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The Patient Experience of Living With Knee Osteoarthritis Pain: Development of a Conceptual Model

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ABSTRACT

Background: Knee osteoarthritis (KOA) is a chronic degenerative condition. Pain is the most prominent symptom of KOA, which can be exacerbated by obesity. The US Food and Drug Administration recommends using patient-reported outcome (PRO) measures to assess KOA pain and function in clinical trials, but none have been validated for patients with KOA and obesity/overweight. The objective of this study was to explore and document the patient experience of signs, symptoms, and health-related quality of life (HRQoL) impacts of KOA pain, including the impact of obesity/overweight, to facilitate future validation studies.

Methods: A targeted literature review and interviews with US participants with KOA pain (including some with comorbid obesity) were conducted. Publications and interview transcripts were analysed using content analysis methods to develop a conceptual model of KOA pain experience.

Results: Eighteen publications were reviewed and 25 participants were interviewed. All participants in the interviews reported knee pain and described that their physical functioning had been negatively affected. Many experienced a negative emotional/psychological impact. Many participants believed that there was a relationship between their weight and experience of KOA pain, reporting a 'vicious cycle' of pain and weight gain due to KOA.

Conclusions: This study highlights the burden of living with KOA pain and the negative impact of obesity/overweight on patients' HRQoL. A conceptual model was developed, which may be used to explore the content validity of PRO measures and promote a robust understanding of the patient experience of living with KOA pain during the development of new therapies.

1 | Introduction

Knee osteoarthritis (KOA) is a chronic degenerative condition that involves the entire joint, with the most critical changes occurring in the articular cartilage (French et al. 2022). There is no cure for KOA (Geng et al. 2023), but available treatments focus on symptom management strategies and include the reduction of modifiable risk factors (e.g., obesity), analgesic medications, intraarticular therapy, exercise, physical therapy, and surgery (Geng et al. 2023; Suarez-Almazor et al. 2010; Tan et al. 2024). Pain is the most prominent symptom for patients with KOA, as well as stiffness, swelling, and loss of mobility (Abramoff and Caldera 2020). Patients with higher BMI classes have reported higher pain scores on measurements of pain severity (Raud et al. 2020), and increasing weight (i.e., weight gain) in adults is associated with worsening clinical KOA features for example, pain, function, and quality of life (Solanki et al. 2023). Symptomatic, radiologically confirmed KOA is a

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leading cause of disability globally (Hall et al. 2022), with a global age-standardized prevalence of 4307 cases per 100,000 (GBD 2021 Osteoarthritis Collaborators 2023). In US and Australian studies, KOA affected approximately 16% of people aged > 45 years and 20% of patients with obesity, respectively (Ackerman and Osborne 2012; Hall et al. 2022).

In the evaluation of treatments (new or existing) for KOA, the US Food and Drug Administration (FDA) recommends using patient-reported outcome measures (PROMs) to assess KOA pain and function in clinical trials (Food and Drug Administration (FDA) 2018). PROMs capture and assess what is important and relevant to patients directly from the patient. As pain is a multi-dimensional and subjective experience, the patient-reported experience of pain and its impacts are critical to understanding the effectiveness of therapies and the meaningfulness of improvements to patients' lives. Thus, PROMs used in KOA studies should be evaluated in the intended population to ensure they capture relevant concepts of interest within the context of use. Qualitative evidence can be used to evaluate whether PROMs are conceptually relevant and comprehensive; however, there is no existing study in the literature that fully explores the patient experience of KOA and obesity/overweight; thus, it is currently difficult to assess the content validity of existing PROMs in this population.

The overall objective of this qualitative study was to explore and document patient experience of signs, symptoms, and health-related quality of life (HRQoL) impacts of pain associated with KOA, as well as the impact of obesity/overweight using a targeted literature review (TLR) and qualitative interviews with individuals experiencing KOA pain. This qualitative study was conducted to conceptualise and inform a robust understanding of the patient experience of living with KOA pain.

2 | Methods

2.1 | Targeted Literature Review

An electronic search was conducted of the Medline, EMBASE, and PsycINFO databases to identify published qualitative research describing the patient experience of KOA pain. Hand-searching was used as a supplementary measure to ensure that all relevant studies were included in the literature review; this included a review of recent (past 3 years) conference proceedings of Osteoarthritis Research Society International (OARSI), European Congress of Rheumatology (EULAR), and American College of Rheumatology (ACR) Convergence, and a review of the reference lists of included studies and relevant review papers identified in the electronic database searches. Database searches were conducted in June 2023 using pre-defined search strategies combining terms for osteoarthritis with terms for qualitative research (e.g., interview). Eligible articles were published 1980 to present, while conference proceedings were searched from 2021 to 2023, inclusive. Articles meeting pre-specified eligibility criteria were reviewed and reported descriptions of the experiences of patients with KOA pain underwent secondary directed content analysis to identify relevant concepts. For full methods, for example, eligibility criteria, see Supporting Information S1: Additional file 1.

2.2 | Participant Interviews

Non-interventional, observational, cross-sectional qualitative interviews were conducted with individuals living with KOA pain based in the US. The study was designed in accordance with FDA patient-reported outcome (PRO) Guidance for Industry and Patient Focused Drug Development (PFDD) (final and draft) guidance (Food and Drug Administration (FDA) 2019, 2020, 2022a, 2022b). Efforts were made to ensure diversity of the interview sample in terms of race/ethnicity, sex, BMI, and educational level (e.g., equal male/female, BMI < 27 kg/m^2 and ≥ 27 kg/m^2). The eligibility (inclusion and exclusion) criteria for this study are described in Table 1. Participants were recruited by a professional healthcare research recruitment agency using a variety of methods including patient databases, physician referrals, social media advertisements, and/or patient association websites.

Open-ended interviews, lasting up to 90 min, were conducted using web-assisted software (Microsoft Teams) between August and November 2023. Unique identifiers were assigned to all participants to ensure anonymity and protect their identity. A semi-structured discussion guide was developed by experienced clinical outcome assessment (COA) researchers to explore the symptoms and impacts experienced by individuals living with KOA pain. Participants were also asked to describe the impact of their weight on their KOA pain during the interviews. Open-ended questions were broad to promote spontaneous discussion of experiences by participants (‘*Can you tell me about your experiences with osteoarthritis pain?*’, ‘*Does the pain from your osteoarthritis affect you in your daily life?*’). Specific follow-up probes to determine the relevance of the symptom and impact concepts identified in the TLR were also included for use where participants did not discuss these topics unprompted (e.g. ‘*Does the pain from your osteoarthritis affect your sleep?*’, ‘*Have you had to miss any work or take time off because of your osteoarthritis?*’). All participants received an honorarium for the time spent participating in the interviews.

Analyses were conducted by experienced COA researchers. Demographic and clinical information were descriptively summarised. The interviews were audio recorded and transcribed verbatim to allow in-depth qualitative analysis. De-identified transcripts were analysed using semantic, qualitative, directed content analysis methods (Hsieh and Shannon 2005) and facilitated by ATLAS.ti 9 software; descriptive codes were assigned to the quotes to identify, define, and refine relevant concepts and domains. The analysis took an experiential, realist approach, focussing on participants' perspectives and experiences (Lincoln and Guba 1985). For each included concept, frequency counts were calculated to understand the number of participants reporting the experience to broadly explore the participant experience and obtain in-depth descriptions of the concepts. To confirm an adequate sample size had been recruited and to determine whether the patient experience had

TABLE 1 | Eligibility criteria for interviews.

Criteria	Inclusion
Location; age; BMI	• Resides in the US • Age ≥ 40 years • BMI (subgroups of < 27 kg/m^2 and ≥ 27 kg/m^2)
Diagnosis	• Has a clinician-confirmed diagnosis of KOA **and** at least one of the following: ○ Age > 50 years ○ Morning stiffness in the index joint less than 30 min in duration ○ Crepitus in the index joint
Pain	• Has self-reported experience of KOA pain for at least 3 months • Has had osteoarthritis pain for > 15 days over the previous month or ≥ 4 days over the past week • Has moderate to severe osteoarthritis pain over the last week, as indicated by a score of ≥ 4 on a pain severity NRS[a]
	Exclusion
Joint status	• Participant has prior joint replacement in the index joint • Participant has a history of potentially causative and/or confounding conditions that can be reasonably considered to interfere with the results of this study

Abbreviations: BMI, body mass index; KOA, knee osteoarthritis; NRS, numerical rating scale.

[a] "Over the past 7 days, how would you rate the usual level of your knee pain? Please select an answer from a scale of 0 to 10, where 0 is "no pain" and 10 is "worst possible pain"'.

been understood in appropriate depth and breadth, saturation analysis was conducted following industry standards (Patrick et al. 2011). Sequential transcripts were organised into sets of 4–5 participants and spontaneously elicited concepts were compared between the sets to determine whether each concept had been identified before the final set of interviews, thus demonstrating an appropriate breadth of data collection. Subsequently, concepts were reviewed to determine if they were discussed in depth by a notable number of participants, and whether a full understanding of each concept had been obtained. Saturation was deemed to be met if each concept was understood in sufficient depth and/or breadth.

2.3 | Harmonised Conceptual Model

Qualitative results from the TLR and patient interviews were compared, and homogeneous concepts were merged based on similar patient-reported and literature-based descriptions. All merged and stand-alone concepts were constructed and presented in a harmonised conceptual model (CM), in line with PFDD guidance (Food and Drug Administration (FDA), 2019, 2020, 2022a, 2022b), to characterise the patient experience of KOA from the literature and patient perspective.

3 | Results

3.1 | Targeted Literature Review

In total, 3343 articles were identified (see Supporting Information S1: Figure S2). After the removal of 651 duplicates, 2612 publications were excluded from eligibility reasons (see Supporting Information S1: Additional file 1). Eight publications, identified via hand-searching of reference lists, were included in the list of eligible studies. In total, 88 papers meeting the study eligibility criteria were identified. The 18 most relevant and generalisable publications were selected for data extraction (see Supporting Information S1: Additional file 1). Some eligible papers were not selected for extraction due to the limited amount of relevant data (n = 55), enrolment of a comparatively less generalisable population (n = 7), publication in only conference abstract/poster format (n = 5), or exploration of only one concept (n = 3). The included publications were published between 2007 and 2022; therefore, all studies were less than 20 years old. The included publications are summarised in Table 2.

Five key signs and symptoms associated with KOA, including pain, stiffness, swelling, clicking/grinding (crepitus), and joint locking, were reported in the studies from the TLR. Signs and symptoms of KOA have been reported to cause multiple physical impacts, which, in a bidirectional fashion, may also further trigger the signs and symptoms of KOA. Other HRQoL impacts were on daily activities, work, social and leisure time, sleep, and strain on emotional and psychological well-being and relationships. Weight gain was noted as a relevant factor of KOA in six publications, with a bidirectional relationship between weight and the key signs and symptoms of KOA. The frequency of concept reporting from the TLR is summarised in Table 3.

3.2 | Participant Interviews

3.2.1 | Sample Characteristics

Demographic and clinical characteristics of the 25 participants are shown in Table 4. One additional participant was interviewed but excluded post-hoc, as they had a concurrent diagnosis of hip OA, revealed during their interview, which could be reasonably considered to interfere with the results of this study. Sample diversity based on sex, race, ethnicity, and education level was attained. Five patients had KOA pain and a BMI < 27 kg/m^2, and 20 patients had KOA pain with BMI ≥ 27 kg/m^2.

3.2.2 | Patient Experience of KOA Pain

Among the 25 participants, the most frequently reported descriptors of pain were 'ache' (n = 10/25) and 'sharp' (n = 8/25). Participants reported that the severity of their pain fluctuated (n = 19/25) and that they experienced KOA pain every day (n = 17/25) (Table 5). The severity and frequency were the most bothersome aspects of pain. Participants also reported the

TABLE 2 | Summary of publications identified from the TLR.

Author, year, country (Reference)	Study population with knee OA BMI (mean) kg/m^2	Aim of study	Data collection method
Al-Khlaifat, 2020, Jordan (Al-Khlaifat et al. 2020)	*N* = 14 BMI: 32.4	To explore the knowledge of the pathology and the experience of people diagnosed with KOA living in Jordan.	Semi-structured interviews and focus groups
Allison, 2019, Australia (Allison et al. 2019)	*N* = 13 BMI: 34.3	To explore the attitudes of individuals with KOA towards the role of physiotherapists in weight management in KOA.	Semi-structured interviews
Battista, 2022, Italy (Battista et al. 2022)	*N* = 6 BMI: 27.8	To investigate how patients with OA experience their disease and care process, highlighting potential elements that can enhance or spoil it, to optimise their quality of care.	Semi-structured interviews
Carmona-Teres, 2017, Spain (Carmona-Terés et al. 2017a)	*N* = 10 BMI: NR	To further understand the experiences, perceptions, cognitive evaluations, values, emotions, beliefs and coping strategies of patients with KOA and the influence of all these factors in the self-management of OA.	Semi-structured interviews
Chan, 2011, China (Chan and Chan 2011)	*N* = 20 BMI: NR	To evaluate the influence of different pain patterns of patients' quality of life and to investigate their interpretation and coping strategies for the disease.	Semi-structured interviews
Hall, 2008, Canada (Hall et al. 2008)	*N* = 15 BMI: NR	To examine individuals' experiences living with KOA and what their expectations are of arthroplasty and physiotherapy.	Semi-structured interviews
Hawker, 2008, Canada (Hawker et al. 2008)	*N* = 91 BMI: NR	To examine the pain experience of people with hip or knee OA, particularly changes over time and most distressing features.	Semi-structured interviews and focus groups
Hochman, 2010, Canada (Hochman et al. 2010)	*N* = 80 BMI: NR	To determine whether people with chronic, symptomatic KOA use pain descriptors that are suggestive of underlying neuropathic pain.	Focus groups
Hsu, 2018, Tiawan (Hsu et al. 2018)	*N* = 79 BMI: NR	To explore triggers of and decision-making patterns for older adults with KOA to receive total knee arthroplasty.	Semi-structured interviews
Kamsam, 2020, Malaysia (Kamsan et al. 2020)	*N* = 16 BMI: NR	To explore older adults' knowledge about KOA and their perspectives on the information required to enable self-management.	Focus groups
Kanavaki, 2022, UK (Kanavaki et al. 2022)	*N* = 6 BMI: NR	To understand how physical activity and sedentary behaviour are actualised and experienced in the daily lives of people living with knee and hip OA, and how these link to people's sense of well-being.	Semi-structured interviews
Maly, 2007, Canada (Maly and Krupa 2007)	*N* = 3 BMI: NR	To understand the experience of living with KOA in the older adult.	Semi-structured interviews
Murphy, 2015, US (Murphy et al. 2015)	*N* = 45 BMI: 30.9 (for *n* = 40)	To characterise pain flares in individuals with KOA.	Qualitative log book recordings
Nyvang, 2016, Sweden (Nyvang et al. 2016)	*N* = 12 BMI: NR	To describe patients' experiences of living with KOA when scheduled for surgery and further their expectations for future life after surgery.	Semi-structured interviews

(Continues)

TABLE 2 | (Continued)

Author, year, country (Reference)	Study population with knee OA BMI (mean) kg/m^2	Aim of study	Data collection method
Parsons, 2009, UK (Parsons et al. 2009)	$N = 3$ BMI: NR	To explore the lived experiences of patients with severe OA of the hip or knee joint while awaiting joint replacement surgery.	Unstructured interviews
Stone, 2017, Canada (Stone and Baker 2017)	$N = 13$ BMI: NR	To gain a broader understanding of the facilitators and barriers towards regular physical activity being perceived by adults with OA within the context of their experiences with physician-recommended treatment strategies.	Semi-structured interviews
Tollefsrud, 2010, Norway (Tollefsrud and Mengshoel 2020)	$N = 8$ BMI: NR	To examine how individuals manage to live a life with OA in the knee or hip.	Focus groups
Woolhead, 2010, UK (Woolhead et al. 2010)	$N = 76$ BMI: NR	To explore the experience of night pain in people with hip or knee OA.	Focus groups

Abbreviations: BMI, body mass index; KOA, knee osteoarthritis; NR, none reported; OA, osteoarthritis; UK, United Kingdom.

TABLE 3 | Frequency table of KOA symptoms and impact concepts from the TLR.

Concept	Frequency of report (number of articles)	References reporting concept
Key signs/symptoms		
Pain	17	(Al-Khlaifat et al. 2020; Battista et al. 2022; Carmona-Terés et al. 2017a; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Hochman et al. 2010; Hsu et al. 2018; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Murphy et al. 2015; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017; Tollefsrud and Mengshoel 2020; Woolhead et al. 2010)
Stiffness	8	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Stone and Baker 2017)
Swelling	6	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hall et al. 2008; Kamsan et al. 2020; Nyvang et al. 2016; Tollefsrud and Mengshoel 2020)
Clinking/Grinding (Crepitus)	3	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hawker et al. 2008)
Joint locking	4	(Hall et al. 2008; Hawker et al. 2008; Kanavaki et al. 2022; Murphy et al. 2015)
Other signs/symptoms		
Instability/joint gives way	6	(Hawker et al. 2008; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Parsons et al. 2009; Tollefsrud and Mengshoel 2020)
Weakness	5	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hawker et al. 2008; Kamsan et al. 2020; Tollefsrud and Mengshoel 2020)
Numbness	3	(Chan and Chan 2011; Hawker et al. 2008; Hochman et al. 2010)
Decreased range of motion	3	(Chan and Chan 2011; Hawker et al. 2008; Kanavaki et al. 2022)
Cramping/muscle spasms	2	(Hawker et al. 2008; Kamsan et al. 2020)
Deformity	2	(Chan and Chan 2011; Hall et al. 2008)

(Continues)

TABLE 3 | (Continued)

Concept	Frequency of report (number of articles)	References reporting concept
Muscle tightness	2	(Al-Khlaifat et al. 2020; Kamsan et al. 2020)
Weight gain worsens OA symptoms	6	(Al-Khlaifat et al. 2020; Allison et al. 2019; Battista et al. 2022; Chan and Chan 2011; Hall et al. 2008; Kanavaki et al. 2022)
HRQoL impacts of pain		
Physical function		
Difficulty with the following movements:		
Walking	14	(Al-Khlaifat et al. 2020; Battista et al. 2022; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Hsu et al. 2018; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Murphy et al. 2015; Nyvang et al. 2016; Stone and Baker 2017; Tollefsrud and Mengshoel 2020; Woolhead et al. 2010)
Climbing stairs	12	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Murphy et al. 2015; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017; Tollefsrud and Mengshoel 2020)
Bending/kneeling/squatting	11	(Al-Khlaifat et al. 2020; Battista et al. 2022; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Hsu et al. 2018; Kamsan et al. 2020; Kanavaki et al. 2022; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017)
Standing up (e.g., from seated)	7	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Kamsan et al. 2020; Kanavaki et al. 2022; Murphy et al. 2015; Parsons et al. 2009; Woolhead et al. 2010)
Lifting heavy objects	3	(Chan and Chan 2011; Nyvang et al. 2016; Woolhead et al. 2010)
Turning in bed	3	(Nyvang et al. 2016; Tollefsrud and Mengshoel 2020; Woolhead et al. 2010)
Running	1	(Maly and Krupa 2007)
Balancing	1	(Hawker et al. 2008)
Transferring (e.g. in/out bath)	1	(Hall et al. 2008)
Inactivity/held positions:		
Sitting for prolonged time	7	(Al-Khlaifat et al. 2020; Hall et al. 2008; Hawker et al. 2008; Kamsan et al. 2020; Kanavaki et al. 2022; Murphy et al. 2015; Nyvang et al. 2016)
Standing for a prolonged period of time	4	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hsu et al. 2018; Murphy et al. 2015)
Emotional/psychological functioning		
Sad/depressed	13	(Battista et al. 2022; Carmona-Terés et al. 2017a; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Hsu et al. 2018; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017; Tollefsrud and Mengshoel 2020)
Negative view of self (e.g. poor body image, feel embarrassed/ashamed)	13	(Battista et al. 2022; Carmona-Terés et al. 2017a; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Hsu et al. 2018; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017; Tollefsrud and Mengshoel 2020)

(Continues)

TABLE 3 | (Continued)

Concept	Frequency of report (number of articles)	References reporting concept
Angry/Frustrated/Irritated	10	(Al-Khlaifat et al. 2020; Carmona-Terés et al. 2017a; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Kamsan et al. 2020; Kanavaki et al. 2022; Nyvang et al. 2016; Parsons et al. 2009; Tollefsrud and Mengshoel 2020)
Anxious/worried/fearful: Of falling/injury	8	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Kanavaki et al. 2022; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017)
Anxious/worried/fearful: Of disease progression	7	(Al-Khlaifat et al. 2020; Carmona-Terés et al. 2017a; Chan and Chan 2011; Hawker et al. 2008; Hsu et al. 2018; Kamsan et al. 2020; Kanavaki et al. 2022)
Stressed	4	(Chan and Chan 2011; Hawker et al. 2008; Kanavaki et al. 2022; Tollefsrud and Mengshoel 2020)
Anxious/worried/fearful: Of flares	3	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Tollefsrud and Mengshoel 2020)
Feel isolated	3	(Chan and Chan 2011; Maly and Krupa 2007; Parsons et al. 2009)
Anxious/worried/fearful: Of life in the future	1	(Chan and Chan 2011)
Other HRQoL impacts		
Social and leisure time	14	(Al-Khlaifat et al. 2020; Allison et al. 2019; Carmona-Terés et al. 2017a; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Hsu et al. 2018; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017; Tollefsrud and Mengshoel 2020)
Sleep	13	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Hsu et al. 2018; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017; Tollefsrud and Mengshoel 2020; Woolhead et al. 2010)
Daily activities	12	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hall et al. 2008; Hawker et al. 2008; Hsu et al. 2018; Kamsan et al. 2020; Kanavaki et al. 2022; Maly and Krupa 2007; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017; Tollefsrud and Mengshoel 2020)
Fatigue/tiredness	9	(Al-Khlaifat et al. 2020; Chan and Chan 2011; Hawker et al. 2008; Hsu et al. 2018; Nyvang et al. 2016; Parsons et al. 2009; Stone and Baker 2017; Tollefsrud and Mengshoel 2020; Woolhead et al. 2010)
Relationships	7	(Carmona-Terés et al. 2017a; Chan and Chan 2011; Hall et al. 2008; Kamsan et al. 2020; Kanavaki et al. 2022; Nyvang et al. 2016; Parsons et al. 2009)
Work	6	(Chan and Chan 2011; Hsu et al. 2018; Kanavaki et al. 2022; Nyvang et al. 2016; Parsons et al. 2009; Tollefsrud and Mengshoel 2020)

Abbreviations: HRQoL, health-related quality of life; KOA, knee osteoarthritis; TLR, targeted literature review.

unpredictability of pain, the prospect of needing surgery, using medication to manage their pain, and the impact on day-to-day life as bothersome impacts. All participants with KOA reported experiencing pain in their knee or knees ($n = 25/25$). The most frequently reported method for alleviation of pain was medication ($n = 20/25$), including oral and topical pain relief treatments (in the form of tablets, creams, and gels) and injections (including steroids and hyaluronic acid). Participants reported a range of triggers for pain, with the most frequently reported triggers including walking ($n = 16/25$), weather ($n = 11/25$), sitting ($n = 8/25$), standing ($n = 7/25$), and using stairs ($n = 7/25$).

TABLE 4 | Demographic characteristics of participants with KOA.

Demographic and clinical characteristic	Total sample ($N = 25$)
Age, years, Mean (SD) [range]	57.9 (8.5) [40.0–75.0]
Sex, *n* (%)	
Male	10 (40%)
Female	15 (60%)
Race, *n* (%)	
White	19 (76%)
Black or African-American	6 (24%)
Ethnicity, *n* (%)	
Hispanic or Latino	2 (8%)
Not Hispanic or Latino	23 (92%)
Highest level of education, *n* (%)	
High school or equivalent	8 (32%)
Associate degree	3 (12%)
Bachelor's degree	11 (44%)
Graduate/post-graduate degree	3 (12%)
Time since diagnosis, years, Mean [range]	4.4 (3.5) [0.3–12.3]
Pain NRS score,[a] *n* (%)	
4	1 (4%)
5	3 (12%)
6	10 (40%)
7	5 (20%)
8	6 (24%)
Mean (SD) NRS score	6.5 (1.12)
BMI kg/m^2, Mean (SD) [range]	32.4 (8.9) [20.4–58.8]
< 27, *n* (%)	5 (20%)
27–30, *n* (%)	9 (36%)
31–40, *n* (%)	7 (28%)
≥ 40, *n* (%)	4 (16%)
Current treatment,[b,c] *n* (%)	
Non-steroidal anti-inflammatory drugs	15 (60%)
Prescription opioids	4 (16%)
Antidepressants	2 (8%)
Non-opioid analgesics	11 (44%)
Steroids	5 (20%)
Other	4 (16%)
No medication	0 (0%)
Comorbidities,[b] *n* (%)	
Anxiety	3 (12%)
Asthma	1 (4%)
Cancer	1 (4%)
Chronic obstructive pulmonary disease	1 (4%)
Diabetes (type 2)	3 (12%)
High blood pressure	8 (32%)
Kidney disease	1 (4%)
Liver disease	1 (4%)
Migraines	1 (4%)
Thyroid disease	2 (8%)

Abbreviations: BMI, body mass index; KOA, knee osteoarthritis; NRS, numerical rating score; SD, standard deviation.

[a] Provided at recruitment in response to the question: 'Over the past 7 days, how would you rate the usual level of your knee pain? Please select an answer from a scale of 0 to 10, where 0 is "no pain" and 10 is "worst possible pain"'.

[b] Not mutually exclusive, participants could select more than one category.

[c] Medications and co-morbidities were collected in the case report form and were tick boxes (open space for 'other medications' where patients could write information in).

3.2.3 | HRQoL Impacts of Pain

All 25 participants reported that their physical function had been negatively impacted by their KOA pain. Impacts on walking were described by most participants (*n* = 20/25). These included impacts on the patient's ability to walk quickly (*n* = 5/25), walk up inclines (*n* = 4/25), walk for long distances (*n* = 4/25), walk for long periods (*n* = 3/25), as well as limping (*n* = 3/25), and changes to their walking posture/gait (*n* = 2/25) (Table 5). Physical impacts were chosen by 11 participants as one of their top three most bothersome impacts. When asked, physical impacts mentioned included issues with walking, sitting in a chair, bending down, flexibility, and a general dislike about being more sedentary than they had been prior to their pain developing. When elaborating on why physical impacts were the most bothersome to them, participants cited their 'lack of endurance', not being able to do what they used to be able to do, and the frustration that their pain made them 'even more sedentary'.

Participants also reported negative emotional/psychological impacts of their KOA pain (*n* = 23/25) (Table 5). Emotional/psychological impacts included feeling depressed/sad (*n* = 14/25), feeling angry/frustrated/irritated (*n* = 12/25), having a negative view of self (*n* = 9/25), and feeling anxious/worried/fearful (*n* = 4/25). Emotional/psychological impacts were chosen by nine (36%) participants as one of their top three most bothersome impacts. Participants described how knowing they had KOA caused them to have feelings of worry for the present and the future.

Most participants reported that daily activities were negatively impacted (*n* = 18/25) including difficulty completing chores/errands (*n* = 13/25), difficulty travelling (*n* = 6/25), loss of independence (*n* = 4/25), difficulty with self-care/hygiene activities (*n* = 3/25), and difficulty getting dressed (*n* = 2/25).

KOA pain also negatively impacted participants' social and leisure time (*n* = 25/25) and relationships (*n* = 15/25) (Table 5).

TABLE 5 | Patient experience quotations.

Domain	Concept	Example quote
Symptom		
Experience of pain	Ache ($n = 10$, 40%)	'*So, it's, it's just a constant-constant. It's just a constant ache that's always there*'. *(Female, 52 years, BMI ≥ 40)*
	Sharp ($n = 8$, 32%)	'*Sometimes you get a sharp pain, you know, depending on, you know, what you're doing*'. *(Female, 50 years, BMI 31–40)*
	Severity (fluctuates) ($n = 19$, 76%)	'*I would say it, it varies from not, not bad to moderately bad and severe at times. It just varies. Overall, I guess you'd call it moderate, but it just varies so much from day-to-day. It can be anywhere from not bad to rather severe*'. *(Female, 57 years, BMI 27–30)*
	Frequency (every day) ($n = 17$, 68%)	'*Every day I'm, I'm in pain. Um, there's some level of pain every day*'. *(Male, 63 years, BMI 27–30)*
HRQoL impacts		
Physical function	Walking ($n = 20$, 80%)	'*I have some, like I say, problems with keeping up with some people, like I can't walk fast or run, or do any of that kind of stuff, because it's just too painful to do that*'. *(Male, 70 years, BMI 27–30)*
	Going up/down stairs ($n = 12$, 48%)	'*Stairs are just about out of the question, even just up on the kerb, just trying to get into my office*'. *(Female, 64 years, BMI ≥ 40)*
Emotional/ psychological	Sad/depressed ($n = 14$, 56%)	'*I've had to stop being able to do things with my family and my grandkids because I simply just can't get out the—in the condition that I'm in without hurting so much more that I just sit there and cry. Err, so arthritis definitely affects me*'. *(Female, 64 years, BMI ≥ 40)*
	Feeling angry/frustrated/irritated ($n = 12$, 48%)	'*Oh yeah. I-I'm very cranky, um, I snap easy, you know, um, I have a temperament that I didn't have before, because I'm angry that I don't feel good. I think that's the way to put it, I'm very angry that I'm not the way I used to be*'. *(Female, 60 years, BMI 27–30)*
	Having a negative view of self ($n = 9$, 36%)	'*There are times where I will decide not to go something because I am having a flare-up, or I feel l like the activities that my friends want to go do, I would be embarrassed in attempting to do them. Um, I think a lot of times, my decisions is not—that I would say 80% of the time, my decisions are made based on pain, and 20% of the time due to, um, feeling like an embarrassment, um, because I don't want people to see me struggle*'. *(Female, 44 years, BMI ≥ 40)*
	Feeling anxious/worried/fearful ($n = 4$, 16%)	'*I know it's only going to get worse, and I need to walk more, not walk less. And I am worried that, you know, in two or 3 years, I'll be barely walking a mile*'. *(Female, 62 years, BMI 31–40)*
Social and leisure time	Impaired ability/reduced levels of participation ($n = 17$, 68%)	'*I can swim up to half an hour and then, my leg gets tired. I used, I used to swim for up to an hour*'. *(Female, 65 years, BMI 31–40)*
	Unable to participate ($n = 17$, 68%)	'*Back when I was in my twenties and thirties, I used to dance six and 7 days a week. Well, I can't do that anymore. Um, can't dance at all*'. *(Female, 64 years, BMI ≥ 40)*
Relationships	Decreased quality time with loved ones ($n = 14$, 56%)	'*Friends and I would say, you know, not being able to do the things that I like to do with my sister go to, um, fairs and flea*

(Continues)

Domain	Concept	Example quote
		markets and do things that involve a lot of walking that we've always liked to do'. *(Female, 57 years, BMI 27–30)*
	Decreased relationship quality (n = 5, 20%).	'*All the relationships I have, like relationship with my family, relationship with my friends, relationship with, err, colleagues and co-workers, are also a little bit hampered*'. *(Male, 40 years, BMI 31–40)*
Sleep (n = 19, 76%)		'*I'm usually a very sound sleeper, but like I said, sometimes in the middle of the night, the pain will wake me up and then, I either have to—I sleep with a pillow between my knees. So, I either—I have to bend my left knee to a comfortable position on the pillow. That usually works, but if it doesn't, then I'll get up and I'll put on the topical cream*'. *(Female, 65 years, BMI 31–40)*
Daily activities (n = 18, 72%)		'*I just try to get through the, um, the day-to-day work, try to take care of my house. Um, I can't, err, scrub the floors and things like that, that I used to be able to do, um, so I have to get help*'. *(Female, 64 years, BMI ≥ 40)*
Work (n = 15, 60%)		'*I work in an office and, err, the pain's gotten so severe that I'm on a walker. So, therefore, like, I have my, um, my assistants at the office will come take my faxes, will come take, you know, my papers round to my bosses and stuff like that because I, literally I—every bit I walk, it makes it harder*'. *(Female, 64 years, BMI ≥ 40)*
Tiredness/fatigue (n = 7, 28%)		'*I used to go out and walk at 8 o'clock in the morning for an hour to 2 h before work. I, I always worked—I worked at home for many years, and I can't do that. Like, it's just—it'll be too tiring*'. *(Female, 62 years, BMI 31–40)*
Other key signs/ symptoms	Stiffness (n = 22, 88%)	'*That morning stiffness, you feel dry, like there is no greasing in the joint. There is, like—it-it-it's, it's just as if the joint was not meant to move in the first place*'. *(Male, 40 years, BMI 31–40)*
	Crepitus (n = 6, 24%)	'*when I get up in the morning, my, err, left knee talks to me, you know. Yeah, I mean, it, it cracks and it crackles*'. *(Male, 55 years, BMI 31–40)*
	Joint locking (n = 2, 8%)	'*Sometimes, it—err, the joint will lock, and I need to, like, just bend my knee a few times*'. *(Female, 44 years, BMI ≥ 40)*
Weight gain	Impact on pain (n = 9, 36%)	'*By not being as active, we tend to put on weight, obviously, and so, you know, I get yelled at for that by the Doctor, of course, and it's a vicious cycle. You know, you try to lose weight, but you can't because you can't be as active as you want to be, and so, you know, what do you do?*' *(Female, 50 years, BMI 31–40)*
	Impact on stiffness (n = 8, 32%)	'*I don't know, because again—maybe so, because it's not as stiff as it used to be, like, maybe a year ago. So, I would say so. I hadn't thought about that before*'. *(Female, 60 years, BMI ≥ 40)*

Abbreviations: HRQoL, health-related quality of life.

Participants reported negative impacts on their ability to participate in social and leisure time activities (such as social events, hobbies, and exercise) by having an impaired ability/ reduced levels of participation (n = 17/25), or being unable to participate (n = 17/25) because of their KOA pain. Participants reported negative impacts on their relationships because of their KOA pain, such as decreased quality time with loved ones (n = 14/25), and decreased relationship quality (n = 5/25). Social and leisure time impacts were chosen by 13 (52%) participants as one of their top three most bothersome impacts, and was the most frequently chosen domain. Participants felt that their social and leisure activities had been affected and subsequently changed their lifestyle. KOA pain also reduced the enjoyment of doing things with people.

KOA pain negatively impacted other HRQoL concepts. Participants ($n = 15/25$) reported negative impacts to their work, such as requiring reduced hours/time off or needing to take breaks at work ($n = 9/25$), difficulty completing work tasks ($n = 8/25$), and being unable to perform their role ($n = 2/25$). Participants reported that sleep was negatively impacted ($n = 19/25$), including difficulty staying asleep ($n = 11/25$), difficulty falling asleep ($n = 7/25$), poor sleep quality ($n = 5/25$), changing position during sleep (e.g. needing to 'flip-over' sides) ($n = 4/25$), and needing to nap during the day ($n = 1/25$). Some participants ($n = 7/25$) reported that their KOA pain made them feel fatigued and/or tired. Descriptions of fatigue and tiredness included both physical and mental experiences.

3.2.4 | Experience and Impacts of Other Signs/Symptoms

Participants reported experiencing stiffness ($n = 22/25$), crepitus ($n = 6/25$), swelling ($n = 3/25$), locking of their joint ($n = 2/25$), redness ($n = 2/25$), decreased range of motion ($n = 1/25$), numbness ($n = 1/25$), and instability in their joint ($n = 1/25$) as part of their KOA experience (Table 5). Participants described how stiffness negatively impacted physical functioning, such as walking and getting up from bed or sitting positions. Stiffness also impacted participants' work routines.

3.2.5 | Impact of Weight

Majority of participants ($n = 22/25$), across all BMI subgroups, stated that they believed there was a relationship between their weight and their experience of KOA pain. Participants indicated that their pain had resulted in an inability to exercise or not be as active as desired ($n = 10/25$). Participants reported gaining weight as a factor associated with their KOA pain ($n = 9/25$) (Table 5). Participants described the situation as a 'vicious cycle', as the inability to exercise had caused them to gain more weight. Participants with obesity/overweight noted that they thought their experience of pain had been impacted by their weight, indicating an awareness that increased body weight can cause pressure on joints, which impacted the pain they felt in their knee joints ($n = 12/25$). Three (12%) participants reported that their experience of pain severity increased with weight gain. Two participants also noticed that their pain severity reduced with weight loss ($n = 2/25$).

Participants also described relationships between their weight and other (non-pain) symptoms of KOA, including stiffness ($n = 8/25$; all BMI subgroups), crepitus ($n = 2/25$; BMI > 27 kg/m^2), joint locking ($n = 1/25$; BMI > 31 kg/m^2) and swelling ($n = 1/25$; BMI > 31 kg/m^2).

3.3 | Conceptual Model

A draft CM was developed based on the TLR. This draft model was then updated based on the interview data to present a full illustration of the lived experience of KOA pain based on the concepts extracted from the interviews. A conceptual saturation analysis was conducted. Most descriptions and impacts of pain were elicited spontaneously in the first two sets (4–5 patients per set) of interviews, and all were discussed in depth by a notable number of participants. Thus, analysts concluded that a full understanding of the patient experience of KOA pain was obtained and saturation was achieved.

The final CM summarises the KOA symptoms experienced and the subsequent impact on aspects of HRQoL. The model has four major domains: signs and symptoms, the experience of pain, HRQoL impacts, and weight gain (Figure 1). The majority of concepts and sub-concepts were elicited in both the TLR findings and the patient interviews. However, some concepts/sub-concepts were unique to each source, as summarised in Figure 1.

4 | Discussion

4.1 | Summary of Findings

This study explored participants' experiences of signs, symptoms, and HRQoL impacts of pain associated with KOA, as well as the impact of obesity/overweight through a TLR and patient interviews. To our knowledge, this is the first qualitative study to explore patients' experiences of KOA that includes discussion of the impact of body weight. To date, there is a lack of evidence of content validity for any PROMs for patients with KOA and obesity/overweight. The TLR identified studies describing the signs, symptoms, and impacts of KOA that influence patients' experience, while interviews were conducted to validate the most relevant and important concepts to patients with KOA pain, with a focus on patients' descriptions of pain associated with KOA, and how it impacts their daily lives. The TLR and interviews each identified unique and overlapping concepts; 15 concepts were unique to the participant interviews and six arose only in the literature (Figure 1). The resulting CM summarises key patient-reported outcomes that should be considered in studies of KOA.

All interview participants reported that they experienced pain due to KOA, as this was an inclusion criterion. Many participants reported experiencing pain every day, although, for the majority of these participants, the severity fluctuated and depended on their levels of activity and rest. This demonstrates the heterogeneity of participants' experiences while highlighting severity and frequency as important factors in KOA pain management. Participants identified that pain due to KOA impacted all aspects of HRQoL, including physical, emotional, social and leisure activities, daily activities, work, and sleep. These findings align with those from other studies which also found pain to be a key symptom of KOA (Carmona-Terés et al. 2017b; Murphy et al. 2015; Özkan et al. 2021) that impacts patients' HRQoL (Battista et al. 2022; Jackson et al. 2020). The most bothersome

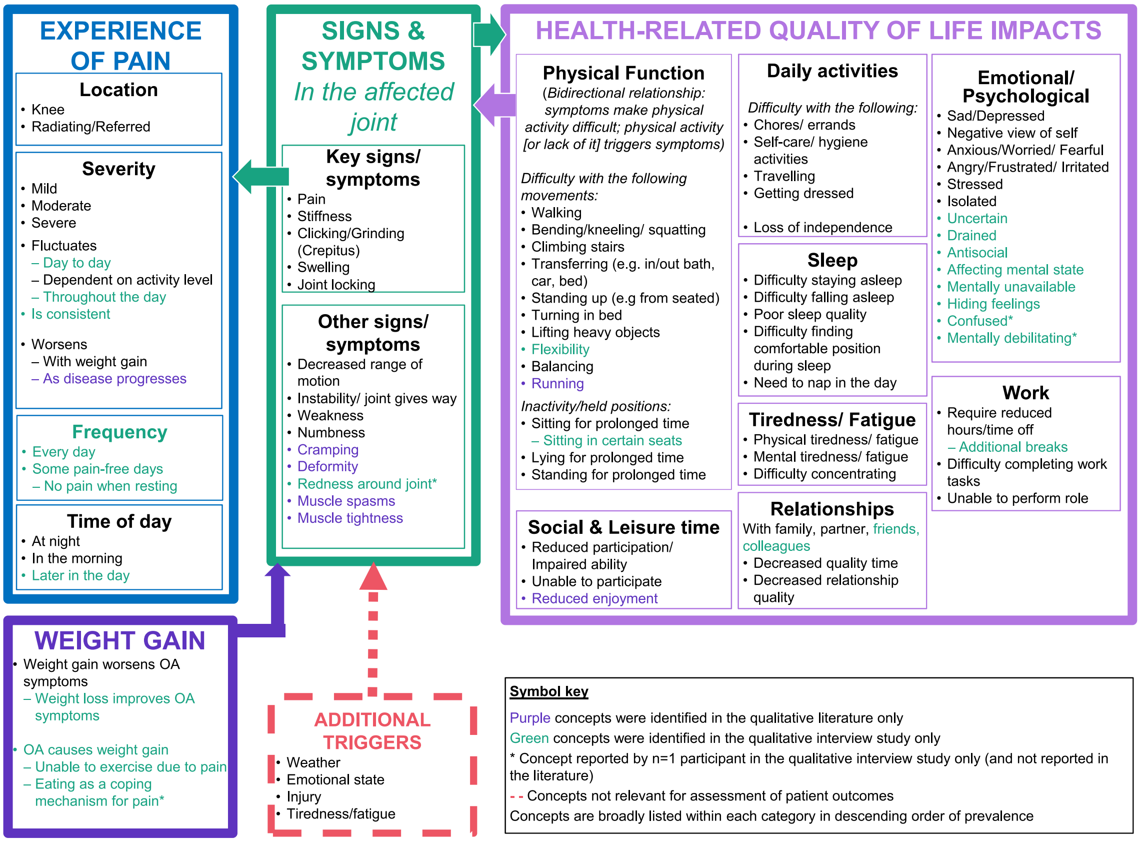

FIGURE 1 | CM of the patient experience of KOA. CM, conceptual model; KOA, knee osteoarthritis; OA, osteoarthritis.

HRQoL impacts reported by patients included physical function impacts, emotional/psychological impacts, and impacts on social and leisure time. As the most bothersome to patients, these concepts may be of greater relevance for measurement in clinical trials during the development of therapies for the management of KOA.

This study explored the impact of weight on pain in patients with KOA. Obesity/overweight is associated with higher KOA pain intensity (Raud et al. 2020) and weight gain is associated with worsening KOA pain (Solanki et al. 2023). The majority of participants in the interviews perceived their weight to be related to their experience of KOA pain. Participants reported a vicious cycle of pain and weight gain due to KOA; pain associated with KOA resulted in reduced levels of physical activity, which ultimately caused participants to gain weight and led to an inability to exercise, further exacerbating KOA pain. Participants with obesity/overweight reported that their KOA pain had been exacerbated by their weight, causing excess pressure on their joints.

This study highlights the substantial impact of living with KOA pain and the impact of obesity/overweight on the patient experience of living with KOA. Findings from the CM can be utilised to assess the content validity of PROMs and to develop clinical outcome assessment strategies for patients with KOA pain. This model may be used to assist management strategies of KOA and provide clinicians with greater insights into the HRQoL consequences of KOA pain.

4.2 | Study Strengths and Limitations

Conceptual saturation for the study was achieved, and the study harmonised information from the literature and patient interviews to describe the full experience of patients living with KOA.

Limitations of this study are acknowledged. The literature review was targeted; therefore, a number of eligible studies were not included for review and analysis, and others may have been inadvertently missed during study identification. All participants included in this study had self-reported KOA pain; therefore, our results may not be generalisable to all patients with KOA. Regarding the patient interviews, while the captured sample population was diverse, not all soft target quotas were met, and the sample lacked representation for some demographics (e.g., no Asian participants). Recruitment was limited to US participants only and our findings may not be generalisable to other countries; however, other settings were represented from the TLR findings.

5 | Conclusion

This study has provided an in-depth understanding of KOA pain and the negative impact it has on patients' HRQoL, including the impact of obesity/overweight. A CM was developed based on the qualitative data obtained via a TLR and patient interviews. The majority of participants were able to link their obesity/overweight to their KOA pain, and vice versa. Findings will provide supportive evidence for the selection of appropriate and content-valid PROMs for inclusion in future measurement strategies evaluating novel treatments for KOA pain, particularly in patients with overweight/obesity (e.g. the Western Ontario and McMaster Universities Arthritis Index [WOMAC] or Short-Form 36 [SF-36]). This study also suggests that, despite available medications, an unmet need exists for effective therapies to manage the wide-ranging and often debilitating symptoms of KOA, most notably pain, and mitigate their impact on patients' lives.

Author Contributions

The authors provided substantial contributions to the conception (C.K., E.S.) and design of the work (C.K., E.S., S.K., N.A., K.M), the acquisition, analysis, or interpretation of data for the work (all authors), and drafting the work and/or revising it critically for important intellectual content (all authors). All authors have approved the final version to be published. Each author participated sufficiently in the work to take public responsibility for appropriate portions of the content.

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Ethics Statement

The study protocol and associated documents were submitted for review to the Western Copernicus Group Institutional Review Board (WCG IRB) and received approval on 26 August 2023 (IRB Study Number: 1359396). Unique identifiers were used to anonymise interview participants. Interview transcripts were anonymised by removing any potentially identifiable information (e.g., names of people, places, etc.) from the transcript.

Conflicts of Interest

CK, ES, RR, KG, and JFB are employees and stockholders of Eli Lilly and Company. NVJA, HE, KM and SK are employees of Clarivate. NVJA, HE, and SK are stockholders of Clarivate.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.