, shoes removed) measurements using a scale and stadiometer (Model 402 KL, Pelstar, McCook, IL, USA).

2.5.4. Isometric Knee Strength

Normalized isometric knee extensor and flexor strength of the injured (index) limb were measured using handheld dynamometry (Model 01163, Lafayette Instrument, Lafayette, IN, USA) [25]. Prior to testing, all examiners were given a written description of testing and scoring. Each examiner practiced under the guidance of an experienced examiner over a minimum of three 1-hour training sessions before testing study participants [35]. For knee extension, participants were seated with hips and knees in 90° and 60° flexion, respectively, and a handheld dynamometer placed 5 cm proximal to the distal tip of the lateral malleolus on the shin. For knee flexion, participants were in a prone position with the knee in 60° flexion and a dynamometer placed 5 cm proximal to the distal tip of the lateral malleolus on the calf. In all strength tests, the dynamometer was secured to the leg with an immovable strap. After a practice trial, participants completed three experimental trials consisting of 5 s of maximum effort pushing into the dynamometer followed by 15 s of rest. Peak isometric strength scores (N) were converted to peak torque (Nm; force x distance between joint line and dynamometer) and normalized to body weight (Nm/kg). Isometric knee muscle strength testing has sufficient intra- (pooled intraclass correlation coefficient > 0.90) [36,37] and inter-rater reliability (pooled intraclass correlation coefficient > 0.84) [36].

2.5.5. Intermittent Knee Pain

Intermittent knee pain was assessed with the intermittent pain subscale of the ICOAP [38]. This subscale consists of six items that asks patients about "pain that comes and goes" over the past week. Each item is scored on a 5-point Likert scale, summed, and transformed to a subscale score ranging from 0–100 with lower scores indicating better outcomes. The ICOAP has not been evaluated in active youth populations but demonstrates sufficient internal consistency (Cronbach's alpha 0.93) and test-retest reliability (intraclass correlation coefficient 0.85) in individuals with knee osteoarthritis [38].

2.5.6. Physical Activity

Physical activity participation was self-reported using the GLTEQ [39]. Participants reported the number of 15-minute bouts of mild (minimal effort), moderate (not exhausting), and strenuous (heart beats rapidly) physical activity in which they engaged over a typical seven-day period. The total activity in metabolic equivalents (METs) is calculated by multiplying the number of mild, moderate, and strenuous bouts by 3, 5, and 9, respectively, and then summing these values. One MET equals the amount of energy expended by an individual seated at rest. The GLTEQ has been validated to assess physical activity [40,41]. Weekly moderate-to-strenuous METs were the focus of these analyses.

2.6. Data Analysis

Statistical analyses were performed using STATA (v12.1, Stata Corp., College Station, TX, USA). Descriptive statistics [median (range), proportion (95%CI)] were calculated for all participant characteristics and outcomes by study group (knee injury history or not).

Univariable linear regression models (95%CI), accounting for clustering on sex (female/male) and main sport type (e.g., soccer, ice hockey, basketball), were used to assess the association between previous injury history (yes/no) and HRQoL outcome (EQ-5D-5L index, EQ-VAS, and KOOS QOL). To better understand what factors might influence the relationship between injury history and HRQoL outcomes, separate multivariable linear regression models (95%CI), accounting for clustering on sex and main sport type, including sex, time since injury (years), type of injury (ACL tear or other), BMI (kg/m^2), normalized peak knee extensor and flexor strength (Nm/kg), intermittent knee pain (ICOAP intermittent pain subscale), and moderate-to-strenuous physical activity (GLTEQ weekly METs) were considered. Biological sex [7,8], ACL tear [42,43], BMI [7], and knee strength [24] are established risk factors for osteoarthritis disease, whereas sex [16], age [17], BMI [21], pain [44], and physical activity [19], have been associated with generic and/or condition-specific HRQoL outcomes. Time since injury for uninjured participants was coded the same as that of matched injured participants on recruitment and indicate an equivalent injury-free time. Regression analyses began with models that included injury history (primary exposure variable), sex, time since injury, type of injury, BMI, knee extensor and flexor strength, intermittent knee pain, moderate-to-strenuous physical activity, and a two-way interaction term for injury history and sex. After evaluating the significance of the interaction term (i.e., likelihood ratio test, $\geq$0.05), we followed a backwards stepwise elimination approach where covariates with a *p*-value <0.05 were retained and the most parsimonious model was reported. All assumptions for linear regression analyses were assessed and met.

3. Results

A total of 253 participants were recruited, including 124 youth with a previous sport-related knee injury and 129 uninjured controls. The median age of the participants at follow-up was 23 years (range 14–29) and 55% of the participants were females (Table 1). Soccer was the most common pre-injury sport (35%) with ice hockey (21%), basketball (12%), skiing or snowboarding (8%), football (5%), rugby (4%), running (4%), volleyball (4%), dance or gymnastics (2%), horseback riding or rodeo (2%), baseball (1%), figure skating (1%), lacrosse (1%), and field hockey (1%) also identified. Of the injured group, 69 participants (56%) sustained a complete ACL tear, all of whom underwent ACL reconstruction. Twenty participants (16%) had meniscus injuries, 15 (12%) had other ligament injuries (i.e., grade I-II ACL or posterior cruciate ligament injury, grade I-III medial or lateral collateral ligament injury), 18 had a patellofemoral subluxation or dislocation (15%), and two (2%) had a fracture. The median time since injury was 6.7 years (range 2.9–11.6).

For generic HRQoL, the median EQ-5D-5L index score for the uninjured and injured participants was 0.911 (range 0.634–0.949) and 0.911 (range 0.561–0.949), respectively, and the median EQ-VAS score for the uninjured and injured participants was 85 (range 20–100) and 80 (range 10–100), respectively. For condition-specific HRQoL, uninjured participants had a median KOOS QOL score of 100 (range 83–100) whereas injured participants had a median score of 92 (range 64–100). One injured participant did not complete the EQ-5D-5L and three injured participants did not complete the EQ-VAS.

Univariable associations between injury history and HRQoL outcomes are summarized in Table 2. Injury history was not associated with EQ-5D-5L index (−0.0074, 95%CI −0.0238, 0.0089) or EQ-VAS scores (−3.82, 95%CI −8.77, 1.14). However, a negative association was found between injury history and KOOS QOL scores (−8.41, 95%CI −10.76, −6.06).

Table 1. Participant characteristics, outcomes, and covariates by study group.

Characteristic	Uninjured (*n* = 129)	Injured (*n* = 124)
Sex (% female, 95%CI)	56 (47, 64)	53 (44, 62)
Age at injury (years)	-	16 (9–19)
Age at follow-up (years)	23 (14–29)	22 (16–29)
Time since injury (years)	-	6.7 (2.9–11.6)
Type of injury (% ACL tear, 95%CI)	-	56 (47, 64)
Subsequent injury (% yes, 95%CI)	1 (0, 7)	27 (29, 46)
Subsequent surgery (% yes, 95%CI)	-	21 (15, 29)
Radiographic osteoarthritis (% yes, 95%CI) *	0 (0, 0)	7 (3, 15)
MRI-defined osteoarthritis (% yes, 95%CI) †	3 (1, 10)	28 (19, 38)
Main sport (% soccer, 95%CI)	35 (27, 44)	35 (27, 44)
Sport participation in last 12 months (% yes, 95%CI)	95 (90, 98)	89 (81, 93)
EQ-5D-5L index	0.911 (0.634–0.949)	0.911 (0.561–0.949)
EQ-VAS	85 (20–100)	80 (10–100)
KOOS QOL	100 (83–100)	92 (64–100)
BMI (kg/m^2)	23.5 (18.1–33.1)	24.8 (18.6–38.9)
Knee extensor strength (Nm/kg)	1.92 (0.73–4.21)	1.84 (0.40–3.53)
Knee flexor strength (Nm/kg)	1.09 (0.38–2.08)	0.95 (0.37–2.09)
ICOAP intermittent pain	0 (0–33)	0 (0–54)
GLTEQ moderate-to-strenuous physical activity (METs/week)	45 (0–93)	42 (4–136)

Values represent median (range) unless otherwise indicated. Subsequent injury = any tibiofemoral or patellofemoral injury that resulted in seeking medical attention and time-loss from sport participation. Subsequent surgery = any surgery to the index or non-index knee during the follow-up period. Radiographic osteoarthritis of index knee = grade ≥ 2 on the Kellgren-Lawrence Grading System [45]. MRI-defined osteoarthritis of index knee = met criteria for tibiofemoral (medial or lateral compartment), mixed tibiofemoral, or patellofemoral MRI-defined osteoarthritis as per Hunter et al. (2011) [46]. * Data available for 86 uninjured and 84 injured participants. † Data available for 88 uninjured and 87 injured participants. ACL, anterior cruciate ligament; BMI, body mass index; EQ-5D-5L, EuroQoL five-dimension, five-level; EQ-VAS, EuroQoL visual analog scale; GLTEQ, Godin Leisure-Time Exercise Questionnaire; ICOAP, Intermittent and Constant Osteoarthritis Pain Score; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score quality of life subscale; m, metre; MET, metabolic equivalent; MRI, magnetic resonance imaging; *n*, number of participants; Nm, Newton-metre; 95%CI, 95% confidence interval.

Table 2. Univariable linear regression models for injury history and HRQoL outcomes.

Model	*n*	Injury History *	r^2
1. EQ-5D-5L	252	−0.0074 (−0.0238, 0.0089)	0.005
2. EQ-VAS	250	−3.82 (−8.77, 1.14)	0.022
3. KOOS QOL	253	**−8.41 (−10.76, −6.06)**	0.305

Values represent coefficient and 95%CI. All models accounted for clustering by sex and sport. Bolded font represents 95%CI does not encompass zero. * Reference = uninjured participants. EQ-5D-5L, EuroQoL five-dimension, five-level; EQ-VAS, EuroQoL visual analog scale; KOOS QOL, Knee injury and Osteoarthritis Outcome Score quality of life subscale; *n*, number of participants; r^2, coefficient of determination; 95%CI, 95% confidence interval.

Multivariable linear regression models that considered the influence of sex, time since injury, type of injury, BMI, knee extensor and flexor strength, intermittent knee pain, and moderate-to-strenuous physical activity on the relationship between youth sport-related knee injury history and HRQoL outcomes are summarized in Table 3. Regardless of injury history, higher levels of intermittent pain (ICOAP) were associated with poorer generic HRQoL (EQ-5D-5L index −0.0024, 95%CI −0.0034, −0.0015) and, higher levels of moderate-to-strenuous physical activity (GLTEQ) were associated with better generic HRQoL (EQ-VAS 0.10, 95%CI 0.03, 0.17). A significant interaction between injury and sex suggested that injured males have slightly higher generic HRQoL (EQ-5D-5L index 0.0232, 95%CI 0.0042, 0.0422) than uninjured males. Finally, injury history (−5.14, 95%CI −6.90, −3.38), an ACL tear (−1.41, 95%CI −2.77, −0.06), and higher levels of intermittent pain (ICOAP −0.40, 95%CI −0.45, −0.36) were associated with lower condition-specific HRQoL (KOOS QOL). No other associations were found.

Table 3. Multivariable linear regression models for injury history and HRQoL outcomes considering determinants of HRQoL and osteoarthritis disease.

Model	Injury History *	Sex †	Time Since Injury	ACL ‡	BMI (kg/m^2)	Extensor Strength (Nm/kg)	Flexor Strength (Nm/kg)	ICOAP	GLTEQ (MET/wk)	Injury × Sex	r^2
1. EQ-5D-5L	−0.0032 (−0.0170, 0.0107)	−0.0090 (−0.0227, 0.0047)						**−0.0024 (−0.0034, −0.0015)**		**0.0232 (0.0042, 0.0422)**	0.220
2. EQ-VAS	−3.47 (−7.98, 1.04)								**0.10 (0.03, 0.17)**		0.047
3. KOOS QOL	**−5.14 (−6.90, −3.38)**			**−1.41 (−2.77, −0.06)**				**−0.40 (−0.45, −0.36)**			0.587

Values represent coefficient and 95%CI. All models accounted for clustering by sex and sport. Bolded font represents 95%CI does not encompass zero. Shaded cells represent variables that were removed due to lack of evidence of modification or confounding. * Reference = uninjured participants. † Reference = female sex. ‡ Reference = no ACL tear. ACL, anterior cruciate ligament tear; BMI, body mass index; EQ-5D-5L, EuroQoL five-dimension, five-level; EQ-VAS, EuroQoL visual analog scale; GLTEQ, Godin Leisure-Time Exercise Questionnaire moderate-to-strenuous physical activity; ICOAP, Intermittent and Constant Osteoarthritis Pain intermittent pain subscale; kg, kilogram; KOOS QOL, Knee injury and Osteoarthritis Outcome Score quality of life subscale; m, metre; MET, metabolic equivalent; Nm, Newton-metre; r^2, coefficient of determination; wk, week; 95% CI, 95% confidence interval.

4. Discussion

Currently, most of what is known about risk factors for osteoarthritis is relative to markers of osteoarthritis disease (e.g., structural changes, biomechanics), not osteoarthritis illness (e.g., occupational or recreational time-loss, functional limitations, reduced HRQoL). This contrasts the fact that it is the illness that motivates people to seek healthcare and drives the individual and societal burden of osteoarthritis.

We present a novel examination of generic and condition-specific HRQoL in individuals with a previous youth sport-related knee injury compared to uninjured controls of similar age, sex, and sport. Our findings indicate that a 3–12 year history of a youth sport-related knee injury is not associated with generic HRQoL but is negatively associated with condition-specific HRQoL. Exploratory analyses revealed that more intermittent knee pain or less self-reported moderate-to-strenuous physical activity are associated with worse generic HRQoL, as measured by the EQ-5D-5L index and EQ-VAS scores, respectively. Regarding condition-specific HRQoL (KOOS QOL), injury history, a previous ACL tear, and more intermittent knee pain were associated with a poorer outcome. These data imply that there may be distinct determinants of generic and condition-specific HRQoL following a youth sport-related knee injury; therefore, these two outcomes, although related, need to be considered as unique parts of a broad construct. Furthermore, these preliminary analysis suggests that risk factors for osteoarthritis illness, including intermittent knee pain and participation in moderate-to-strenuous physical activity, may differ from osteoarthritis disease.

The finding that generic HRQoL was not associated with a 3–12 year history of a previous youth sport-related knee injury is consistent with a systematic review examining adults (n = 2493, mean age 34 years) at a mean of nine years following ACL reconstruction who reported similar or even better generic HRQoL (Short-Form 36) compared to population norms [14]. In contrast, individual analyses of Australian and Danish cohorts report lower generic HRQoL (Assessment of Quality of Life 4D instrument and EQ-5D-5L index, respectively) in relatively young individuals (n = 147, mean age 48 years) with radiographic osteoarthritis [47] and older individuals (n = 24,513, mean age 64.7 years) with radiographic and/or symptomatic osteoarthritis [48] compared to population norms [49]. With that said, few studies have assessed generic HRQoL in people with osteoarthritis while considering differences based on injury history.

It is plausible that the link between intermittent pain and generic HRQoL may be explained by its physical (e.g., sleep disturbance [50]), psychological (e.g., depression [51]), and social (e.g., activity or hobby limitation [50]) manifestations. Similarly, physical inactivity may influence generic HRQoL through its negative impact on physical (e.g., increased sedentary behaviour [52]), psychological (e.g., depression [53]), and social (e.g., isolation from sports/recreational community [54]) well-being. It is important to note that generic HRQoL could be influenced by factors not assessed here, including but not limited to other injuries, medical conditions (e.g., anxiety, depression, diabetes), and socioeconomic status. Although intermittent pain and moderate-to-strenuous physical activity may be determinants of generic HRQoL of young adults, the influence of many other aspects of physical, psychological, and social health should be investigated.

Current evidence indicates that individuals who have undergone an ACL reconstruction and those who have post-traumatic osteoarthritis may demonstrate deficits in condition-specific HRQoL. Specifically, reduced KOOS QOL scores have been observed at two years post-ACL reconstruction compared to uninjured controls (n = 120, mean age 19 years) [13] and persist up to 5–20 years post-op compared to population norms [14]. Reduced condition-specific HRQoL has also been identified by former collegiate athletes (n = 100, mean age 53.1 years) diagnosed with post-traumatic osteoarthritis compared to athletes with no knee surgery history [55]. Our findings expand beyond these observations to include individuals with a broad range of traumatic knee injuries that occurred in their youth. Taken together, these findings suggest that injury history is an important determinant of condition-specific HRQoL following a sport-related knee injury, regardless of age at injury and injury type.

Intermittent pain was identified as a possible determinant of condition-specific HRQoL, likely due to similar physical, psychological, and social manifestations as those mentioned above. It is also important to consider there is a moderate correlation between the KOOS QOL and pain subscales (Pearson's correlation coefficient 0.603) [25], indicating that there may be some overlap of the constructs measured by these two subscales. Sustaining an ACL tear is a well-established risk factor for osteoarthritis disease [42] and, as our findings suggest, may also contribute to greater reductions in condition-specific HRQoL and possibly osteoarthritis illness. This is unsurprising as an ACL tear is associated with substantial physical impairments (e.g., knee muscle weakness [56]), psychological consequences (e.g., heightened fear of reinjury [57]), and social limitations (e.g., isolation from sport community [54]) as well as a relatively long rehabilitation period.

Aside from a past ACL tear, we found no association between other established risk factors for osteoarthritis disease (i.e., sex [7,8], BMI [7], knee strength [24]) and generic or condition-specific HRQoL, an important feature of osteoarthritis illness. Instead, what has emerged is the possible influence of intermittent pain and physical inactivity on generic and/or condition-specific HRQoL. These findings suggest that the forces leading to osteoarthritis disease and osteoarthritis illness following knee joint trauma may be somewhat distinct. They also suggest that intermittent pain and physical inactivity might be important targets for preventing osteoarthritis illness and highlight the need to consider both determinants of disease and illness when designing and evaluating prevention programs. Ultimately, a better understanding of the determinants of osteoarthritis disease and illness following a knee joint injury could contribute to the individualization of osteoarthritis prevention programs.

The strengths of this study are the inclusion of uninjured controls of similar age, sex, and sport exposure and a broad definition of knee injury (i.e., beyond an ACL tear) confirmed at the time of injury. In contrast, this study was not specifically powered for our research questions. However, these preliminary findings can be used to inform an adequately powered study to fully address related objectives. Many of the participants in the Alberta Youth PrE-OA cohort may be from middle-to-high socioeconomic status given the recruitment sources and their ability to access organized sport, post-secondary education, and healthcare which limits the generalizability of our findings. Future studies should seek diverse and inclusive samples to better understand what happens to people from all backgrounds following a youth sport-related knee injury. It is important to highlight that the KOOS QOL subscale only consists of four items which may not capture the breadth and complexity of condition-specific HRQoL. Although only limited to people with an ACL injury, a possible alternative is the Anterior Cruciate Ligament-Quality of Life questionnaire (ACL-QOL) [58] which comprehensively assesses multiple domains of condition-specific HRQoL (i.e., symptoms and physical complaints, work-related concerns, recreational activities and sports participation, lifestyle, and social and emotional). Using a self-report measure of physical activity also introduces possible recall bias. When possible, accelerometry should be utilized as it is a more valid measure of physical activity. Lastly, only data on biological sex is available for the Alberta Youth PrE-OA study. Arguably, one's biological sex and socially constructed gender could influence HRQoL and, therefore, both the influence of sex and gender should be examined going forward [59].

More research is required to better understand osteoarthritis illness, particularly in individuals who have sustained a previous youth sport-related knee injury. Further investigation of both generic and condition-specific HRQoL outcomes as it relates to osteoarthritis prevention is needed as they likely represent related yet separate constructs. Future studies should confirm and continue to explore the determinants of generic and condition-specific HRQoL and assess how these outcomes change in the short-, medium-, and long-term after a youth sport-related knee injury. In addition to building upon previous evidence, we recommend engaging patients as research partners to ensure relevant constructs related to HRQoL and osteoarthritis illness are examined. This information can be leveraged to develop osteoarthritis prevention programs that target aspects of both osteoarthritis disease and illness.

5. Conclusions

The findings of this study suggest that generic and condition-specific HRQoL are distinct from one another and, therefore, both should be measured in research and clinical practice. Injury history appears to be associated with condition-specific but not generic HRQoL. Based on exploratory analyses, intermittent knee pain and moderate-to-strenuous physical activity may be factors that influence generic HRQoL whereas injury history, injury type, and intermittent knee pain may be factors that influence condition-specific HRQoL. Targeting intermittent knee pain and physical activity, particularly in youth and young adults who have sustained an ACL injury, may help optimize HRQoL. This study provides preliminary evidence that risk factors for osteoarthritis illness may differ from osteoarthritis disease. This finding can inform the design of future studies and osteoarthritis prevention strategies.

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Appendix Q: Bespoke Study Questionnaire for the Alberta PrE-OA Cohort Study Conducted at the University of Calgary (Chapter 3)

Consequences of Knee Joint Injury in Youth Sport: Implications for OA and Other Health Outcomes
2013-2016

UNIVERSITY OF CALGARY

Follow-up 1 Questionnaire:

Participants with NO History of Knee Injury

Sport Injury Prevention Research Centre
UNIVERSITY OF CALGARY

Please complete this form before baseline testing and bring it with you on the testing day. You may seek help from a parent or guardian.

office use only	
Study Subject ID#	
Past SIPRC study:	

SECTION A: Demographics

1. Name:	**11. If female: are you pregnant?** ☐ Yes ☐ No ☐ Do not know
2. Sex: ☐ Male ☐ Female	
3. Current Mailing Address (include postal code):	**12. If female: how many childbirths have you had?**
	13. If female: When did you start to menstruate? month/year: /
4. Permanent Mailing Address (e.g., parent's address):	**14. If female: on average, how many periods do you have per year?** ☐ 0-3 ☐ 4-6 ☐ 7-9 ☐ 10 or more
5. Email:	
6. Phone number: ( )	
7. Permanent phone number (parents): ( )	
8. Date of birth: / / Day Month Year	
9. Current age:	
10. Today's Date: / / Day Month Year	

SECTION C: Healthcare Utilization in the Past Year

Please indicate if in the PAST YEAR you have visited the following practitioners or received the following services for ANY REASON (exclude visits and services recieved as an inpatient)

Practitioners and Services	Visited	No Visits
physician - emergency room doctor		
physician - general practitioner/ family		
physician - sport medicine doctor		
surgeon		
physiotherapist		
chiropractor		
massage therapist		
athletic therapist		
magnetic resonance imaging (MRI)		
computer tomography (CT scan)		
radiographs (x-rays)		
other (please specify)		

questionnaire continues

Consequences of Knee Joint Injury in Youth Sport: Implications for OA and Other Health Outcomes 2013-2016

In the past year, have you been admitted to the hospital for any reason.

☐ no   If you answered 'no' to this question, please skip to Section D.

☐ yes

Please describe ANY hospitalisations you have had in the **past year** below. If you have had more than 2 hospitalisations, use a separate sheet to describe.

Primary reason for hospitalisation	Number of nights in hospital	Did you have a surgery while in hospital?	
		I **DID NOT** have surgery	I **DID** have surgery: Please name and describethe surgery to best of your ability.
		☐	
		☐	

SECTION D: Sport and Physical Activity Participation in the Past Year

Based on the **PAST YEAR** (last 12 months), have you participated in any sports?

☐ no, I have not participated in any sports in the past year.

☐ yes, I have participated in sports in the past year.

If ***no,*** please skip to Section E: Medical History. If ***yes,*** please estimate the average number of hours per week you participated in each sport

SPORT	hrs/wk, mo/yr	SPORT	hrs/wk, mo/yr	SPORT	hrs/wk, mo/yr
☐ Aerobics	,	☐ Floor hockey	,	☐ Soccer	,
☐ Backpacking	,	☐ Football	,	☐ Squash	,
☐ Badminton	,	☐ Golf	,	☐ Speed skating	,
☐ Baseball	,	☐ Gymnastics	,	☐ Swimming	,
☐ Basketball	,	☐ Hiking/ Scrambling	,	☐ Tennis	,
☐ Boxing (incl. kick)	,	☐ Hockey	,	☐ Track and field	,
☐ Canoeing	,	☐ Horse riding	,	☐ Triathlon	,
☐ Caving	,	☐ Kayaking	,	☐ Ultimate Frisbee	,
☐ Climbing - Alpine	,	☐ Lacrosse	,	☐ Volleyball	,
☐ Climbing - Ice	,	☐ Martial arts	,	☐ Waterpolo	,
☐ Climbing - Traditional	,	☐ Rafting	,	☐ Weight training	,
☐ Cycling - Mountain	,	☐ Rollerblading	,	☐ Wrestling	,
☐ Cycling - Road	,	☐ Rugby	,	☐ *Other:	,
☐ Dance	,	☐ Running	,	**Please describe other:*	
☐ Dirt biking	,	☐ Skateboarding	,		
☐ Diving	,	☐ Skiing - Downhill	,		
☐ Field hockey	,	☐ Skiing - Cross-country	,		
☐ Figure skating	,	☐ Snowboarding	,		

SECTION E: Medical History

1.a) Have you had any other major injuries that have required medical attention **AND** resulted in at least 1 day of missed participation from sport and recreational activities?

☐ Yes   ☐ No   If you answered 'no' to this question, please skip to question 3

if "Yes", please describe this injury(s) to the best of your ability: ____________________

questionnaire continues

Consequences of Knee Joint Injury in Youth Sport: Implications for OA and Other Health Outcomes 2013-2016

1.b) What were you doing when you were injured (i.e., what caused the injury)?

☐ Sport or recreation ☐ Other

1.c) Injury details:

Injury Date *Month/Year*	Did the injury occur:	Injury Type *sprain, bruise, etc.*	Body Part (include side of body) *left knee, nose, etc.*	Sport of Occurrence *soccer, hockey, etc.*	Treatment description *first aid, physiotherapy, etc.*	Time loss before FULL return to sport *1 day, 3 weeks, etc.*
	□ 0-3 months ago □ 3-12 months ago □ more than 12 months ago					
	□ 0-3 months ago □ 3-12 months ago □ more than 12 months ago					
	□ 0-3 months ago □ 3-12 months ago □ more than 12 months ago					

2a. Do you have any ongoing injuries?

☐ No ☐ Yes ☐ Do not know

*If **yes**, describe these injuries to the best of your ability:*

2b. Are you currently receiving treatment for this / these injury(s)?

☐ No ☐ Yes ☐ Do not know ☐ Not Applicable (i.e. no ongoing injury)

*If **yes**, describe the treatments to the best of your ability:*

3. Are you currently taking medication **for ANY injuries**? (Please check all the apply)

☐No ☐Yes ☐ibuprofen (e.g., Advil)

☐acetominophen (e.g., Tylenol)

☐Other; please describe:

4. Do you take medications for any other reasons (i.e., not for injuries) on a regular basis? (e.g., asthma inhaler, antidepressants, birth control pills etc.)

☐No ☐Yes

*If **yes**, please list:*

5. Are you currently taking any supplements (vitamins, minerals, protein powder, etc.) ?

☐No ☐Yes

*If **yes**, please list:*

Have you been diagnosed by a physician with any of the following:	No	Yes	Do not know	*If **yes**, describe your condition(s) to the best of your abilit **(include side of body)**:*	Year of diagnosis	Do not know
6. a bone fracture, arthritis, or other muscle or bone related condition	☐	☐	☐			☐
7. a systemic disease (e.g., cancer, thyroid disease, heart disease)	☐	☐	☐			☐
8. a circulation or heart-related problem (e.g., heart murmur, irregular heart beat, congenital heart deformity)	☐	☐	☐			☐
9. a neurological disorder (e.g., brain injury, cerebral palsy, pinched nerve, "stinger", multiple sclerosis, etc.)	☐	☐	☐			☐

Thank you for your time and effort in completing this questionnaire. Please bring this with you on the testing day to the Sport Medicine Centre at the University of Calgary.

Consequences of Knee Joint Injury in Youth Sport: Implications for OA and Other Health Outcomes
2013-2016

UNIVERSITY OF CALGARY

Follow-up 1 Questionnaire:

Participants with History of Knee Injury

Please complete this form before baseline testing and bring it with you on the testing day. You may seek help from a parent or guardian.

Sport Injury Prevention Research Centre
UNIVERSITY OF CALGARY

office use only	
Study Subject ID#	
Past SIPRC study:	

SECTION A: Demographics

1. Name:	
2. Sex:	☐ Male ☐ Female
3. Current Mailing Address (include postal code):	
4. Permanent Mailing Address (e.g., parent's address):	
5. Email:	
6. Phone number: ( )	
7. Permanent phone number (parents): ( )	
8. Date of birth:	/ / Day Month Year
9. Current age:	
10. Today's Date:	/ / Day Month Year
11. If female: are you pregnant?	☐ Yes ☐ No ☐ Do not know
12. If female: how many childbirths have you had?	
13. If female: When did you start to menstruate? month/year: /	
14. If female: on average, how many periods do you have per year?	☐ 0-3 ☐ 4-6 ☐ 7-9 ☐ 10 or more

SECTION B: Knee Injury Details

1. STUDY (injured) KNEE:	**RIGHT**
2. Dominant Leg (e.g., for kicking a soccer ball):	Right ☐ Left ☐
3. Type of knee injury (check all that apply):	☐ Anterior Cruciate Ligament (ACL) ☐ Posterior Cruciate Ligament (PCL) ☐ Medial Collateral Ligament (MCL) ☐ Lateral Collateral Ligament (LCL) ☐ Meniscus ☐ Other (describe): ____________ ☐ Do not know
4. Age when injured:	
5. Date of knee injury:	/ / Day Month Year
6. How was the knee injury treated? (check all that apply)	☐ surgery ☐ physiotherapy ☐ other (describe):
7. Number of *major flare-ups (event that led to missed work, school or sport) of RIGHT knee in the past month:	
8. Number of *major flare-ups (event that led to missed work, school or sport) of RIGHT knee in the past year:	

SECTION C: Healthcare Utilization in the Past Year

Please indicate if In the **PAST YEAR**, have you visited the following practitioners or received the following services (exclude visits/services as an inpatient)

Practitioners and Services	Visited	Number of visits **for** the **RIGHT** knee	Number of visits **not for** to the **RIGHT** knee	No Visits
physician - emergency room doctor	✎			✎
physician - general practitioner/ family	✎			✎
physician - sport medicine doctor	✎			✎
surgeon	✎			✎
physiotherapist	✎			✎
chiropractor	✎			✎
massage therapist	✎			✎
athletic therapist	✎			✎
magnetic resonance imaging (MRI)	✎			✎
computer tomography (CT scan)	✎			✎
radiographs (x-rays)	✎			✎
other (please specify)	✎			✎

questionnaire continues

In the past year, have you been admitted to the hospital for any reason.

☐ no — If you answered 'no' to this question, please skip to Section D.

☐ yes

Please describe ANY hospitalisations you have had in the **past year** below. If you have had more than 2 hospitalisations, use a separate sheet to describe.

Primary reason for hospitalisation	Number of nights in hospital	Did you have a surgery while in hospital?	
		I **DID NOT** have surgery	I **DID** have surgery: Please name and describethe surgery to best of your ability.
		☐	
		☐	

SECTION D: Sport and Physical Activity Participation in the Past Year

Based on the **PAST YEAR** (last 12 months), have you participated in any sports?

☐ no, I have not participated in any sports in the past year.

☐ yes, I have participated in sports in the past year.

If ***no,*** please skip to Section E: Medical History. If ***yes,*** please estimate the average number of hours per week you participated in each sport

SPORT	hrs/wk, mo/yr	SPORT	hrs/wk, mo/yr	SPORT	hrs/wk, mo/yr
☐ Aerobics	,	☐ Floor hockey	,	☐ Soccer	,
☐ Backpacking	,	☐ Football	,	☐ Squash	,
☐ Badminton	,	☐ Golf	,	☐ Speed skating	,
☐ Baseball	,	☐ Gymnastics	,	☐ Swimming	,
☐ Basketball	,	☐ Hiking/ Scrambling	,	☐ Tennis	,
☐ Boxing (incl. kick)	,	☐ Hockey	,	☐ Track and field	,
☐ Canoeing	,	☐ Horse riding	,	☐ Triathlon	,
☐ Caving	,	☐ Kayaking	,	☐ Ultimate Frisbee	,
☐ Climbing - Alpine	,	☐ Lacrosse	,	☐ Volleyball	,
☐ Climbing - Ice	,	☐ Martial arts	,	☐ Waterpolo	,
☐ Climbing - Traditional	,	☐ Rafting	,	☐ Weight training	,
☐ Cycling - Mountain	,	☐ Rollerblading	,	☐ Wrestling	,
☐ Cycling - Road	,	☐ Rugby	,	☐ *Other:	,
☐ Dance	,	☐ Running	,	**Please describe other:*	
☐ Dirt biking	,	☐ Skateboarding	,		
☐ Diving	,	☐ Skiing - Downhill	,		
☐ Field hockey	,	☐ Skiing - Cross-country	,		
☐ Figure skating	,	☐ Snowboarding	,		

SECTION E: Medical History

1.a) **Since your RIGHT knee injury**, have you had any other major injuries that have required medical attention AND resulted in at least 1 day of missed participation from sport and recreational activities?

☐ Yes ☐ No — If you answered 'no' to this question, please skip to question 3

if "Yes", please describe this injury(s) to the best of your ability: ________________

questionnaire continues

Consequences of Knee Joint Injury in Youth Sport: Implications for OA and Other Health Outcomes 2013-2016

1.b) What were you doing when you were injured (i.e., what caused the injury)?

☐ Sport or recreation ☐ Other

1.c) Injury details:

Injury Date *Month/Year*	Did the injury occur:	Injury Type *sprain, bruise, etc.*	Body Part (include side of body) *left knee, nose, etc.*	Sport of Occurrence *soccer, hockey, etc.*	Treatment description *first aid, physiotherapy, etc.*	Time loss before FULL return to sport *1 day, 3 weeks, etc.*
	□ 0-3 months ago □ 3-12 months ago □ more than 12 months ago					
	□ 0-3 months ago □ 3-12 months ago □ more than 12 months ago					
	□ 0-3 months ago □ 3-12 months ago □ more than 12 months ago					

2a. Do you have any ongoing injuries?

☐ No ☐ Yes ☐ Do not know

*If **yes**, describe these injuries to the best of your ability:*

2b. Are you currently receiving treatment for this / these injury(s)?

☐ No ☐ Yes ☐ Do not know ☐ Not Applicable (i.e. no ongoing injury)

*If **yes**, describe the treatments to the best of your ability:*

3. Are you currently taking medication **for ANY injuries**? (Please check all the apply)

☐No ☐Yes ☐ibuprofen (e.g., Advil)

☐acetominophen (e.g., Tylenol)

☐Other; please describe:

4. Do you take medications for any other reasons (i.e., not for injuries) on a regular basis? (e.g., asthma inhaler, antidepressants, birth control pills etc.)

☐No ☐Yes

*If **yes**, please list:*

5. Are you currently taking any supplements (vitamins, minerals, protein powder, etc.) ?

☐No ☐Yes

*If **yes**, please list:*

Have you been diagnosed by a physician with any of the following:	No	Yes	Do not know	*If **yes**, describe your condition(s) to the best of your abilit **(include side of body)**:*	Year of diagnosis	Do not know
6. a bone fracture, arthritis, or other muscle or bone related condition	☐	☐	☐			☐
7. a systemic disease (e.g., cancer, thyroid disease, heart disease)	☐	☐	☐			☐
8. a circulation or heart-related problem (e.g., heart murmur, irregular heart beat, congenital heart deformity)	☐	☐	☐			☐
9. a neurological disorder (e.g., brain injury, cerebral palsy, pinched nerve, "stinger", multiple sclerosis, etc.)	☐	☐	☐			☐

Thank you for your time and effort in completing this questionnaire. Please bring this with you on the testing day to the Sport Medicine Centre at the University of Calgary.

Appendix R: EuroQoL-5D-5L index score (EQ-5D-5L) and EuroQoL-visual analogue scale (EQ-VAS) (Chapter 3)

EQ-5D-5L

Health Questionnaire

English version for the UK

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about ☐

I have slight problems in walking about ☐

I have moderate problems in walking about ☐

I have severe problems in walking about ☐

I am unable to walk about ☐

SELF-CARE

I have no problems washing or dressing myself ☐

I have slight problems washing or dressing myself ☐

I have moderate problems washing or dressing myself ☐

I have severe problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ☐

I have slight problems doing my usual activities ☐

I have moderate problems doing my usual activities ☐

I have severe problems doing my usual activities ☐

I am unable to do my usual activities ☐

PAIN / DISCOMFORT

I have no pain or discomfort ☐

I have slight pain or discomfort ☐

I have moderate pain or discomfort ☐

I have severe pain or discomfort ☐

I have extreme pain or discomfort ☐

ANXIETY / DEPRESSION

I am not anxious or depressed ☐

I am slightly anxious or depressed ☐

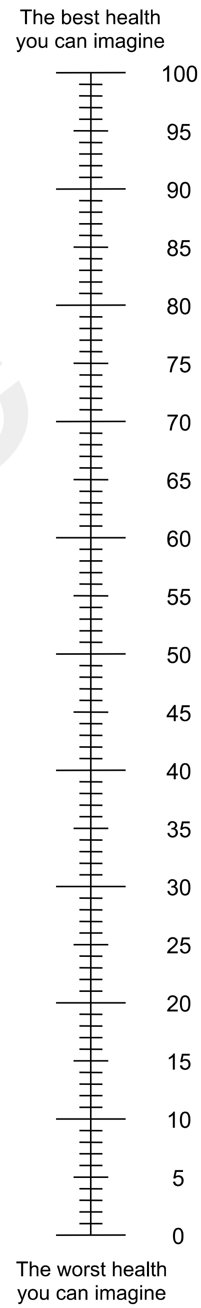
I am moderately anxious or depressed ☐

I am severely anxious or depressed ☐

I am extremely anxious or depressed ☐

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Please mark an X on the scale to indicate how your health is TODAY.
- Now, write the number you marked on the scale in the box below.

YOUR HEALTH TODAY =



Appendix S: Knee injury and Osteoarthritis Outcome Score (KOOS) (Chapters 3-5)

KOOS KNEE SURVEY

Today's date: _____/______/______ Date of birth: _____/______/______

Name: ____

INSTRUCTIONS: This survey asks for your view about your knee. This information will help us keep track of how you feel about your knee and how well you are able to perform your usual activities.
Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

Symptoms
These questions should be answered thinking of your knee symptoms during the **last week**.

S1. Do you have swelling in your knee?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S3. Does your knee catch or hang up when moving?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S4. Can you straighten your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

S5. Can you bend your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

Stiffness
The following questions concern the amount of joint stiffness you have experienced during the **last week** in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

S6. How severe is your knee joint stiffness after first wakening in the morning?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

S7. How severe is your knee stiffness after sitting, lying or resting **later in the day**?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Pain

P1. How often do you experience knee pain?

Never	Monthly	Weekly	Daily	Always
☐	☐	☐	☐	☐

What amount of knee pain have you experienced the **last week** during the following activities?

P2. Twisting/pivoting on your knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P3. Straightening knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P4. Bending knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P5. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P6. Going up or down stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P7. At night while in bed

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P8. Sitting or lying

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P9. Standing upright

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, daily living

The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A1. Descending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A2. Ascending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A3. Rising from sitting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A4. Standing

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A5. Bending to floor/pick up an object

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A6. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A7. Getting in/out of car

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A8. Going shopping

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A9. Putting on socks/stockings

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A10. Rising from bed

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A11. Taking off socks/stockings

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A12. Lying in bed (turning over, maintaining knee position)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A13. Getting in/out of bath

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A14. Sitting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A15. Getting on/off toilet

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A17. Light domestic duties (cooking, dusting, etc)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, sports and recreational activities

The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the **last week** due to your knee.

SP1. Squatting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP2. Running

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP3. Jumping

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP4. Twisting/pivoting on your injured knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP5. Kneeling

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Quality of Life

Q1. How often are you aware of your knee problem?

Never	Monthly	Weekly	Daily	Constantly
☐	☐	☐	☐	☐

Q2. Have you modified your life style to avoid potentially damaging activities to your knee?

Not at all	Mildly	Moderately	Severely	Totally
☐	☐	☐	☐	☐

Q3. How much are you troubled with lack of confidence in your knee?

Not at all	Mildly	Moderately	Severely	Extremely
☐	☐	☐	☐	☐

Q4. In general, how much difficulty do you have with your knee?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Thank you very much for completing all the questions in this questionnaire.

Appendix T: Intermittent and Constant Osteoarthritis Pain (ICOAP) Measure (Chapters 3 & 5)

A Measure of Intermittent and Constant Osteoarthritis Pain, ICOAP: KNEE Version

People have told us that they experience different kinds of pain (including aching or discomfort) in their knee. To get a better sense of the different types of knee pain you may experience, we would like to ask you about any "constant pain" (pain you have all the time) separately from any pain that you may experience less often, that is, "pain that comes and goes". The following questions will ask you about the pain that you have experienced in your knee in the PAST WEEK. Please answer ALL questions.

A) CONSTANT PAIN

For each of the following questions, please select the response that best describes, on average, your *constant knee pain* in the PAST WEEK.

1. In the past week, how intense has your *constant knee pain* been?

0	1	2	3	4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

2. In the past week, how much has your *constant knee pain* affected your sleep?

0	1	2	3	4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

3. In the past week, how much has your *constant knee pain* affected your overall quality of life?

0	1	2	3	4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

4. In the past week, how frustrated or annoyed have you been by your *constant knee pain?*

0	1	2	3	4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

5. In the past week, how upset or worried have you been by your *constant knee pain*?

0	1	2	3	4
Not at all/ No constant knee pain	Mildly	Moderately	Severely	Extremely

B) PAIN THAT COMES AND GOES

For each of the following questions, please select the response that best describes your *__knee pain that comes and goes__, on average,* in the PAST WEEK.

6. In the past week, how intense has your most severe *__knee pain that comes and goes__* been?

0	1	2	3	4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

7. In the past week, how frequently has this *__knee pain that comes and goes__* occurred?

0	1	2	3	4
Never/ No knee pain that comes and goes	Rarely	Sometimes	Often	Very Often

8. In the past week, how much has your *__knee pain that comes and goes__* affected your sleep?

0	1	2	3	4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

9. In the past week, how much has your *__knee pain that comes and goes__* affected your overall quality of life?

0	1	2	3	4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

10. In the past week, how frustrated or annoyed have you been by your *__knee pain that comes and goes__*?

0	1	2	3	4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

11. In the past week, how upset or worried have you been by your *__knee pain that comes and goes__*?

0	1	2	3	4
Not at all/ No knee pain that comes and goes	Mildly	Moderately	Severely	Extremely

THANK YOU!

Appendix U: Godin Leisure-Time Exercise Questionnaire (GLTEQ) (Chapter 3)

Godin Leisure-Time Exercise Questionnaire

INSTRUCTIONS

In this excerpt from the Godin Leisure-Time Exercise Questionnaire, the individual is asked to complete a self-explanatory, brief four-item query of usual leisure-time exercise habits.

CALCULATIONS

For the first question, weekly frequencies of strenuous, moderate, and light activities are multiplied by nine, five, and three, respectively. Total weekly leisure activity is calculated in arbitrary units by summing the products of the separate components, as shown in the following formula:

Weekly leisure activity score = (9 · Strenuous) + (5 · Moderate) + (3 · Light)

The second question is used to calculate the frequency of weekly leisure-time activities pursued "long enough to work up a sweat" (see questionnaire).

EXAMPLE

Strenuous = 3 times/wk

Moderate = 6 times/wk

Light = 14 times/wk

Total leisure activity score = (9 · 3) + (5 · 6) + (3 · 14) = 27 + 30 + 42 = 99

Godin, G., Shephard, R. J.. (1997) Godin Leisure-Time Exercise Questionnaire. Medicine and Science in Sports and Exercise. 29 June Supplement: S36-S38.

Godin Leisure-Time Exercise Questionnaire

1. During a typical **7-Day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your free time (write on each line the appropriate number).

	Times Per Week
a) STRENUOUS EXERCISE (HEART BEATS RAPIDLY) (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)	________
b) MODERATE EXERCISE (NOT EXHAUSTING) (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)	________
c) MILD EXERCISE (MINIMAL EFFORT) (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking)	________

2. During a typical **7-Day period** (a week), in your leisure time, how often do you engage in any regular activity **long enough to work up a sweat** (heart beats rapidly)?

OFTEN	SOMETIMES	NEVER/RARELY
1.	2.	3.

Appendix V: Bespoke Study Questionnaire for the Alberta PrE-OA Cohort Study Conducted at the University of Alberta (Chapters 4 & 5)

Baseline Sport Participation, Medical and Rehabilitation Questionnaire

As part of this study we need to collect some vital information about you, your health status, healthcare use, physical activity participation and beliefs.

This will be done by having you complete a series of five questionnaires. These questionnaires will take approximaltey 20 minutes in total to complete.

Keep in mind that you can save your responses, exit and return to the questionniares at any point.

For some of the questionnaires you will be asked questions related to your knee or a knee injury. If you HAVE recently had a knee injury then answer these questions in relation to your injured knee. If you have NOT had a knee injury please answer these question in relation to one of your knees and your beliefs had you recently injured injured it.

Please answer each question to the best of your ability. If you have any questions feel free to email the research team at kneestdy@ualberta.ca

CONSENT TO PARTICIPATE

I understand that completing these questionnaires implies my consent to participate in this study. I am also aware that I (or my legal guardian if I am under 18 years of age) will be asked to sign a written consent form at my first testing session.

Please click yes to provide your consent. If you do not provide your consent, you will not be able to access the questionnaire.

○ Yes

Today's date

____
(YYYY-MM-DD)

SECTION A: DEMOGRAPHIC DETAILS

Date of birth	__________________ (YYYY-MM-DD)
Age	__________________ (age in years)
Sex	◯ Female ◯ Male
Current occupation	◯ Student ◯ Other
If you chose 'Other' for your occupation, please describe it here:	__________________
If you were to asked to kick a soccer ball as far as you could which leg would you use?	◯ Right ◯ Left
Are you in this study because?	◯ I have had a recent (in the last 6 months) knee injury ◯ I have never had a knee injury

BIOLOGICAL MATURITY	
FEMALE - Are you pregnant?	◯ Yes ◯ No ◯ I do not know ◯ I prefer not to answer
FEMALE - On average how many periods do you have per year?	◯ 0-3 ◯ 4-6 ◯ 7-9 ◯ 10 or more ◯ I do not know ◯ I prefer not to answer
FEMALE - What year and month did you start to menstruate?	____________________ (YYYY-MM)
MALE - What year and month did you start to shave?	____________________ (YYYY-MM)
FEMALE - How many childbirths have you had?	____________________
MALE & FEMALE - What year and month did you start to have acne?	____________________ (YYYY-MM)

SECTION B: KNEE INJURY DETAILS

Which knee is your recently (in the last 6 months) injured knee? The following questions are about this knee which will be referred to as your INJURED or STUDY KNEE.	◯ Right ◯ Left
Did your knee injury involve contact with another person or object?	◯ No (there was no contact with another person or object) ◯ Yes (there was contact with another person or object)
What type of knee injury do you have? (choose all that apply to your STUDY KNEE)	☐ Anterior Cruciate Ligament (ACL) ☐ Posterior Cruciate Ligament (PCL) ☐ Medial Collateral Ligament (MCL) ☐ Lateral Collateral Ligament (LCL) ☐ Meniscus ☐ Other (please describe below) ☐ I do not know
If you chose 'Other' for your type of knee injury please describe it here.	______________________
How old were you when you injured your STUDY KNEE?	______________________ (age in years)
What was the date of your STUDY KNEE injury? (please indicate year, month and if known day)	______________________ (YYYY-MM-DD)
What treatments have you had for your STUDY KNEE injury? (choose all that apply)	☐ Surgery ☐ Physiotherapy ☐ No treatment ☐ Other ☐ I do not know ☐ I prefer not to answer ☐ Not applicable
If you chose 'Other' for treatments you have had for your STUDY KNEE please describe here.	______________________

SECTION C: HEALTHCARE USE

Please indicate the number of times in the PAST 6 MONTHS you have visited the following practitioners or received the following services for ANY REASON (exclude visits and services received as in inpatient).

	No Visit	1	2	3	4	5 or more	I don't know	I prefer not to say
Physician - emergency room doctor	○	○	○	○	○	○	○	○
Physician - general pracitioner	○	○	○	○	○	○	○	○
Physician - sports medicine	○	○	○	○	○	○	○	○
Surgeon	○	○	○	○	○	○	○	○
Physiotherapist	○	○	○	○	○	○	○	○
Chiropractor	○	○	○	○	○	○	○	○
Massage Therapist	○	○	○	○	○	○	○	○
Athletic Therapist	○	○	○	○	○	○	○	○
Magnetic Resonance Imaging (MRI)	○	○	○	○	○	○	○	○
Computer Tomography (CT)	○	○	○	○	○	○	○	○
Ultrasound Imaging (USI)	○	○	○	○	○	○	○	○
Radiographs (x-ray)	○	○	○	○	○	○	○	○

If you are in this study because you have had a recent knee injury, how many times in the PAST 6 MONTHS did you see the following practitioners or receive the following services (excluding visits/services as an inpatient) for your STUDY KNEE INJURY?

If you have NOT had a recent knee injury please disregard this section header.

	No Visit	1	2	3	4	5 or more	I don't know	I prefer not to say	No response
Physician - emergency room doctor	○	○	○	○	○	○	○	○	○
Physician - general practitioner	○	○	○	○	○	○	○	○	○
Physician - sports medicine	○	○	○	○	○	○	○	○	○
Surgeon	○	○	○	○	○	○	○	○	○
Physiotherapist	○	○	○	○	○	○	○	○	○
Chiropractor	○	○	○	○	○	○	○	○	○
Massage Therapist	○	○	○	○	○	○	○	○	○
Athletic Therapist	○	○	○	○	○	○	○	○	○
Magnetic Resonance Imaging (MRI)	○	○	○	○	○	○	○	○	○
Computer Tomography	○	○	○	○	○	○	○	○	○
Ultrasound Imaging (USI)	○	○	○	○	○	○	○	○	○
Radiography (x-ray)	○	○	○	○	○	○	○	○	○

In the PAST 6 MONTHS have you been admitted to the hospital FOR ANY REASON

○ Yes
○ No
○ I do not know
○ I prefer not to answer

If you have been admitted to the hospital in the PAST 6 MONTHS please indicate the primary reason for the hospitalization

____

If you were admitted to the hospital in the PAST 6 MONTHS, how many nights were you in the hospital?

____

If you were admitted to the hospital in the PAST 6 MONTHS did you have a surgery while you were in the hospital?

○ Yes
○ No
○ I do not know
○ I prefer not to answer

If you had surgery during your hospital stay please name and describe the surgery to the best of your ability

____

SECTION D: SPORT AND PHYSICAL ACTIVITY PARTICIPATION

Have you participated in any sports in the PAST YEAR?

- ◯ Yes
- ◯ No
- ◯ I do not know
- ◯ I prefer not to answer

Which sports have you participated in over the LAST 12 MONTHS? (choose all that apply)

- ☐ Aerobic
- ☐ Backpacking
- ☐ Badminton
- ☐ Baseball
- ☐ Basketball
- ☐ Boxing (including kick-boxing)
- ☐ Canoeing
- ☐ Caving
- ☐ Climbing - Alpine
- ☐ Climbing - Ice
- ☐ Climbing - Traditional
- ☐ Cycling - Mountain
- ☐ Cycling - Road
- ☐ Dance
- ☐ Dirt biking
- ☐ Diving
- ☐ Field hockey
- ☐ Figure skating
- ☐ Floor hockey
- ☐ Football
- ☐ Golf
- ☐ Gymnastics
- ☐ Hiking / Scrambling
- ☐ Hockey
- ☐ Horse riding
- ☐ Kayaking
- ☐ Lacrosse
- ☐ Martial arts
- ☐ Rafting
- ☐ Rollerblading
- ☐ Rugby
- ☐ Running
- ☐ Skateboarding
- ☐ Skiing - Downhill
- ☐ Skiing - Cross-country
- ☐ Snowboarding
- ☐ Soccer
- ☐ Squash
- ☐ Speed skating
- ☐ Swimming
- ☐ Tennis
- ☐ Track and field
- ☐ Triathlon
- ☐ Ultimate Frisbee
- ☐ Volleyball
- ☐ Waterpolo
- ☐ Weight Training
- ☐ Wrestling
- ☐ Other
- ☐ I do not know
- ☐ I prefer not to answer

How many weeks per year do you participate in Aerobics?

____
(weeks)

How many hours per week do you participate in Aerobics?	______________ (hours)
How many weeks per year do you Backpack?	______________ (weeks)
How many hours per week do you Backpack?	______________ (hours)
How many weeks per year do you play Badminton?	______________ (weeks)
How many hours per week do you play Badminton?	______________ (hours)
How many weeks per year do you play Baseball?	______________ (weeks)
How many hours per week do you play Baseball?	______________ (hours)
How many weeks per year do you play Basketball?	______________ (weeks)
How many hours per week do you play Basketball?	______________ (hours)
How many weeks per year do you participate in Boxing (including kick-boxing)?	______________ (weeks)
How many hours per week do you participate in Boxing (including kick-boxing)?	______________ (hours)
How many weeks per year do you Canoe?	______________ (weeks)
How many hours per week do you Canoe?	______________ (hours)
How many weeks per year do you participate in Caving?	______________ (weeks)

How many hours per week do you participate in Caving?

(hours)

How many weeks per year do you Alpine Climb?

(weeks)

How many hours per week do you Alpine Climb?

(hours)

How many weeks per year do you Ice Climb?

(weeks)

How many hours per week do you Ice Climb?

(hours)

How many weeks per year do you participate in Traditional Climbing?

(weeks)

How many hours per week do you participate in Traditional Climbing?

(hours)

How many weeks per year do you Mountain Bike?

(weeks)

How many hours per week do you Mountain Bike?

(hours)

How many weeks per year do you Road Cycle?

(weeks)

How many hours per week do you Road Cycle?

(hours)

How many weeks per year do you Dance?

(weeks)

How many hours per week do you Dance?

(hours)

How many weeks per year do you participate in Dirt Biking?

(weeks)

How many hours per week do you participate in Dirt Biking?	______ (hours)
How many weeks per year do you Dive?	______ (weeks)
How many hours per week do you Dive?	______ (hours)
How many weeks per year do you play Field Hockey?	______ (weeks)
How many hours per week do you play Field Hockey?	______ (hours)
How many weeks per year do you Figure Skate?	______ (weeks)
How many hours per week do you Figure Skate?	______ (hours)
How many weeks per year do you play Floor Hockey?	______ (weeks)
How many hours per week do you play Floor Hockey?	______ (hours)
How many weeks per year do you play Football?	______ (weeks)
How many hours per week do you play Football?	______ (hours)
How many weeks per year do you Golf?	______ (weeks)
How many hours per week do you Golf?	______ (hours)
How many weeks per year do you participate in Gymnastics?	______ (weeks)

How many hours per week do you participate in Gymnastics?	______________ (hours)
How many weeks per year do you Hike / Scramble?	______________ (weeks)
How many hours per week do you Hike / Scramble?	______________ (hours)
How many weeks per year do you play Hockey?	______________ (weeks)
How many hours per week do you play Hockey?	______________ (hours)
How many weeks per year do you participate in Horse riding?	______________ (weeks)
How many hours per week do you participate in Horse riding?	______________ (hours)
How many weeks per year do you participate in Kayaking?	______________ (weeks)
How many hours per week do you participate in Kayaking?	______________ (hours)
How many weeks per year do you participate in Lacrosse?	______________ (weeks)
How many hours per week do you participate in Lacrosse?	______________ (hours)
How many weeks per year do you participate in Martial Arts?	______________ (weeks)
How many hours per week do you participate in Martial Arts?	______________ (hours)
How many weeks per year do you go Rafting?	______________ (weeks)

How many hours per week do you go Rafting?

______________ (hours)

How many weeks per year do you Rollerblade?

______________ (weeks)

How many hours per week do you Rollerblade?

______________ (hours)

How many weeks per year do you play Rugby?

______________ (weeks)

How many hours per week do you play Rugby?

______________ (hours)

How many weeks per year do you participate in Running?

______________ (weeks)

How many hours per week do you participate in Running?

______________ (hours)

How many weeks per year do you Skateboard?

______________ (weeks)

How many hours per week do you Skateboard?

______________ (hours)

How many weeks per year do you Downhill Ski?

______________ (weeks)

How many hours per week do you Downhill Ski?

______________ (hours)

How many weeks per year do you Cross-country Ski?

______________ (weeks)

How many hours per week do you Cross-country Ski?

______________ (hours)

How many weeks per year do you Snowboard?

______________ (weeks)

How many hours per week do you Snowboard?	______________ (hours)
How many weeks per year do you play Soccer?	______________ (weeks)
How many hours per week do you play Soccer?	______________ (hours)
How many weeks per year do you play Squash?	______________ (weeks)
How many hours per week do you play Squash?	______________ (hours)
How many weeks per year do you Speed Skate?	______________ (weeks)
How many hours per week do you Speed Skate?	______________ (hours)
How many weeks per year do you Swim?	______________ (weeks)
How many hours per week do you Swim?	______________ (hours)
How many weeks per year do you play Tennis?	______________ (weeks)
How many hours per week do you play Tennis?	______________ (hours)
How many weeks per year do you participate in Track and Field?	______________ (weeks)
How many hours per week do you participate in Track and Field?	______________ (hours)
How many weeks per year do you participate in Triathlon?	______________ (weeks)

How many hours per week do you participate in Triathlon?	______________ (hours)
How many weeks per year do you play Ultimate Frisbee?	______________ (weeks)
How many hours per week do you play Ultimate Frisbee?	______________ (hours)
How many weeks per year do you play Volleyball?	______________ (weeks)
How many hours per week do you play Volleyball?	______________ (hours)
How many weeks per year do you play Waterpolo?	______________ (weeks)
How many hours per week do you play Waterpolo?	______________ (hours)
How many weeks per year do you Weight Train?	______________ (weeks)
How many hours per week do you Weight Train?	______________ (hours)
How many weeks per year do you Wrestle?	______________ (weeks)
How many hours per week do you Wrestle?	______________ (hours)
If you chose 'Other' under sports you have participated in over the LAST 12 MONTHS, please name your 'Other' sport here:	______________
How many weeks per year do you participate in your 'Other' sport?	______________ (weeks)
How many hours per week do you participate in your 'Other' sport?	______________ (hours)

MAIN SPORT

Which sport would you classify as your MAIN SPORT?	__________________________
How would you classify your level of participation in your MAIN SPORT? If you have recently injured your knee, please answer based on your MAIN SPORT before your injury.	◯ Recreational (done for enjoyment, minimal organization) ◯ Club (competitive, organized training and competition schedule) ◯ School (selected to represent a junior or high school) ◯ Varsity (selected to represent a university or college) ◯ Provincial (selected to represent a province) ◯ National (selected to represent a nation) ◯ I do not know ◯ I prefer not to answer
In an average week how many training (practice) sessions do you participate in related to your MAIN SPORT? If you have recently injured your knee, please answer based on your MAIN SPORT before your injury.	__________________________ (number of sessions / week)
What is the average length of your MAIN SPORT training (practice) session? If you have recently injured your knee, please answer based on your MAIN SPORT before your injury.	__________________________ (minutes)
In an average week how many games or competitions do you participate in related to your MAIN SPORT? If you have recently injured your knee, please answer based on your MAIN SPORT before your injury.	__________________________ (number of games or competitions)
Since your knee injury, have you attempted to train (practice) or play any sport?	◯ Yes ◯ No

Since your knee injury, have you attempted to train (practice) or compete (game) in your MAIN SPORT before your injury?	◯ No ◯ Yes, attempted competition in my MAIN SPORT at the SAME or HIGHER level (frequency and intensity) than before injury ◯ Yes, attempted competition in my MAIN SPORT but at a LOWER level (frequency and intensity) than before injury ◯ Attempted training (practice) ONLY in my MAIN SPORT ◯ I do not know ◯ I prefer not to answer
Since your knee injury, have you attempted to train (practice) or compete in a sport OTHER than your main sport?	◯ No ◯ Yes, attempted COMPETITION a sport other than my MAIN SPORT before injury (specify sport) ◯ Yes, attempted TRAINING (practice) only in a sport other than my MAIN SPORT before injury (specify sport) ◯ I do not know ◯ I prefer not to answer
Please specify what sport(s) you have attempted COMPETITION in, that is NOT your MAIN SPORT before your knee injury	________________
Please specify what sport(s) you have attempted TRAINING in, that is NOT your MAIN SPORT before your knee injury.	________________
If you have not yet attempted to train (practice) or play any sport since your knee injury, do you still have intentions of returning to your MAIN SPORT?	◯ Yes ◯ No
If you DO NOT wish to return to your MAIN SPORT, please indicate why by selecting all responses that are appropriate from the list below:	☐ Knee feels unstable ☐ Lack of motion ☐ Knee hurts with activity ☐ Physical unable to participate at the same level as prior to injury ☐ Job prevents ☐ School prevents ☐ No longer eligible for same level of participation ☐ Pregnancy ☐ Parenting responsibility prevents ☐ Knee feels weak ☐ Knee swelling ☐ Other knee symptoms ☐ Parents not wanting me to return ☐ Health concerns ☐ Lack of interest ☐ Fear of reinjury ☐ Advised not to return to sport ☐ Other life event ☐ I do not know ☐ I prefer not to answer
If you chose 'Other knee symptom(s)' as a reason, why you DO NOT wish to return to your MAIN SPORT? Please list the symptom(s) here.	________________

If chose 'Other life event' as a reason, why you DO NOT wish to return to your MAIN SPORT? Please describe this life event here. ____________________

SECTION E: MEDICAL HISTORY

In the PAST 6 MONTHS, have you had any injuries (OTHER than your current knee injury) that required medical attention AND made you miss at least 1 day of sport and/or recreational activities?

- ◯ Yes
- ◯ No
- ◯ I do not know
- ◯ I prefer not to answer

In the PAST 6 MONTHS, have you had any injuries that required medical attention AND made you miss at least 1 day of sport and/or recreational activities?

- ◯ Yes
- ◯ No
- ◯ I do not know
- ◯ I prefer not to answer

How many other injuries have you had in the PAST 6 MONTHS?

- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5 or more
- ◯ I do not know
- ◯ I prefer not to answer

Injury #1: Injury type (sprain, bruise, fracture etc.)

____

Injury #1: Body part (include side of the body, e.g. left arm)

____

Injury #1: Date of injury

____
(YYYY-MM-DD)

Injury #1: What were you doing when you were injured (i.e., what caused the injury)?

- ◯ Sport and recreation activity
- ◯ Occupation related
- ◯ Other
- ◯ I do not know
- ◯ I prefer not to say

Injury #1: If you chose 'Other', please briefly describe the nature of your injury.

____

Injury #1: If you were participating in sport and recreation activity when you were injured, please indicate the sport.

____

Injury #1: Please describe what treatments you received for this injury (e.g. first aid, physiotherapy, surgery etc).

____

Injury #1: How many days passed before you were able to FULLY return to sport after this injury (i.e., 7 days).

____
(days)

Injury #2: Injury type (sprain, bruise, fracture etc.)

____

Injury #2: Body part (include side of the body, e.g. left arm)

____

Injury #2: Date of injury	______________ (YYYY-MM-DD)
Injury #2: What were you doing when you were injured (i.e., what caused the injury)?	◯ Sport and recreation activity ◯ Occupation related ◯ Other ◯ I do not know ◯ I prefer not to say
Injury #2: If you chose 'other' please briefly describe the nature of your injury.	______________
Injury #2: If you were participating in a sport and recreation activity when you were injured please indicate the sport.	______________
Injury #2: Please describe what treatments you received for this injury (e.g. first aid, physiotherapy, surgery etc).	______________
Injury #2: How many days passed before you were able to FULLY return to sport after this injury (i.e., 7 days).	______________ (days)
Injury #3: Injury type (sprain, bruise, fracture etc.)	______________
Injury #3: Body part (include side of the body, e.g. left arm)	______________
Injury #3: Date of injury	______________ (YYYY-MM-DD)
Injury #3: What were you doing when you were injured (i.e., what caused the injury)?	◯ Sport and recreation activity ◯ Occupation related ◯ Other ◯ I do not know ◯ I prefer not to say
Injury #3: If you chose 'other' please briefly describe the nature of your injury.	______________
Injury #3: If you were participating in a sport and recreation activity when you were injured please indicate the sport.	______________
Injury #3: Please describe what treatments you received for this injury (e.g. first aid, physiotherapy, surgery etc).	______________
Injury #3: How many days passed before you were able to FULLY return to sport after this injury (i.e., 7 days).	______________ (days)

Injury #4: Injury type (sprain, bruise, fracture etc.)	__________________________________
Injury #4: Body part (include side of the body, e.g. left arm)	__________________________________
Injury #4: Date of injury	__________________________________ (YYYY-MM-DD)
Injury #4: What were you doing when you were injured (i.e., what caused the injury)?	○ Sport and recreation activity ○ Occupation related ○ Other ○ I do not know ○ I prefer not to say
Injury #4: If you chose 'other' please briefly describe the nature of your injury.	__________________________________
Injury #4: If you were participating in a sport and recreation activity when you were injured please indicate the sport.	__________________________________
Injury #4: Please describe what treatments you received for this injury (e.g. first aid, physiotherapy, surgery etc).	__________________________________
Injury #4: How many days passed before you were able to FULLY return to sport after this injury (i.e., 7 days).	__________________________________ (days)
Injury #5: Injury type (sprain, bruise, fracture etc.)	__________________________________
Injury #5: Body part (include side of the body, e.g. left arm)	__________________________________
Injury #5: Date of injury	__________________________________ (YYYY-MM-DD)
Injury #5: What were you doing when you were injured (i.e., what caused the injury)?	○ Sport and recreation activity ○ Occupation related ○ Other ○ I do not know ○ I prefer not to say
Injury #5: If you chose 'other' please briefly describe the nature of your injury.	__________________________________
Injury #5: If you were participating in a sport and recreation activity when you were injured please indicate the sport.	__________________________________
Injury #5: Please describe what treatments you received for this injury (e.g. first aid, physiotherapy, surgery etc).	__________________________________

Injury #5: How many days passed before you were able to FULLY return to sport after this injury (i.e., 7 days).	______________ (days)
Apart from your knee injury, do you have any ongoing injuries? An ongoing injury is one that has been bothering you for MORE than 6 months.	◯ Yes ◯ No ◯ I do not know ◯ I prefer not to answer
If you have an ongoing injury, please describe it to the best of your ability	______________
Are you currently receiving treatment for an ongoing injury?	◯ Yes ◯ No ◯ I do not know ◯ I prefer not answer
If you are receiving treatment for an ongoing injury, please describe the treatments to the best of your ability	______________
Are you currently receiving medication for ANY INJURIES?	◯ Yes ◯ No ◯ I prefer not to answer
What medications are you currently taking for ANY INJURIES? (please check all that apply)	☐ Ibuprofen (e.g. Advil) ☐ Acetaminophen (e.g. Tylenol) ☐ Other ☐ I do not know ☐ I prefer not to answer
If you are taking an 'Other' medication please describe it here	______________
Do you take medication(s) for any OTHER reasons (i.e., not for an injury) in a regular basis? (i.e., asthma inhaler, antidepressants, birth control pills, etc)	◯ Yes ◯ No ◯ I prefer not to answer
If you are taking medication(s) on a regular basis not related to your injuries please describe here	______________
Are you currently taking any supplement(s)? (i.e., vitamins, minerals, protein powder, etc)	◯ Yes ◯ No ◯ I do not know ◯ I prefer not to answer
If you are taking any supplement(s) (i.e., vitamins, minerals, protien powder, etc) please describe them here	______________

Have you been diagnosed by a physician with any of the following:

	Yes	No	I do not know	I prefer not to answer
Bone fracture, arthritis, or other muscle or bone related condition	○	○	○	○
Systemic disease (i.e., cancer, thyroid disease)	○	○	○	○
Circulation or heart-related problem (i.e., heart murmur, irregular heart beat, congenital heart deformity)	○	○	○	○
Neurological disorder (i.e., concussion, brain injury, cerebral palsy, pinched nerve, "stinger", multiple sclerosis)	○	○	○	○

Please describe your bone or muscle condition to the best of your ability (include side of body)

____

Please describe your systemic disease to the best of your ability (include side of body)

____

Please describe your circulation problem to the best of your ability (include side of body)

____

Please describe your neurological disorder to the best of your ability (include side of body)

____

Year of bone or muscle condition diagnosis

____
(YYYY)

Year of systemic disease diagnosis

____
(YYYY)

Year of circulation disease diagnosis

____
(YYYY)

Year of neurological disorder diagnosis

____
(YYYY)

QUALITY OF LIFE	
How much does your knee health impact your happiness?	◯ Not at all ◯ Slightly ◯ Moderately ◯ Significantly ◯ I prefer not to answer
At this moment, how satisfied are you with your knee health?	◯ Not at all ◯ Slightly ◯ Moderately ◯ Significantly ◯ I prefer not to answer
Do you ever play sports despite knowing you are at a greater risk of injury?	◯ Never ◯ Sometimes ◯ Always ◯ I prefer not to answer
What is your favourite way to exercise?	◯ Team sports (e.g. soccer, hockey) ◯ Individual sports (e.g. swimming, track & field) ◯ Other ◯ I prefer not to answer
Please describe "Other exercise":	______________________________

Appendix W: Accelerometer Log for Study Participants (Chapters 4 & 5)

INSTRUCTIONS: HOW TO WEAR THE PHYSICAL ACTIVITY MONITOR

This small activity monitor records general movement and gives us a better understanding of your overall activity level. We will not be able to tell what kind of specific activity you are doing, only the intensity and duration of physical activity. At first, the belt may feel slightly awkward, but after a few hours, you will not notice it as much. It is very important for our study that you wear the monitor correctly. Please follow these instructions carefully:

- ✓ Wear the monitor attached to the belt around your waist, **JUST ABOVE YOUR RIGHT HIPBONE**.
- ✓ Wear the monitor so that the sticker is facing **UP**.
- ✓ Wear the monitor snug against your body. If you have to, you can adjust the end of the strap to make it tighter. Or, to loosen the belt, push more of the strap through the loop. **WEAR THE MONITOR TIGHT ENOUGH SO THAT IT DOES NOT MOVE WHEN YOU ARE BEING ACTIVE.**
- ✓ The monitor can be worn underneath or on top of your clothes or in your belt loop.
- ✓ Keep the monitor on **ALL DAY AND ALL NIGHT** for 8 days.
- ✓ **DO NOT SUBMERGE IN THE WATER** (swimming, bathing, etc). You can remove it for showering but remember to put it back on as soon as possible and record the times you do not have it on.
- ✓ **Record all stationary activities (i.e., stationary cycling) or those that require you to remove your activity monitor such as swimming, wrestling, judo etc.**
- ✓ Do not let anyone else wear it.

Details for dropping off/collection of monitor: **PLEASE SEE CHECKLIST PAGE**

If you have any questions related to the activity monitor, please email: *kneestdy@ualberta.ca*

There is no 'ON' or 'OFF' switch that you need to worry about. The activity monitor runs on a battery and is programmed to run continuously from when we give it to you. Please do not try to open the monitor.

OFFICE USE ONLY	
Start Date and Time: ____________________	Participant ID: ________________________
Testing Timepoint: ____________________	Age: ________________________
Valid days: ____________________	ActiGraph ID: ________________________

MONITOR LOG

NON-EXERCISE ACTIVITIES – Please use Table 1 to record every time you take the monitor off for more than 5 minutes for **non-exercise** activities such as **showering and bathing**.

Table 1: Log every time you take the monitor off for more than 5 minutes for non-exercise activities

	Date	Day	Time OFF	Time ON	Reason
Example:	December 1, 2016	Thursday	8:00 AM	8:15 AM	Shower
START:			-----		
FINISH:				-----	

EXERCISE ACTIVITIES – Please use Table 2 to record all stationary activities (e.g., stationary bike, weight lifting) that the monitor may not detect or those that require you to remove the activity monitor (e.g., swimming, wrestling, judo, etc). In the last column, please note how hard you thought this exercise session was (see definitions below).

Table 2: Log exercise-related activities that the monitor may not detect

	Date	Day	Was the Monitor ON?	Activity	Activity Start Time	Activity End Time	Intensity (see below)
Example:	December 1	Thursday	No	Swimming	5:00 PM	6:00 PM	10 min – light 50 min - moderate

Light: requires minimal effort and does not noticeably accelerate the heart rate
Moderate: requires moderate effort and noticeably accelerates the heart rate but not exhausting
Vigorous: requires a large amount of effort and causes rapid breathing and substantial increase in heart rate

Appendix X: Tampa Scale for Kinesiophobia (TSK) (Chapters 4 & 5)

Tampa Scale for Kinesiophobia

(Miller , Kori and Todd 1991)

1 = strongly disagree
2 = disagree
3 = agree
4 = strongly agree

1. I'm afraid that I might injury myself if I exercise	1	2	3	4
2. If I were to try to overcome it, my pain would increase	1	2	3	4
3. My body is telling me I have something dangerously wrong	1	2	3	4
4. My pain would probably be relieved if I were to exercise	1	2	3	4
5. People aren't taking my medical condition seriously enough	1	2	3	4
6. My accident has put my body at risk for the rest of my life	1	2	3	4
7. Pain always means I have injured my body	1	2	3	4
8. Just because something aggravates my pain does not mean it is dangerous	1	2	3	4
9. I am afraid that I might injure myself accidentally	1	2	3	4
10. Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my pain from worsening	1	2	3	4
11. I wouldn't have this much pain if there weren't something potentially dangerous going on in my body	1	2	3	4
12. Although my condition is painful, I would be better off if I were physically active	1	2	3	4
13. Pain lets me know when to stop exercising so that I don't injure myself	1	2	3	4
14. It's really not safe for a person with a condition like mine to be physically active	1	2	3	4
15. I can't do all the things normal people do because it's too easy for me to get injured	1	2	3	4
16. Even though something is causing me a lot of pain, I don't think it's actually dangerous	1	2	3	4
17. No one should have to exercise when he/she is in pain	1	2	3	4

Reprinted from:
Pain, Fear of movement/(re) injury in chronic low back pain and its relation to behavioral performance, 62, Vlaeyen, J., Kole-Snijders A., Boeren R., van Eek H., 371.

Scoring Information
Tampa Scale for Kinesiophobia
(Miller et al 1991)

A total score is calculated after inversion of the individual scores of items 4, 8, 12 and 16.

Appendix Y: Missing Data at Baseline and Follow-Up by Study Group (Chapter 4)

		Uninjured (n=73)		Injured (n=93)	
Timepoint	**Outcome**	**Number of Missing Participants**	**Reasons**	**Number of Missing Participants**	**Reasons**
Baseline	Knee-specific HRQoL[a]	–	–	n=1	• Did not fully complete online questionnaires, n=1
	Index knee muscle strength[b]	–	–	n=13	• Pain or swelling from recent knee injury or surgery, n=13
	Physical activity[c]	n=3	• Not enough wear time, n=2 • Did not return ActiGraph, n=1	n=5	• Not enough wear time, n=4 • Did not return ActiGraph, n=1
	Fat mass index[d]	n=1	• BIA unit error, n=1	n=1	• BIA unit error, n=1
	Kinesiophobia[e]	–	–	n=1	• • Did not fully complete online questionnaires, n=1
6-Month Follow-Up	Knee-specific HRQoL[a]	–	–	n=1	• Did not fully complete online questionnaires, n=1
	Index knee muscle strength[b]	n=9	• Out of town, n=1 • Partially withdrew and chose to only complete questionnaires, n=4 • Lab closure due to COVID-19, n=4	n=11	• Pain or swelling from knee injury or recent surgery, n=4 • Restricted by surgeon, n=1 • Partial withdraw and chose to only complete questionnaires, n=3 • Lab closure due to COVID-19, n=3
	Physical activity[c]	n=11	• Out of town, n=1 • Not enough wear time, n=2 • Partially withdrew and chose to only complete questionnaires, n=4 • Lab closure due to COVID-19, n=4	n=22	• Not enough wear time, n=17 • Partial withdraw and chose to only complete questionnaires, n=3 • Lab closure due to COVID-19, n=3
	Fat mass index[d]	n=9	• Out of town, n=1 • Partial withdraw and chose to only complete questionnaires, n=4 • Lab closure due to COVID-19, n=4	n=7	• BIA unit error, n=1 • Partial withdraw and chose to only complete questionnaires, n=3 • Lab closure due to COVID-19, n=3
	Kinesiophobia[e]	–	–	n=1	• • Did not fully complete online questionnaires, n=1

[a]Measured using the Knee injury and Osteoarthritis Outcome Score knee-related quality of life subscale
[b]Measured using isokinetic dynamometry
[c]Measured using accelerometry (ActiGraph)
[d]Measured using bioelectrical impedance

[e]Measured using the Tampa Scale for Kinesiophobia

BIA, bioelectrical impedance analysis; HRQoL, health-related quality of life; n, number of participants;

Appendix Z: CONSERVE Checklist for the PrE-OA Cohort Study Conducted at the University of Alberta (Chapters 4 & 5)

Item	Item Title	Description
I.	Extenuating circumstances	COVID-19 and subsequent university- and government-mandated restrictions[a], including: a) Research laboratory closures from March 23, 2020-June 9, 2020 and December 14, 2020-January 22, 2021. b) Youth sport restrictions from March 17, 2020-June 12, 2020 and November 12, 2020-February 8, 2021.
II.	Important modifications	Impacts: a) Lab closures: Unable to complete in-person data collection (knee muscle strength and body composition) 6-month follow-up with 7 participants (4 uninjured, 3 injured) and 12-month follow-up with 5 participants (4 uninjured, 1 injured). b) Youth sports restrictions: Changes in the physical function behaviours and HRQoL may have been present at 6-month follow-up for 16 participants (10 uninjured, 6 injured) and 12-month follow-up for 21 participants (14 uninjured, 7 injured)[b]. Mitigation strategies: a) Lab closures: Participants with follow-up appointments during the impacted periods completed online questionnaires only. b) Youth sports restrictions: Participants who attended data collection after the onset of COVID-19 were asked to indicate if their physical activity levels were the same, less, or more at the time of testing compared to pre-pandemic levels. Eight participants (8 uninjured) responded at baseline testing (1 reported having the same level of activity, 4 reported less, and 4 reported more); 15 participants (13 uninjured, 2 injured) responded at 6-month testing (1 reported having the same level of activity, 10 reported less, and 4 reported more); and 8 participants (5 uninjured, 3 injured) responded at 12-month testing (5 reported having the same level of activity and 3 reported less).
III.	Responsible parties	The principal investigator (JW) and research staff were involved in planning and reviewing modifications. The university research ethics committee was involved in approving modifications. Study participants were given the option to not attend in-person data collection during COVID-19 if they were not comfortable with it.
IV.	Interim data	No interim data were used to inform the modifications.

[a]Refers to the University of Alberta and Government of Alberta
[b]The COVID-19 pandemic has been shown to negatively impact physical activity (Moore et al., 2020)[1] and quality of life (McGuine et al., 2021)[2] in youth.

Appendix AA: Sample Size Calculation (Chapter 5)

The sample size was calculated using the primary outcome of the Knee injury and Osteoarthritis Outcome Score (KOOS) knee-related quality of life (QOL) subscale score (STATA v14.2, College Station, Texas, USA). Based on previous research,[1] we assumed the mean (standard deviation, SD) of the KOOS QOL subscale score for the uninjured group would be 98.1 (3.8) and for the injured group would be 89.7 (8.2).

KQ_U: uninjured group – mean (SD): 98.1 (3.8)
KQ_I: injured group – mean (SD): 89.7 (8.2)
Null hypothesis: $KQ_U = KQ_I$
Alternative hypothesis: $KQ_U \neq KQ_I$

```
. sampsi 98.1 89.7, p(0.8) sd1(3.8) sd2(8.2)

Estimated sample size for two-sample comparison of means

Test Ho: m1 = m2, where m1 is the mean in population 1
                    and m2 is the mean in population 2
Assumptions:

         alpha =   0.0500  (two-sided)
         power =   0.8000
            m1 =     98.1
            m2 =     89.7
           sd1 =      3.8
           sd2 =      8.2
         n2/n1 =     1.00

Estimated required sample sizes:

            n1 =       10
            n2 =       10
```

To perform multivariable regression analyses including 1 covariate and 3 timepoints, sample size was calculated as:

> n = [20 (10 per group x 2 groups) + 20 (1 covariate x 10 per group[2] x 2 groups)] = 40 x 3 (3 timepoints assessed) = 120 (60 per group)

We also accounted for 15% drop-out, adding another 22 participants (11 per group) to our sample size calculation. Therefore, we determined our total a-priori sample size to be 142 participants (71 per group) in order to detect a between-group difference of 8.4 points on the KOOS QOL subscale (1-β=0.8, α=0.05), adjust for 1 covariate, perform 3 separate regression models per timepoint, and account for 15% drop-out.

Appendix AB: Loss to Follow-Up Summary by Study Group (Chapter 5)

Characteristics	Uninjured (n=16)	Injured (n=23)
Sex (n, % female)	10 (63)	14 (61)
Age at injury (years)	-	16.3 (12.7-19.4)
Age at baseline (years)	17.4 (13.6-20.0)	16.4 (12.8-19.6)
BMI (kg/m^2)	21.9 (17.9-27.5)	23.6 (19.1-37.7)
Type of injury (n, % ACL rupture)	-	9 (39)
Main sport (n, % soccer)	7 (44)	6 (26)
Main sport level (n, % club)[a]	9 (56)	15 (71)

Values represent median (range) unless otherwise noted
[a]Categories included recreational, club, school, varsity, provincial, national

ACL, anterior cruciate ligament; BMI, body mass index; CI, confidence interval; kg, kilogram; m, metre; n, number of participants

Appendix AC: Missing Data at Baseline and Follow-Up by Study Group (Chapter 5)

		Uninjured (n=64)		Injured (n=86)	
Timepoint	**Outcome**	**Number of Missing Participants**	**Reasons**	**Number of Missing Participants**	**Reasons**
Baseline	Knee-specific HRQoL[a]	–	–	n=1	• Did not fully complete online questionnaires, n=1
	MVPA[b]	n=1	• Not enough wear time, n=2	n=4	• Not enough wear time, n=3 • Did not return ActiGraph, n=1
	Knee extensor peak torque[c]	–	–	n=13	• Pain or swelling from recent knee injury or surgery, n=13
	Intermittent pain[d]	–	–	n=1	• Did not fully complete online questionnaires, n=1
	Fear of re-injury[e]	–	–	n=1	• Did not fully complete online questionnaires, n=1
	RTS[f]	N/A	N/A	N/A	N/A
6-Month Follow-Up	Knee-specific HRQoL	n=1	• Missed this visit, n=1	n=4	• Missed this visit, n=4
	MVPA	n=9	• Not enough wear time, n=1 • Only completed questionnaires, n=4 • Missed this visit, n=1 • Out of town, n=1 • Lab closure due to COVID-19, n=2	n=21	• Not enough wear time, n=13 • Only completed questionnaires, n=2 • Missed this visit, n=4 • Out of town, n=1 • Lab closure due to COVID-19, n=1
	Knee extensor peak torque	n=8	• Only completed questionnaires, n=4 • Missed this visit, n=1 • Out of town, n=1 • Lab closure due to COVID-19, n=2	n=12	• Pain or swelling from recent knee injury or surgery, n=4 • Only completed questionnaires, n=2 • Missed this visit, n=4 • Out of town, n=1 • Lab closure due to COVID-19, n=1
	Intermittent pain	n=1	• Missed this visit, n=1	n=4	• Missed this visit, n=4
	Fear of re-injury	N/A	N/A	n=4	• Missed this visit, n=4

	RTS	N/A	N/A	n=4	• Missed this visit, n=4
12-Month Follow-Up	Knee-specific HRQoL	–	–	n=1	• Did not fully complete online questionnaires, n=1
	MVPA	n=11	• Not enough wear time, n=3 • Only completed questionnaires, n=1 • Missed this visit, n=1 • Lab closure due to COVID-19, n=4	n=21	• Not enough wear time, n=14 • Only completed questionnaires, n=4 • Missed this visit, n=1 • Out of town, n=1 • Lab closure due to COVID-19, n=1
	Knee extensor peak torque	n=6	• Only completed questionnaires, n=1 • Missed this visit, n=1 • Lab closure due to COVID-19, n=4	n=9	• Pain or swelling from knee injury or recent surgery, n=2 • Only completed questionnaires, n=4 • Missed this visit, n=1 • Out of town, n=1 • Lab closure due to COVID-19, n=1
	Intermittent pain	–	–	n=1	• Did not fully complete online questionnaires, n=1
	Fear of re-injury	N/A	N/A	n=2	• Did not fully complete online questionnaires, n=2
	RTS	N/A	N/A	n=1	• Did not fully complete online questionnaires, n=1

[a]Measured using the Knee injury and Osteoarthritis Outcome Score
[b]Measured using accelerometry (ActiGraph)
[c]Measured using isokinetic dynamometry
[d]Measured using the Intermittent and Constant Osteoarthritis Pain questionnaire
[e]Measured using the Tampa Scale for Kinesiophobia
[f]Measured using a bespoke study questionnaire

HRQoL, health-related quality of life; MVPA, moderate-to-vigorous physical activity; n, number of participants; N/A, not applicable; RTS, return to sport

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