Personalizing non-surgical care in patients with osteoarthritis of the hip or knee

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ISBN: 978-94-6299-918-3
Printing: Ridderprint BV | www.ridderprint.nl

The research presented in this thesis was conducted at the Netherlands Institute for Health Services Research (NIVEL), Utrecht, The Netherlands.

The printing of this thesis was financially supported by the Netherlands Institute for Health Services Research (NIVEL) and the Scientific College Physical Therapy (WCF) of the Royal Dutch Society for Physical Therapy (KNGF).

Personalizing non-surgical care in patients with osteoarthritis of the hip or knee

Gepersonaliseerde, niet-chirurgische zorg bij patiënten met artrose van de heup of knie (met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht op gezag van de rector magnificus, prof.dr. G.J. van der Zwaan, ingevolge het besluit van het college voor promoties in het openbaar te verdedigen op donderdag 24 mei 2018 des ochtends te 10.30 uur

door

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geboren op 13 mei 1985 te Wageningen

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Contents

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General introduction

Osteoarthritis is one of the most common musculoskeletal disorders in developed countries. Approximately 10-12% of the adult population have symptomatic OA[1]. OA can affect several joints, but the knee and the hip joints, are the most commonly affected joints in patients with OA[2]. In the Netherlands, the prevalence of hip/knee OA is estimated on 40.7/1000 males and 73.2/1000 females. Incidence rates for hip/knee OA are 4.0/1000 males and 6.5/1000 females[3]. These numbers are likely to be underestimated, since many patients do not seek help for their complaints. Nevertheless, the economic burden of OA is already high, representing 21.5% of the annual costs concerning musculoskeletal disorders and 1.2% of Dutch national health care costs[4]. Due to the aging population and current Western lifestyle patterns[5,6], the number of people living with hip or knee OA is anticipated to increase largely in the next decades[7]. In the Netherlands, an increase of almost 40% is expected over the period 2011-2030[4]. Considering patients with hip and knee OA are expected to live for prolonged periods with severe complaints due to OA[8], the burden of OA will become a major problem for our health care systems as well.

Pathogenesis of OA

Osteoarthritis is a heterogeneous pathology characterized by a complex and multifactorial nature[9]. Its' pathogenesis is still not completely understood. However, over the last years, it has become evident that OA is characterized by a failure of the entire synovial joint organ[2]. Besides progressive loss of articular cartilage, this failure could be expressed by muscle atrophy, ligament dysfunction, meniscal damage, osteophytes formation, changes in the subchondral bone (sclerosis) and a patchy chronic synovitis[2,10] (figure 1). Structural tissue changes in OA are only to a limited extent related to clinical characteristics presented by patients with OA[10,11].

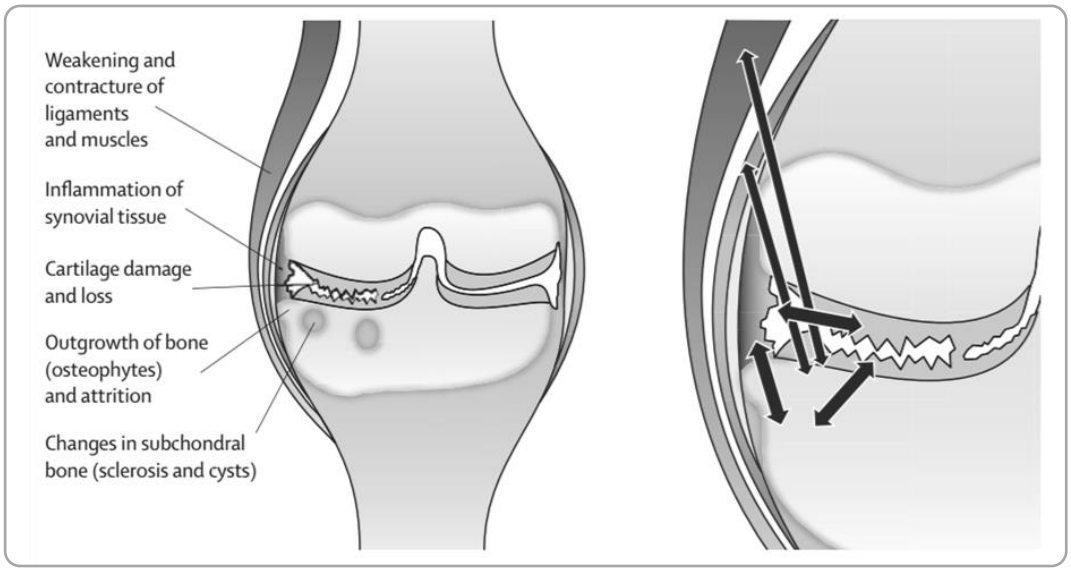

FIGURE 1. Schematic drawing of an osteoarthritic joint (from Bijlsma et al. (2011))[10], printed with permission)

Wide range of functional (dis)ability

As previously mentioned, hip/knee OA is a heterogeneous disease, resulting in varying disabilities in functioning. A patient's functioning could be systematically described by the International Classification of Functioning, Disability, and Health (ICF) (*www.who.int*). The ICF model distinguishes 'impairments in body functions', 'limitations in activities', and 'restrictions in participation' in relation to a medical disorder and influenced by personal and environmental factors. Figure 2 demonstrates the functioning of patients with hip/knee OA classified by the ICF.

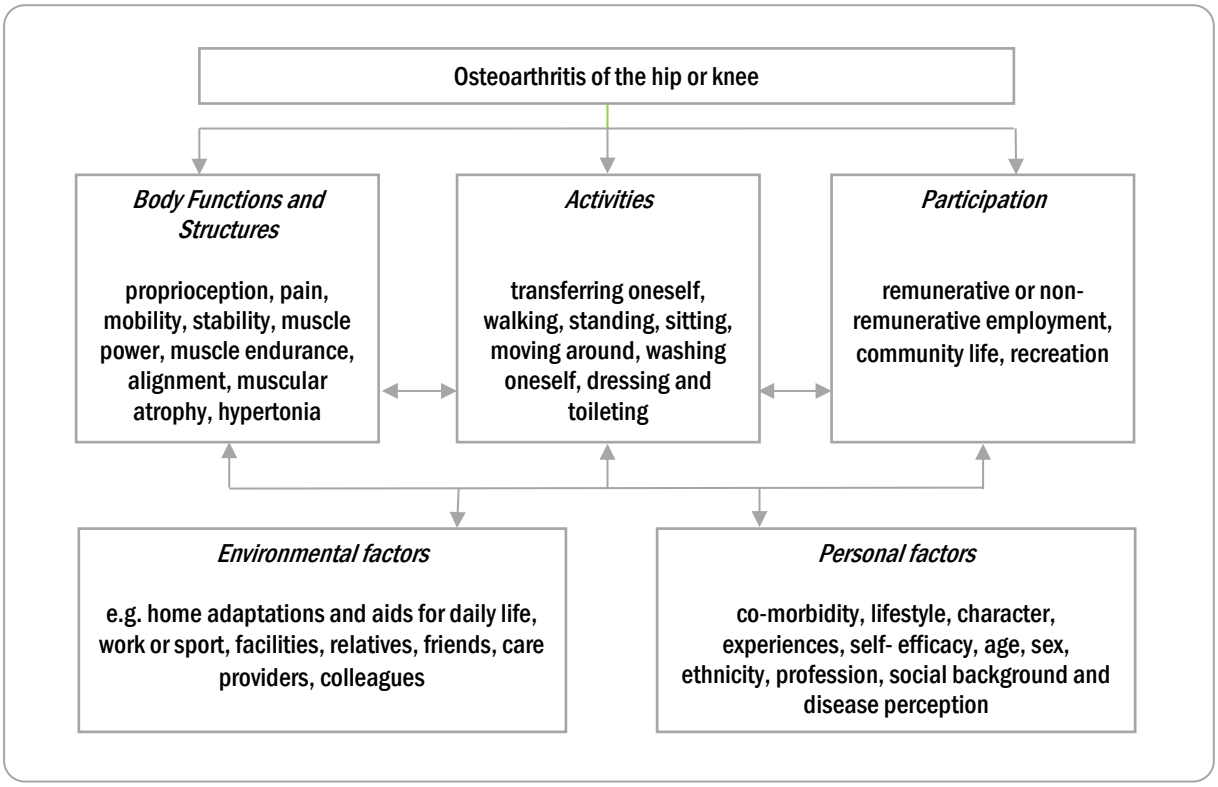

FIGURE 2. Functioning of patients with hip/knee osteoarthritis, classified by he International Classification of Functioning, Disabilities and Health (Peter et al. (2011))[14]

The major impairment in hip/knee OA is (chronic) pain, which typically emerges with weight-loading activities and diminishes with rest. In advanced OA, rest pain and night pain can also occur[12]. Other impairments are short-lasting inactivity-related joint stiffness, cracking of joints (crepitus), loss of joint mobility, muscle atrophy, joint inflammation, and joint instability[10,13]. These impairments are accompanied by limitations in daily functioning and restrictions in a patient's participation in daily life. Commonly mentioned limitations in activities are transferring oneself, moving around and dressing oneself. Potential restrictions in participation are, for instance, absence from work and inability to perform a sport. Contextual factors considerably predispose to the impact of impairments, limitations and restrictions on a patient's life[2]. Personal factors like self-efficacy and pain catastrophizing may attribute to

varying levels of physical disability. The same applies to environmental factors like social support and financial status.

Increasing demand for personalized management of OA

Personalized treatment is recognized as one of the solutions to face the complex and continuously expanding health care demand of patients with (multiple) chronic conditions[15]. Those populations often show high heterogeneity[16,17], high co-morbidity rates[17], low responses to commonly used interventions[16], and high risk of economic burden[16].
Due to its' heterogeneity, and the expected increasing burden of disease, OA would be particularly suitable for personalized treatment[2,7,10,16]. However, current clinical guidelines for treatment of hip/knee OA hardly present personalized recommendations. To date, clinical guidelines generally recommend clinicians to treat OA by pharmacological, non-pharmacological and surgical interventions to diminish impairments in body functions and reduce limitations in activities and restrictions in participation[18,20]. Little attention is paid, for instance, on differences in onset of OA, course of OA, and patient's priorities over time.

Therefore, in this thesis we will explore some opportunities to personalize a patient's treatment. Based on drivers for personalized treatment described by Karsdal et al.[16], we will consider two facets which potentially attribute to personalized treatment: timing of care and focus of care.

Timing of care

Current clinical guidelines provide a clear insight into effective non-pharmacological, pharmacological, and surgical treatment in hip/knee OA. Surgical treatment, by way of Total Joint Replacement (TJR), seems an effective and cost-effective final treatment option in end-stage hip/knee OA[21,22]. The absolute number of TJRs increases annually, up to the amount of 51.680 total hip replacements (+149% compared to 2005) and 57.893 total knee replacements (+297%) in the Netherlands in 2030[23]. Despite the increasing prevalence of OA[24], it has been stated that TJR is overutilized[25]. Appropriate timing of a TJR is important, since the lifespan of a prosthesis is limited, and patient outcomes after a revision are worse compared to a primary prosthesis[26,27]. For that reason, clinical guidelines recommend to start with (combinations of) non-surgical interventions and to reserve TJR for patients who do not respond sufficiently to non-surgical treatment options[28-31]. However, several studies have indicated that non-surgical interventions in patients with hip/knee OA are underutilized[26,28,32-34]. The question arises why surgical treatment in secondary care is relatively often preferred over non-surgical treatment in primary care.

First, the severity of clinical symptoms plays a role. Several research has shown that patients with more pain and more limitations in activities are more likely to receive a TJR[35-38]. The same applies to decreased knee-extension (in patients with knee OA)[37], more severe radiological deviations[39], and absence of comorbidities[38]. Moreover, a patient's willingness and lack of knowledge are associated with greater likelihood of undergoing TJR[38,40]. By way of illustration, in a study by Hofstede et al., almost 30% of the patients who are surgically treated agreed with the statement 'too much loss of cartilage to use non-surgical treatments',[40] despite the fact that cartilage damage is only to a limited extent related to surgical necessity[2,10]. It is remarkable that contextual factors, like a patient's financial status or a patient's psychosocial well-being are rarely involved in research regarding the determination of a patient's individual treatment over time. Besides patient-related factors, clinicians' or organizations' characteristics are currently seldom involved in determining factors associated with the timing and setting of care in patients with hip/knee OA. However, it is reasonable to assume that these characteristics influence a patient's journey in OA care as well. For example, Cottrell et al. showed that insufficient expertise was one of the most mentioned barriers by general practitioners (GPs) for using appropriate non-surgical treatment (e.g. exercise therapy) at the right time in patients with knee OA[41].

One way to facilitate the appropriate use of non-surgical care in patients with hip/knee OA is to phase non-surgical interventions over time. Phasing treatment is expected to reduce inappropriate use of advanced care[30,42]. The recently developed, multidisciplinary, patient-centered Stepped Care Strategy (SCS) phases non-surgical care in patients with hip/knee OA and facilitates clinicians to personalize a patient's treatment over time[43]. An important principle of the SCS is that patients exclusively receive modalities of the subsequent steps if all modalities of the previous steps have been offered. The SCS comprises three consecutive steps. Step 1 comprises optimizing a patients' self-care in primary care by education, lifestyle advices, and the prescription of acetaminophen. In case of persisting complaints after adequate application of all step-1 interventions, (topical) NSAIDs are added or a referral for allied health care (exercise therapy, dietary therapy) will be considered (step 2). Finally, step 3 comprises the application of TENS and intra-articular corticosteroid injections or a referral for interprofessional evaluation in secondary care (Figure 3)[43]. It has not been investigated yet which factors related to the patient respectively the clinician or practice influence the patient journey in OA care after implementation of the SCS. This insight could be helpful to determine the added value of the SCS regarding the timing of care in patients with hip/knee OA.

To date, the implementation of the SCS is limited to only one region in the Netherlands. The vast majority of clinicians in OA care are not facilitated in phasing their treatment over time. Insight into current practice in relation to the SCS will provide guidance for nationwide implementation of the SCS and, subsequently, timely treatment in individual patients with hip/knee OA.

FIGURE 3. Stepped Care Strategy 'Beating osteoARThritis' for non-surgical care in hip/knee osteoarthritis (Smink et al. (2011))[43], printed with permission

Focus of care

Due to the heterogeneity in patients with especially knee OA, it has been hypothesized that this population actually consists of different subgroups[44,45]. Recently, Knoop et al. and van der Esch et al. have succeeded in distinguishing five different phenotypes in patients with knee OA in two large cohorts of patients with knee OA[46,47]. The identified phenotypes are: 'minimal joint disease phenotype', 'strong muscle strength phenotype', 'severe radiographic OA phenotype', 'obese phenotype', and 'depressive mood phenotype'[46,47]. Each phenotype comprises one distinguishing feature (Figure 4). For example, patients fitting in the 'strong muscle phenotype' show high quadriceps muscle strength compared to the remaining phenotypes. It is conceivable that the strong muscle phenotype calls for a different focus of treatment than, for instance, the obese phenotype. Therefore, several authors have considered that the focus of treatment may need to be tailored to specific phenotypes of knee OA to improve treatment results[44-46,48]. The question arises to what extent clinicians, especially physical therapists, currently differentiate their focus of care between phenotypes of knee OA.

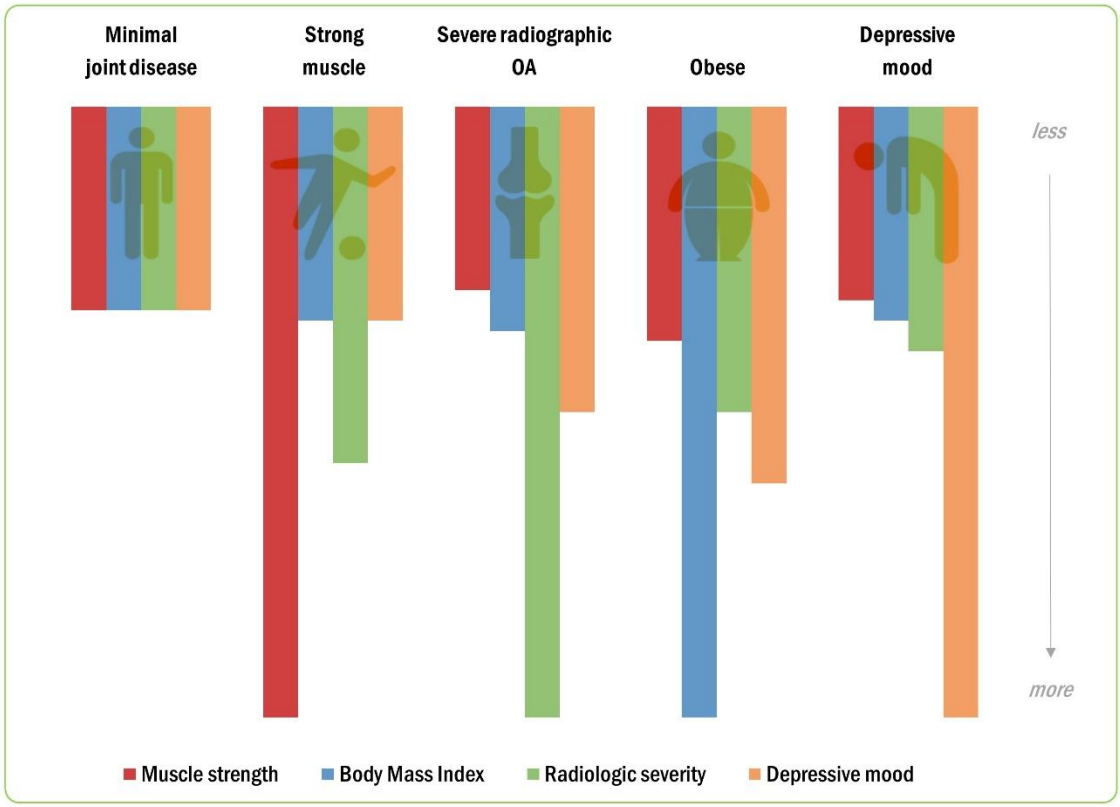

FIGURE 4. Differences in clinical characteristics of five phenotypes of knee osteoarthritis (based on Knoop (2011)[46] and van der Esch (2015) [47])

Measurement tools may facilitate clinicians to focus their treatment to subgroups or individuals with hip/knee OA. To enable diagnostic procedures and evaluation over time focused on the individual patient, patients' priorities should be taken into account[49]. To date, mainly generic and disease-specific tools are used in patients with hip/knee OA. These tools comprise fixed items, which allow comparisons across populations and settings[50]. However, outcomes of generic and disease-specific tools are often difficult to interpret at individual patient level since these tools do not consider patients' preferences and variability in performance on particular activities[49]. Therefore, the use of patient-specific tools has become more and more popular in clinical practice as patients are concerned with the content of the measurement tool[49,51]. An overview of patient-specific measurement tools which could be used in patients with hip/knee OA is still lacking. Furthermore, there is insufficient insight into the psychometric properties of commonly used patient-specific measurement tools like the Patient Specific Functional Scale and, especially used in patients with hip/knee OA, the McMaster Toronto Arthritis Patient Preference Questionnaire (MACTAR)[52]. Providing an overview of commonly used patient-specific measurement tools, including a psychometric evaluation, may facilitate clinicians to focus care to the individual patient with hip/knee OA.

Scope of this thesis

Personalized treatment could be one of the solutions to face the complex and continuously expanding health care demand of patients with chronic conditions like hip/knee OA. To date, personalized treatment is in its' infancy. In this thesis we will explore two drivers which potentially attribute to personalized treatment in hip/knee OA: timing of care and focus of care.

Part I: Timing of care

The first part of this thesis focuses on current timing of non-surgical care in patients with hip/knee OA in Dutch general practice and physical therapy practice. Based on routinely registered data in NIVEL Primary Care Database, we will get insight into current treatment of GPs and physical therapists and to what extent this treatment is in accordance with the Stepped Care Strategy *(Chapter 2)*. The subsequent study focuses on the patient journey in hip/knee OA and provides insight into factors associated with the setting of care (primary care, secondary care) in which patients are treated *(Chapter 3)*. Next to individual determinants, characteristics of their GPs and general practices are involved in the determination of a patients' journey over time.

Research questions are:

- What is the content of current GP care in patients with hip/knee OA, including the compliance to the Stepped Care Strategy?
- To what extent differs the content of physical therapy practice in GP-referred patients compared to self-referred patients with hip/knee OA?
- Which individual factors, GP-related factors and general practice related factors are associated with 1) treatment in primary care, 2) continuation of non-surgical care after a referral, and (3) surgical treatment in patients visiting their GP due to hip/knee OA?

Part II: Focus of care

The topic of the second part of this thesis is the focus of care in patients with hip/knee OA. In *Chapter 4*, clinical vignettes are used to determine to what extent physical therapists tailor their treatment to different phenotypes of knee OA. In *Chapter 5 and 6*, personalized measurement of functioning in hip/knee OA is the central issue. A systematic review is performed to provide a comprehensive overview of measurement properties of patient-specific tools measuring physical function *(Chapter 5)*. *Chapter 6* shows de results of the validation of the Dutch McMaster Toronto Arthritis Patient Preference Questionnaire

(MACTAR). The MACTAR is a patient-specific tool, which could be used in patients with hip/knee OA.

Research questions are:

- To what extent is physical therapists' treatment tailored to the 'minimal joint disease' phenotype, the 'strong muscle strength' phenotype, the 'severe radiographic OA' phenotype, the 'obese' phenotype, and the 'depressive mood' phenotype in patients with knee OA?
- Which patient-specific self-assessment instruments are available to measure physical function in patients with musculoskeletal disorders?
- What are the descriptive properties as well as the psychometric qualities of patient-specific instruments measuring physical function in patients with musculoskeletal disorders?
- What is the content validity, the construct validity and the responsiveness of the Dutch McMaster Toronto Arthritis Patient Preference Questionnaire in patients with OA of the hip or knee?

Chapter 7 provides an overall discussion of the findings of this thesis, including recommendations for clinical practice, policy and future research. Lastly, this thesis will be summarized in English and in Dutch.

The outline of the thesis is graphically presented in Figure 5.

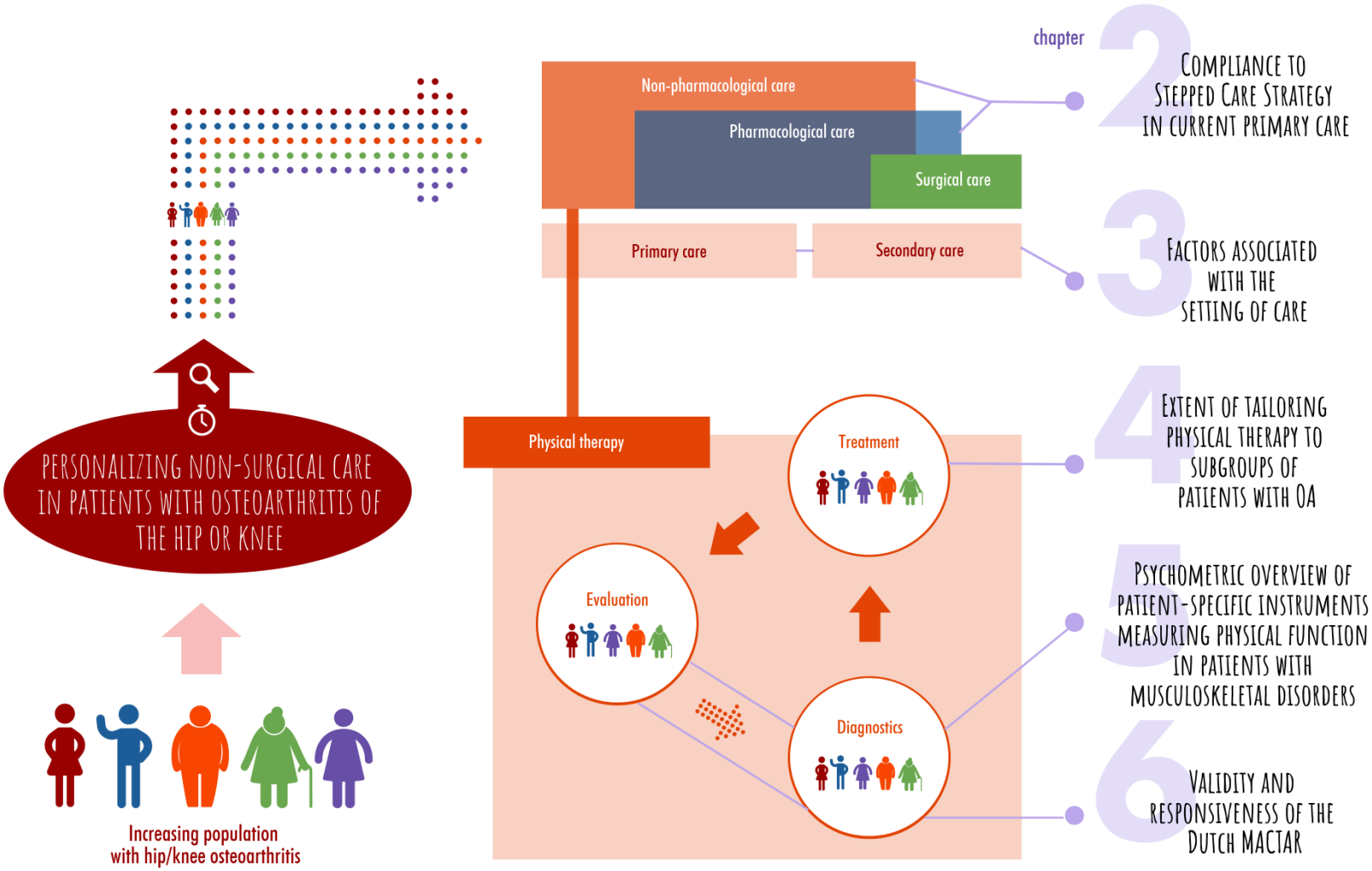

FIGURE 5. Outline thesis 'Personalizing non-surgical care in patients in osteoarthritis of the hip or knee

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2

Treatment of hip/knee osteoarthritis in Dutch general practice and physical therapy practice: an observational study

Published in BMC Fam Pract. 2015 Jun 27;16:75

https://doi.org/10.1186/s12875-015-0295-9

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Abstract

Background A multidisciplinary, guideline-based Stepped-Care-Strategy (SCS), has recently been developed to improve the management of hip and knee osteoarthritis (OA). To date, it is unknown to what extent current Dutch OA care is consistent with the SCS, both with respect to the content of care as well as the sequence of care. Furthermore, there is a lack of clarity regarding the role of different health care providers in the performance of OA care according to the SCS. Therefore, the main purpose of this study is to describe the content of primary care in patients with hip/knee OA, including the compliance to the SCS and taking into account the introduction of patient self-referral to physical therapy.

Methods Data were used from NIVEL Primary Care Database. In total, 12.118 patients with hip/knee OA who visited their GP or physical therapist were selected. Descriptive statistics were used to compare the content of care in GP-referred and self-referred patients to physical therapy.

Results Content of care performed by GPs mostly concerned consultations, followed by NSAID prescriptions and referrals to secondary care. Both prescriptions of acetaminophen and referrals to physical therapy respectively dietary therapy were rarely mentioned. Nevertheless, still 65% of the patients in physical therapy practice were referred by their GP. Compared to GP-referred patients, self-referred patients more often presented recurrent complaints and were treated less often by activity-related exercise therapy. Education was rarely registered as singular intervention, neither in GP-referred nor in self-referred patients.

Conclusion In accordance with the SCS, less advanced interventions are more often applied than more advanced interventions. To optimize the adherence to the SCS, GPs could reconsider the frequent use of NSAIDs instead of analgesics and the low referral rate to allied health care. Self-referral to physical therapy partially distorts both the low referral rate in general practice and the low application rate of education as singular intervention in physical therapy practice. Further research is recommended to evaluate the effects of task-shifting in OA care, taking into account the content of the SCS.

Background

Osteoarthritis (OA) is one of the most common disorders of the musculoskeletal system[1]. As a consequence of the aging process, a large increase of the OA population is expected over the next decades[2]. Considering OA as the major cause of musculoskeletal pain and disability in the elderly, a large increase of demand for care could be expected as well[3]. To cope with this demand, it is important to manage OA in an effective and efficient way. Over the last decades, more than 50 modalities of non-pharmacological, pharmacological and surgical interventions for hip and knee OA have been described in medical literature and integrated in (inter)national, monodisciplinary and interdisciplinary clinical guidelines[3-5]. Recently, Smink et al. developed a multidisciplinary, guideline-based Stepped-Care-Strategy (SCS), known as BART, i.e. Beating Osteoarthritis, to improve the management of hip and knee OA[6]. In addition to current clinical guidelines that recommend appropriate non-surgical treatment modalities, the SCS focuses on the optimal order in which to employ them. It recommends offering all modalities in the previous steps before turning to more advanced modalities in the subsequent steps. According to the SCS, treatment of hip/knee OA starts in primary care with stimulating patients' self-care by emphasizing the usefulness of an adequate dose of acetaminophen and by educating patients about OA and their lifestyle (step 1). Additionally, the use of glucosaminesulphate could be considered for a trial period of three months. In case of persisting complaints, which is identified during an evaluation visit at the general practitioner (GP), (topical) non-steriodal anti-inflammatory drugs (NSAIDs) or tramadol are applied, supplemented by prescribing exercise therapy and, in case of overweight, dietary therapy to diminish the impairments and limitations due to OA (step 2). A referral to secondary care, TENS and intra-articular corticosteroid injections could be applied as final non-surgical interventions (step 3).

To date, it is unknown to what extent current Dutch OA care is consistent with the SCS, both with respect to the content of care as well as the sequence of care. Furthermore, there is a lack of clarity regarding the role of different health care providers in the performance of OA care according to the SCS. The SCS describes several interventions, but do not apportion these interventions to a specific discipline. It stands to reason that step-1 interventions mostly are performed by a GP. In case of unsatisfactory results, the GP refers patients to allied health care providers (step-2) or to an orthopaedic surgeon (step-3). However, the introduction of patient self-referral for physical therapy in 2006[7], possibly has interrupted this natural sequence of care. It is expected that an increasing number of patients will leave out their GP and directly approach a physical therapist in case of experiencing musculoskeletal complaints[8]. In consequence, the question arises to what extent patients using self-referral for physical therapy still receive interventions described in step-1 of the SCS.

Therefore, the two main objectives of the present study are:
1. To describe the content of current GP care in patients with hip/knee OA, including the compliance to the SCS.
2. To describe the content of care in physical therapy practice in GP-referred versus self-referred patients.

Methods

Registration network

'NIVEL Primary Care Database' (NPCD) was used to achieve the research objectives[9]. This database contains data of several, separated primary care health care providers, including GPs and physical therapists (box 1). Participating GPs continuously record data on all patient contacts, including diagnoses, interventions, prescriptions and referrals[10]. GP-data are collected since 1992. For this study, data were used from 84 practices participating in NPCD. These practices provide a representative sample regarding gender and age in comparison with Dutch National Statistics. Participating physical therapists collect longitudinal data on patient characteristics, referrals, diagnoses, interventions and evaluations[11]. This part of the NPCD was constructed in 2001 and contains data of about 100 physical therapists, divided over 35 outpatient practices. The geographical distribution and the degree of urbanisation of the participating practices are in line with all Dutch physical therapy practices. In contrast to the representativeness of participating practices, participating physical therapists are more often male and are older compared to non-participating Dutch physical therapists.

BOX 1. NIVEL Primary Care Database

NIVEL Primary Care Database (*In Dutch: NIVEL Zorgregistraties eerste lijn*) uses routinely recorded data from health care providers to monitor health and utilisation of health services in a representative sample of the Dutch population. It includes data on health problems and treatment. The aim of NIVEL Primary Care Database is to monitor developments in health and the use of primary health services in the Netherlands.

Participants of NIVEL Primary Care Database are:
General practitioners, physical therapists, exercise therapists, dieticians, primary care psychologists, GP out-of-hours services, health centres.
Gathered data are combined and supplemented with data of pharmaceutical care and secondary care collected by other organisations.

Privacy
NIVEL handles the data in accordance with the Dutch Data Protection Act. Researchers have no access to identifiable patient information, such as name, address or citizen service number. Research results cannot be traced back to individual persons, health care providers or health care organisations. Participating health care providers may withdraw from NIVEL Primary Care Database at any time, and without stating reasons.

Governance
Steering committees with representatives from national associations of health care providers decide about the use of the data.

Participants

During 2006 to 2011, all patients with OA of the hip and/or knee who visited their GP and/or a physical therapist were selected from the NPCD. Hip/knee OA was operationalized by the 'International Classification of Primary Care' (ICPC)[12] codes L89 (hip OA) or L90 (knee OA). In physical therapy practice, in case of lacking ICPC codes, patients with hip/knee OA were identified by national diagnosis codes for allied health care, which are mandated by insurers.

Medical record data

General practice – In general practice, first, patient characteristics (gender, age, location of OA (hip/knee/both hip and knee)) were collected. Second, GPs' interventions were gathered, including (telephone) consults, home visits, prescriptions, and referrals. Prescriptions were registered according to the Anatomical Therapeutic Chemical (ATC) classification system[13]. With respect to the referrals, only referrals to physical therapists, dieticians, and orthopaedic surgeons were collected since these health care providers take part in the SCS.

Physical therapy – As in general practice, gender, age, and the location of OA of the participants were collected. Per treatment episode due to hip/knee OA, the applied interventions (information & advise/manual techniques/physical agent modalities/exercise therapy) and the amount of care (duration and number of sessions) were collected. Furthermore, to evaluate the effectiveness of the physical therapy episode, it was examined to what extent the formulated treatment goals were achieved (<25% / 25-50% / 50-75% / >75%) at the end of a treatment episode. Finally, the recurrence rate (recurrent complaint yes/no) and the type of access (referred by GP/referred by medical specialist/direct access) were gathered.

Data analyses

Descriptive statistics were used to describe demographics of the OA population. The content of current care in general practice was described by considering the use of non-surgical treatment modalities proposed by the SCS. Operationalization of these treatment modalities in the NPCD was illustrated in Table 1. Due to the nature of the NPCD, several translations were necessary to enable interpretation of current registered OA care in terms of the SCS. Firstly, since education and lifestyle advises both were not registered in the NPCD, it was assumed that GPs educated their patients when 'consults' or 'visits' were registered in the medical record. Research by Noordman et al. showed that patients' lifestyle is increasingly discussed during consultations in general practice, especially when it is relevant to patients' complaints[14]. Secondly, in the NPCD, prescriptions and referrals were not necessarily directly linked to a specific diagnosis but to treatment episodes in which prescriptions or referrals were performed. Therefore, in case of prescriptions, we first selected the four most common drugs (4-digit ATC) which were applied especially to a diagnosis of hip/knee OA and subsequently counted the application of these prescriptions (NSAIDs, opioids, other analgesics and corticosteroids) in treatment episodes due to hip/knee OA. When appropriate, secondary

analyses were performed to analyse the application of these prescriptions in more detail (7-digit ATC). Analyses of referrals occurred similarly; referrals to exercise therapy, dietary therapy and orthopaedic surgeons were selected.

To determine the compliance of current GP care to the SCS, we assessed the proportion of patients who had been offered at least one treatment modality of step 1, respectively one or more treatment modalities of step-1 in addition to the application of a step-2 intervention, and the proportion of patients who used a step-1 and/or step-2 intervention in addition to a step-3 intervention.

To compare the content of care of self-referred patients and GP-referred patients visiting a physical therapist, two sample t-tests and chi-square tests were used, when appropriate. P-values of <.05 were considered statistically significant.

All statistical analyses were performed using Stata 12 (StataCorp LP, College Station, TX, USA) software.

TABLE 1. Operationalization content of current care in general practice in patients with hip/knee osteoarthritis

	Treatment modality	Positively assessed if NPCD contains:
Step 1 SCS	Education or lifestyle advise	≥1 consult or visit at the GP due to hip/knee OA
	Prescription of acetaminophen	≥1 prescription of other analgesics and antipyretics*
	Prescription of glucosaminesulphate	Not separately assessed but included in anti-inflammatory and anti-rheumatic products, non-steroids **
Step 2 SCS	Prescription of (topical) NSAIDs	≥1 prescription anti-inflammatory and anti-rheumatic products, non-steroids **
	Prescription of tramadol	≥1 prescription of opioids †
	Referral for exercise therapy	≥1 referral to physical therapy due to hip/knee OA
	Referral for dietary therapy	≥1 referral to dietary therapy due to hip/knee OA
Step 3 SCS	Referral to secondary care	≥1 referral to an orthopaedic surgeon due to hip/knee OA
	TENS	Not assessed
	Prescription intra-articular injections	≥1 Cyriax injection due to hip/knee OA
Remaining interventions	Prescription oral corticosteroid	≥1 prescription of corticosteroids for systemic use ‡ (without the application of a Cyriax injection)

Abbreviations: NPCD = NIVEL Primary Care Database, OA = osteoarthritis, SCS = Stepped-care strategy[6], NSAID = non-steroidal anti-inflammatory drug *Anatomical Therapeutic Chemical ((ATC) code N02B[13]; ** ATC code M01A ; † ATC code N02A ; ‡ ATC code H02A

Results

Patient characteristics

In total, 12118 patients with hip/knee OA were included from the NCPD; 11248 patients were extracted from general practice data and 870 patients were identified from physical therapy data. The majority of patients with hip/knee OA is female and suffers from knee OA. More patient characteristics are presented in Table 2.

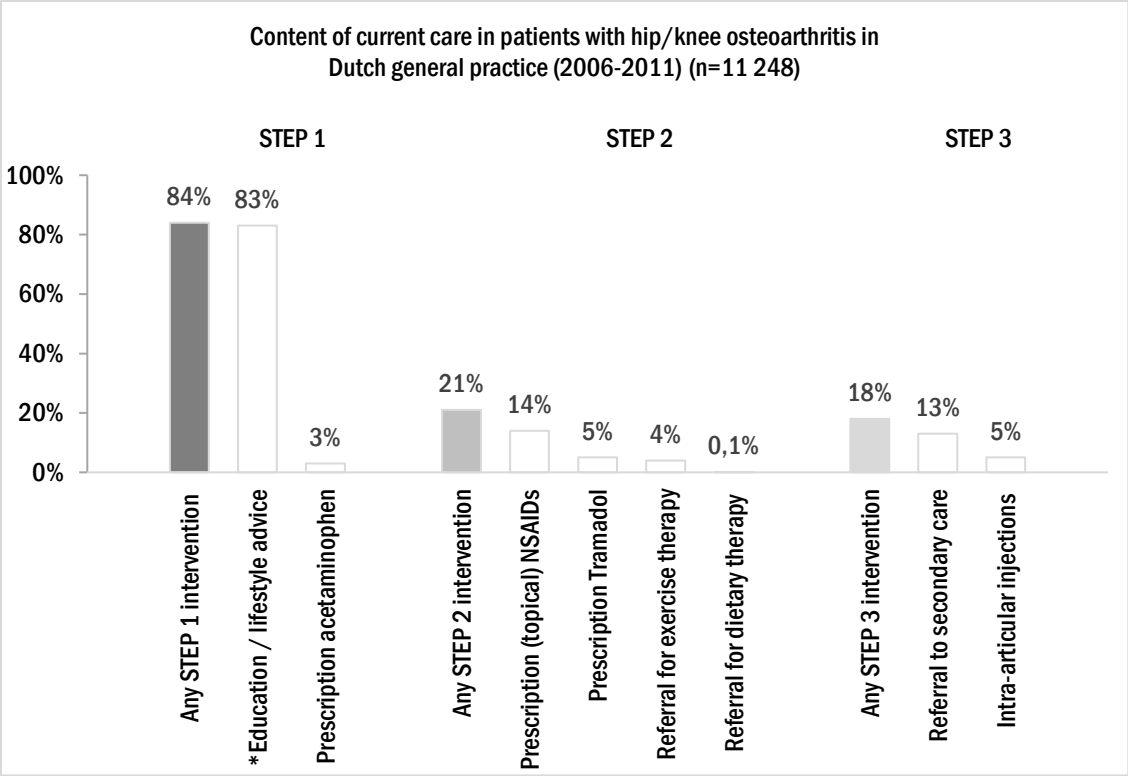
TABLE 2. Characteristics of patients with hip/knee osteoarthritis in general practice and physical therapy practice (2006-2011)

	General practice (n=11248)		Physical therapy practice (n=870)	
Gender, female (n (%))	7552	(67)	581	(67)
Age, years (mean ± sd)	68.7 ± 12.4		66.7 ± 13.2	
Location of OA (n (%))				
Hip	4437	(39)	293	(34)
Knee	6462	(57)	577	(66)
Combination of hip and knee OA	349	(3)	Not applicable	

Abbreviations: OA= osteoarthritis, sd = standard deviation

Content of GP care

Figure 1 summarizes the content of current care in general practice, considering the different steps of the SCS. In total, 84% of the population was treated by at least one of the step-1 modalities, 21% was treated by any step-2 modality, and 18% received any step-3 intervention. Three percent of the patients received analgesics. NSAIDs were more frequently prescribed: more than two out of three patients treated by a step-2 intervention received NSAIDs. In 40% of the cases, the prescription of NSAIDs concerned Diclofenac or Diclophenac combinations. Ibuprofen, Meloxicam and Naproxen were prescribed in respectively 12%, 12% and 11% of the cases. In terms of numbers, referrals to orthopaedic surgeons were more often registered in the medical records than referrals to physical therapists (exercise therapy) and dieticians.



* Since education and lifestyle advises both were not registered in the NIVEL Primary Care Database, it was assumed that GPs educated their patients when 'consults' or 'visits' were registered in the medical record[14].

FIGURE 1. Content of current care in patients with hip/knee osteoarthritis in Dutch general practice (n=11248)

The extent to which GPs currently act in agreement with the SCS is shown in Table 3. It shows that 85% of the population who was treated by a step-2 modality also received any step-1 intervention. Seven percent exclusively received acetaminophen and six percent of the patients treated by a step-2 modality additionally received both step-1 interventions. Furthermore, in addition to the application of a step-3 intervention, 90% was treated by a step-1 modality as well. Twenty-seven percent of the step-3 population additionally received any step-2 intervention, mostly by NSAIDs (18%) and/or tramadol (7%). Two percent received both a prescription of NSAIDs or Tramadol and was referred to an allied health care provider. None of the patients receiving a step-3 intervention was offered all modalities described in step 1 and 2 (Table 3).

TABLE 3. Compliance to the Stepped-Care-Strategy in patients with hip/knee OA in Dutch general practice (n=11 248)

		n	(%)
Step 1:	Number of patients who received ≥1 of the advised step-1 modalities	9396	(84)
	Education or lifestyle advise*	9332	(99)
	Prescription of acetaminophen []H	342	(4)
	Both modalities	278	(3)
Step 2:	Number of patients who received ≥1 of the advised step-2 modalities	2311	(21)
Prior application of step-1 modalities:	Any step 1 modality	1961	(85)
	1. Education or lifestyle advise*	1947	(85)
	2. Prescription of acetaminophen	153	(7)
	Both education (1.) & prescription (2.)	139	(6)
Step 3:	Number of patients who received ≥1 of the advised step-3 modalities	1988	(18)
Prior application of step-1 modalities:	Any step 1 modality	1794	(90)
	1. Education or lifestyle advise*	1791	(90)
	2. Prescription of acetaminophen	68	(3)
	Both education (1.) & prescription (2.)	65	(3)
Prior application of step-2 modalities:	Any step 2 modality	534	(27)
	3. Prescription of (topical) NSAID	365	(18)
	4. Prescription of tramadol	132	(7)
	5. Referral for physical therapy	143	(7)
	6. Referral for dietary therapy	5	(<1)
	Both prescription (3. or 4.) & referral (5. or 6.)	45	(2)
Prior application of step-1&2 modalities:	Both education (1.) & prescription (2. & (3. or 4.)) & referral (5. or 6.)	0	(0)

Abbreviations: OA = osteoarthritis, n=Number, NSAIDs=Non-Steroidal Anti-Inflammatory Drug

* Since education and lifestyle advises both were not registered in the NIVEL Primary Care Database, it was assumed that GPs educated their patients when 'consults' or 'visits' were registered in the medical record[14].

Content of physical therapy

Almost two out of three of the patients suffering from hip/knee OA were referred by a GP (65%), 15% were referred by a medical specialist, and 20% of the patients with hip/knee OA visited a physical therapist on their own initiative. In a very small minority of patients (n=10), physical therapists exclusively provided their patients information and advises. Due to this low number of patients, an extending evaluation of the implementation of (one element of) step-1 of the SCS in physical therapy practice was hindered. Although education rarely was applied as singular intervention, in 36% of the GP-referred population and 37% of the self-referred population, 'information & advise' was represented as a part of physical therapists' treatment (p=.80) (Table 4).

One difference between GP-referred and self-referred patients concerned the recurrence rate. Self-referred patients more often presented a recurrent complaint in comparison to GP-referred patients (p<.01). A trend was indicated with respect to less treatment sessions in the self-referred population compared to the GP-referred population. In both groups, exercise therapy was the most applied intervention, followed by manual techniques, and information & advise (Table 4). The focus of exercise therapy was not equal in both groups; although exercise therapy focussed on improving impairments of body functions was applied similarly in GP-referred and self-referred patients, GP-referred patients more often received exercise therapy focussed on improving limitations in activities compared to self-referred patients (p<.01).

TABLE 4. Treatment characteristics in patients with hip/knee osteoarthritis in Dutch physical therapy practice (n=870)

	Total population (n=870)		Referred by GP (n=523)		Self-referred (n=160)		p-value
Disease characteristics							
Recurrent complaint, yes (n (%)) [a]	297	(37)	171	(35)	70	(46)	.01
Used interventions in ≥50% of the treatment sessions (n (%)) [b] *							
Information & advice	237	(37)	152	(36)	45	(37)	.80
Manual techniques	301	(47)	201	(58)	62	(51)	.47
Physical agent modalities	45	(7)	30	(7)	7	(6)	.61
Exercise therapy – functions	456	(72)	301	(71)	86	(71)	.99
Exercise therapy – activities	225	(35)	164	(39)	31	(26)	<.01
Amount of care [c]							
Number of treatment sessions (mean ± sd)	10.0 ± 12.3		10.9 ± 13.5		8.6 ± 11.7		.07
Duration of treatment, weeks (mean ± sd)	9.1 ± 13.4		9.6 ± 12.8		9.0 ± 15.8		.69
Result* [d]							
Treatment goals, ≥75% reached (n (%))	240	(71)	152	(72)	44	(70)	.78

Abbreviations: GP = general practitioner, sd = standard deviation

* Exclusively reported in finished treatment episodes (n=788); Number of missing values in total population: [a]9%, [b]20%, [c]15%, [d]57%

Discussion

In this study, we described the content of care registered in electronic records of 12.118 patients with hip/knee OA visiting their GP and/or physical therapist during 2006 to 2011, including the compliance to the SCS.

A remarkable result of our study comprised a lower prescription rate of pain medication (NSAIDs and acetaminophen) in patients with hip/knee OA in comparison to previous studies[15, *Belo J, Berger M, Koes B, Bierma Zeinstra SM (unpublished work*]. The lower use of acetaminophen and NSAIDs might be explained by the increasing availability of those (low-dosed) drugs over the counter. As a consequence, the total use of NSAIDs and analgesics in the OA population is probably underestimated in this study.

In line with the SCS, in Dutch general practice less advanced treatment modalities are generally more often applied than more advanced treatment modalities. However, only a small minority of patients is treated by a combination of different interventions belonging to one step before turning to the next step, within the time frame of our study. Most deviations from the SCS concern GPs' prescriptions and their referral policy. With respect to GPs' prescribed pain medication, our results show that NSAIDs (especially Diclophenac (combinations), Ibuprofen, Meloxicam and Naproxen) and tramadol (step-2 interventions) are more often prescribed than analgesics (step-1 intervention). This prescription behaviour has previously been indicated in an observational study by Cardol et al.[15]. Moreover, a more recent study investigating GPs' attitudes regarding SCS recommendations, showed that 21% of the GPs (strongly) agree with

the statement 'NSAIDs should be the first choice of pain medication in patients with OA'[16]. Given the recognized increased risk of several adverse outcomes in older adults due to the frequent use of NSAIDs and to improve guideline adherence, GPs could be advised to optimize the analgesics policy prior to consider NSAIDs prescription in patients with hip/knee OA[17]. Besides the prescription policy, deviations from the SCS are found regarding GPs' referrals as well. In the NPCD, GPs registered fewer referrals to allied health care providers (exercise therapy, dietary therapy (step-2) than to orthopaedic surgeons (step-3). Partially, this could be explained by the moderate quality of the referral-registration in the medical records and the introduction of patient self-referral for allied health care. However, previous work, which has been published prior to the introduction of direct access of allied health care, also showed a lower referral rate for physical therapy compared to orthopaedic surgery[15]. Therefore, the question arises whether GPs could improve care by first ensuring optimal non-surgical care in primary care setting has been delivered, before referring to secondary care[18]. Fortunately, recent (unpublished) research in a population in which the SCS has been implemented showed that patients who are referred to secondary care are significantly more extensively treated by non-surgical interventions in primary care compared to patients who were not referred to secondary care *(Barten JA, Smink AJ, Swinkels ICS, et al.)*

The introduction of direct access to allied health care for example aimed to achieve a rearrangement of health care organization. Translated to OA care, it could have been expected that non-pharmacological step-1 interventions had been integrated in physical therapists' treatment in case of patient self-referral. However, we did not indicate a difference with respect to the application of 'information and advice' between GP-referred and self-referred patients in physical therapy practice. Besides, only a handful of patients exclusively received education. The rearrangement of care, hence, seems to be in its infancy. It should be remarked that almost half of the patients using self-referral presented recurrent complaints (46%). These patients might have been treated by a step-1 intervention by a physical therapist or their GP, prior to the timeframe of this study. Further research is recommended to able an evaluation of the effects of task-shifting in OA-care.

As already mentioned, self-referred patients with hip/knee OA often present recurrent complaints in physical therapy practice. In accordance with studies in the general population and in patients with low back pain, the recurrence rate in self-referred patients significantly exceeds the recurrence rate in GP-referred patients[19,20]. Patients with recurrent complaints might be more aware of direct accessibility and, therefore, are more likely to omit their GP in case of recognizable musculoskeletal complaints. This rationale is confirmed by research of Leemrijse et al.[19], indicating that the use of direct access was significantly higher in patients who received earlier treatment by a physical therapist.

Another difference between self-referred and GP-referred patients concerned the less frequent application of activities-related exercise therapy in self-referred patients. Commonly, treatment starts with improving impairments of body functions and gradually shifts to diminishing limitations in activities of daily life. At the same time, the role of the physical therapist changes from 'hands-on therapist' to 'coach' and the frequency of treatment sessions

decreases. Possibly, this gradual phase out is less often used in patients who refers themselves. Physical therapists might focus on improving impairments, leaving the translation to activities of daily life to patients themselves. This situation stands to reason since a sizeable proportion of the self-referred patients has already gained some experience in the translation to daily life: recurrence rates are high. Furthermore, the lower amount of care in self-referred patients seems to support this rationale.

This study has some limitations. Firstly, in the NPCD, treatment episodes in general practice are constructed retrospectively. As a consequence, applied interventions (consults, prescriptions and referrals) were related to a treatment episode due to OA, unless they were aimed at treating any comorbidity. Secondly, both the increasing use of direct-access and the moderate registration of referrals in the medical record could have induced an underestimation of referrals to other health professionals, including physical therapy and dietary therapy. Since exercise therapy and encouraging weight loss are key recommendations in clinical guidelines for the treatment of lower limb OA[5], a higher referral rate than the indicated 5% respectively <1% could have been expected. Thirdly, we did not take into account the hierarchical structure of the data with patients nested in health professionals, nested in primary care practices both in general practice as well as in physical therapy practice. However, previous work showed that variances in health care use in patients with hip/knee OA were mainly located at patients' level[21]. Fourthly, we were not able to evaluate thoroughly the sequence of the applied interventions in general practice, but evaluated which interventions from each step were applied in patients with hip/knee OA. Furthermore, we did not take into account whether a patient's treatment was evaluated during an evaluation visit before turning to the next step, which is described as an integral part of the SCS[6]. Finally, data were extracted from two voluntary-based, separate registrations, both part of the NPCD. Selection bias could be excluded, as the number of patients objecting to participate in the NPCD is negligible and participating practices reflects the reality of Dutch general practices. As the NPCD comprises several, separate registrations, patients referred for physical therapy were not necessarily represented in the GP data and vice versa, disabling an evaluation of the compliance to the SCS in a singular patient by combining electronic data derived from several health professionals. At this moment, the NPCD is prepared to enable integration of data from several health professionals belonging to a singular patient. This opens the way to evaluate the compliance to the SCS more thoroughly, including the effects of using direct accessibility of allied health care on both patient-outcomes and the process of care.

Conclusion

In accordance with the SCS, less advanced treatment modalities are more often applied in general practice than more advanced treatment modalities. However, completion of each SCS-step is achieved rarely. To optimize the adherence to the SCS, GPs could reconsider their

analgesics policy prior to NSAID prescription and the low referral rate to exercise therapy and/or dietary therapy compared to orthopaedic surgeons. Self-referral to physical therapy partially distorts both the low referral rate in general practice and the low application rate of education as singular intervention in physical therapy practice. Compared to GP-referred patients, self-referred patients seems to be less intensively treated, possibly as a result of a more impairment-minded treatment strategy. This chosen strategy could be related to the higher recurrent rate in self-referred patients. Further research is recommended to evaluate more thoroughly the effects of task-shifting in OA care, taking into account the content and sequence of the SCS.

Acknowledgement

NIVEL Primary Care is funded by the Dutch Ministry of Health, Welfare and Sports. By this funding, data presented on www.nivel.nl/zorgregistraties are collected, analysed and prepared for presentation. The Ministry did not play any role in the content of neither data-collection nor data-analyses. We would like to thank research-assistants concerned in NIVEL Primary Care Database for their cooperation in data-collection and data-analyses.

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Factors associated with referral to secondary care in patients with osteoarthritis of the hip or knee after implementation of a stepped-care strategy

Published in: Arthritis Care Res (Hoboken). 2017 Feb;69(2):216-225
https://doi.org/10.1002/acr.22935

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Abstract

Objective We introduced a Stepped-Care-Strategy (SCS) for hip/knee osteoarthritis focusing on delivery of high quality, and stepped care. In this study, we aimed to identify factors associated with various steps of the SCS.

Methods We used data from a two-year observational prospective cohort study, including 313 patients visiting their general practitioner (GP) with a new episode of hip/knee osteoarthritis. We used logistic multilevel analyses to identify factors at the level of the patient, the GP, and the general practice, related to 1) treatment limited to primary care, 2) referral to non-surgical secondary care, 3) surgical procedures.

Results Patients whose treatment had been limited to primary care, tended to function physically better (OR1.03). Furthermore, they less often received exercise therapy (OR.46), intra-articular injections (OR.08), and radiological assessments (OR.06). Continuation of non-surgical care after referral was more likely in employed patients (OR2.90) and patients who had no exercise therapy (OR.19) nor non-steroidal anti-inflammatory drugs (OR.35). Surgically treated patients more often received exercise therapy (OR7.42). Referral and surgical treatment depend only to a limited extent on the GP or the general practice.

Conclusion After implementation of the SCS in primary care, the performance of exercise therapy seems to play a key role in the decision whether or not to refer for (non)-surgical treatment in secondary care, rather than disease severity or psychological factors. To optimize patient-tailored treatment, future research should be adressed to determine the optimal moment of switch from primary to secondary care in patients with hip/knee osteoarthritis.

Introduction

Management of osteoarthritis (OA) of the hip or knee comprises non-pharmacological, pharmacological and surgical interventions[1]. Clinical guidelines recommend to combine non-pharmacological and pharmacological treatment options prior to the consideration of surgical interventions[1-4]. Surgical treatment, by way of Total Joint Replacement (TJR), is an effective and cost-effective final treatment option in severe hip/knee OA[5,6]. Surgery rates in patients with hip/knee OA differ between 16-23% in primary care cohorts (follow-up time 1-4 years)[7,8] and between 18-50% in patients referred to secondary care (follow-up time 1-3 years)[9-12]. The absolute number of TJRs increases annually, partly due to the increasing prevalence of OA[13]. However, some have suggested that TJR is overutilized[14].

To support physicians to apply non-surgical interventions adequately and to reduce inappropriate use of advanced care including TJRs, several treatment algorithms are developed in OA care[15,16]. These algorithms potentially increase the appropriateness of advanced care, and ascertain that patients with hip/knee OA will receive the right care at the right time. The Stepped-Care-Strategy (SCS) is an example of a treatment algorithm in hip/knee OA. The extended content of the SCS is described elsewhere[16]. In short, non-surgical care in patients with hip/knee OA is prescribed in three steps. Treatment starts in primary care with stimulating patients' self-care (step 1). In case of persisting complaints after adequate application of all step-1 interventions, (topical) NSAIDs or tramadol are applied, supplemented by prescribing exercise therapy and, in case of overweight, dietary therapy to diminish the impairments and limitations due to OA (step 2). TENS and intra-articular corticosteroid injections, and a referral for hospital-based evaluation, may be applied as final non-surgical interventions (step 3) (Appendix). All modalities of step 1 and step 2 of the SCS can be performed in primary care. The performance of step-3 interventions requires a referral to secondary care. TJR should exclusively be considered in case of persisting complaints after completing the SCS.

In 2010, implementation of the SCS in clinical practice has been started. Prior to nation-wide implementation, general practices in one region of the Netherlands were invited to implement the SCS in clinical practice; the implementation strategy was described elsewhere[17]. In this cohort, forty-five percent of the patients were referred to an orthopaedic surgeon, 16% visited a rheumatologist. TJR was applied in 18% of the patients[17]. To date, it is unknown what factors determine the choice for surgery. These factors may relate to patients, practitioners and practice characteristics. Insight into these factors would be useful to optimize nationwide implementation of the SCS in clinical practice.

Therefore, the aim of the present study is to identify patient-related, GP-related and general practice related factors associated with *1*. treatment limited to primary care (step 1 and 2 SCS), *2*. continuation of non-surgical secondary care within the subpopulation that was

referred (step 3 SCS), and *3.* the application of a surgical procedure including TJR in the total patient population visiting their GP due to hip/knee OA.

Methods

Study design

Data were obtained from a two-year observational prospective cohort study, composed within the context of the BART project (Beating osteoARThritis), executed from August 2010 to March 2013 in the region Nijmegen, The Netherlands. The study was designed to test and to evaluate the implementation of the SCS[16]. The study was approved by the Medical Ethics Committee on Research Involving Human Subjects (CMO) Region Arnhem-Nijmegen (approval number: CMO 2009/246).

Study population

General practitioners

GPs from the Nijmegen University Network of General Practitioners (NUHP) were invited to participate in the BART-project and subsequently were encouraged to optimize their non-surgical care prior to a referral for TJR-consideration. The NUHP consists of 157 GPs working in 70 general practices. It is a practice based research network from the department of Primary and Community Care at the Radboud University Nijmegen. Additionaly, six general practices which were not involved in the NUHP were approached to take part in the study.

Patients

Potentially eligible patients were recruited by the participating GPs during visits in their practice. Individuals at least 18 years of age who were seeking help from their GP with a new episode of hip or knee complaints due to OA without a preceding visit accounting to the same complaints in the last three months, were eligible to participate. In addition, patient recruitment occurred on the basis of extractions from medical records of participating GPs; patients with symptomatic hip/knee OA who did not visit the GP due to these complaints in the preceeding three months were selected and approached to participate in this study. Patients were excluded when they had received a total hip or knee replacement in the past, were on a waiting list for such a surgery or were inable to complete the questionnaires due to language barriers or terminal illnesses.

Assessments

Participants completed five similar questionnaires during the time frame of the study (baseline, 6 months, 12 months, 18 months, 24 months after inclusion). Their GPs also completed one questionnaire at baseline and another questionnaire two months after inclusion in the researchproject. For the current study, baseline data were used, completed with data

regarding patients' utilized care during the study period. Box 1 summarizes the collected data at the level of the patient, the GP, and the general practice.

BOX 1. Collected descriptive items at baseline on patient-level, general practitioner level and general practice level

Patient level	
Predisposing #	
Age	Years
Sex	Male / Female
Overweight	Yes / No
Education level	Elementary school / High school; technical or vocational training / Higher eduction
	Paid job / No paid job
Employment status	Alone / With partner / With partner and children / With children / With others
Household composition	Dutch General Self Efficacy Scale (DGSS), range 10-40;
	higher score reflects higher self-efficacy [18]
Self-efficacy	Pain Coping Inventory List (PCI), range 12-48;
	higher score reflects more use of active coping style [19]
Active pain coping	
Enabling #	
Health insurance	Basic / With additional coverage for physiotherapy
Resident urbanity	Rural / Suburban / Urban
Illness related #	
Location of osteoarthritis	Hip / Knee / Both hip and knee
Affected joints	Number
Duration of complaints	<1 year / 1-5 years / 5-10 years / >10 years
Pain severity	Western Ontario McMaster University Index of Osteoarthritis (WOMAC), range 0-100;
	WOMAC, range 0-100 (20, 21); higher score reflect better health status [20,21]
Functional disability	Dutch Arthritis Impact Measurement Scales [22]
Number of comorbidities	
General practitioner level †	
Age	Years
Sex	Male / Female
Years of experience as general practitioner	Years
Special interest in musculoskeletal disorders	Yes / No
Practice nurse involved in osteoarthritis management	Yes / No
Structural collaboration with other discipline(s)	Yes / No
General practice level †	
Practice type	Solo / Duo / Group / GP centre / Health centre
Practice urbanity	Rural / Suburban / Urban
Additional variables	
Previously utilized care	
Education	Yes / No
Lifestyle advise	Yes / No
Dietary therapy	Yes / No
Exercise therapy	Yes / No
Acetaminophen	Yes / No
Glucosaminen	Yes / No
Non-steriod anti-inflammatory drugs	Yes / No
Tramadol	Yes / No
Intra-articular corticosteroid injection	Yes / No
Radiological assessment	Yes / No

Classification according to Andersen et al.[23], distinguishing predisposing factors, enabling factors and factors related the illness level

Dependent variables

Treatment limited to primary care (yes/no) (step 1, step 2 SCS)

Based on data of all participants concerning health care utilization during the study period, it was determined whether or not a patient's treatment due to their hip/knee OA was limited to primary care. Limitation to primary care was defined as 'no patient-reported referral to an orthopaedic surgeon or rheumatologist during the study period'. If a patient reported that he/she was referred to secondary care only for radiological assessment without visiting an orthopaedic surgeon or rheumatologist, the treatment episode was indicated as 'limited to primary care' as well.

Continuation of non-surgical treatment after referral to secondary care (yes/no) (Step 3 SCS)

In the subgroup of patients referred to an orthopaedic surgeon or rheumatologist, it was determined whether or not non-surgical treatment was continued. This variable was scored positively if a patient reported that he/she did not receive any surgical procedure after a referral to secondary care during the study period.

Application of a surgical procedure including TJR (yes/no)

The variable 'application of a surgical procedure including TJR' was scored positively if any participant of the total population reported that he underwent a surgical procedure, mainly a total hip replacement or a total knee replacement in secondary care during the study period.

Figure 1 shows the dependent variabeles in outline.

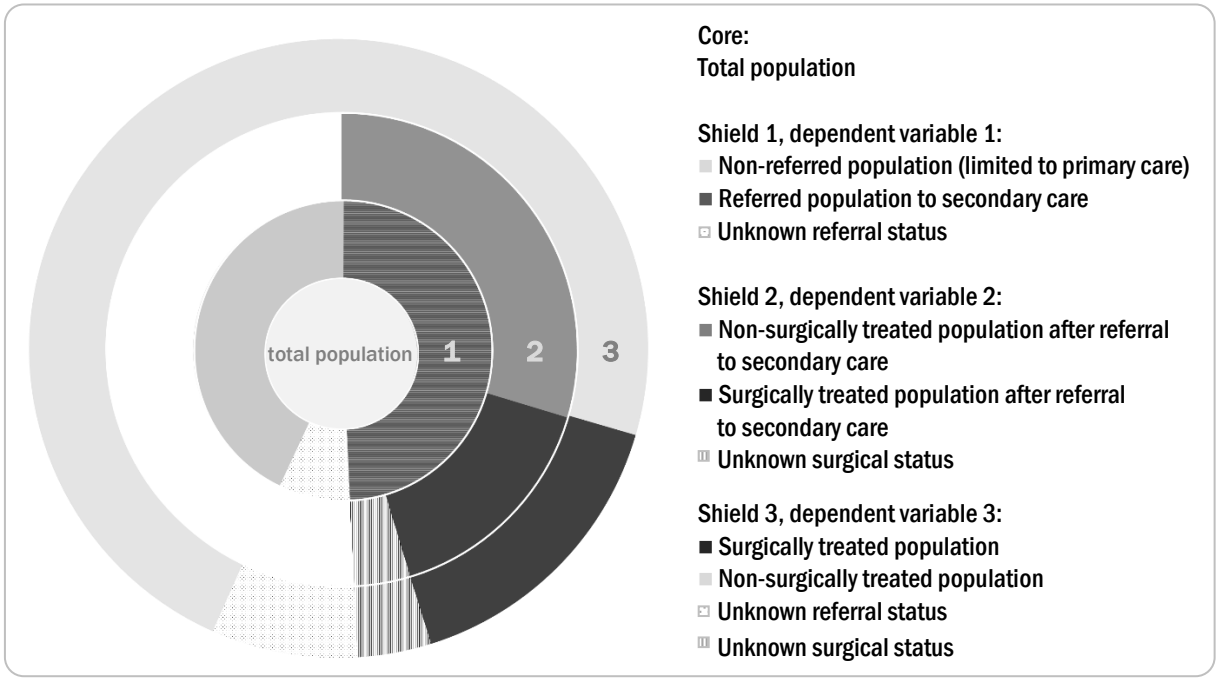

FIGURE 1. Dependent variables (limitation to primary care, non-surgical treatment after referral to secondary care, and surgical treatment) of the study in outline

Potential associative factors

Potential factors associated with referrals to secondary care and subsequent treatment were divided into patient-related factors, factors related to the GP, and factors related to the general practice. We excluded general practice and general practitioner related factors in the determination of factors related to the continuation of non-surgical treatment in patients with hip/knee OA referred to secondary care, since GPs are not involved in the decision to apply a surgical procedure or not. The selection of patient-related potential factors was based on previously reported factors in medical literature[7,11,12,24-31]. Indicated factors were categorized according to Andersen' Behavioural Model of Health Care, distinguishing a predisposing, enabling, and illness level component[23]. Additionally, the content of previously utilized care was collected, including the application of radiological assessment (Box 1).

Statistical analyses

Descriptive statistics

Baseline characteristics were described, both on patient level as well on the level of the GP and the general practice. Subsequently, patient demographics, health status, and disease characteristics were described separately in patients who were not referred to secondary care versus patients who were referred to secondary care. Finally, descriptive properties of the referred group were studied in more detail, comparing referred patients continuing non-surgical treatment and referred patients receiving a surgical procedure. Differences between groups were analysed using unpaired t-tests or chi-square tests, when appropriate.

Identifying factors associated with the provision of care

Given the hierarchical structure of the dataset, i.e. patients (level 1) were nested in the sample of GPs (level 2), who are nested in general practices (level 3), logistic multilevel regression models were built to identify factors associated with the setting of care. To prevent overfitting due to the number of factors[32], the most important factors were selected before fitting the final model. This preselection was started by investigating collinearity between potential factors; variables with a variance inflation factor (VIF) higher than 10 were removed. Subsequently, the selection procedure was performed by classifying the remaining factors into four blocks. The first block included predisposing and enabling factors, the second block comprised disease-related factors, the third block included previously applied treatment modalities, and the fourth block comprised GP and GP-practice variables. Backward stepwise regression based on five imputed datasets was used to select the most important variables per block. Cutoff value for selecting a variable was a mean likelihood ratio $\chi^2 < .05$. The overall final model was constructed by entering simultaneously the selected variables from each of the four blocks and was based on 20 imputed datasets combined using Rubin's rules[33-35]. For each dependent variabele, the percentage of variation (Variance Partition Component (VPC)) belonging to each hierarchical level was calculated, using the latent variable approach[36,37].

All statistical analyses were performed using Stata 10 (StataCorp LP, College Station, TX, USA) software.

Results

Study population

Included patients were treated by 70 GPs working in 38 general practices. Participating GPs were more often male and worked less often in solo-practices compared to Dutch GPs[38]. In total, 313 patients with hip/knee OA participated in the study. Nine out of ten included patients exceeded the age of 51. The majority of the population was female (62%), suffered from at least knee OA (79%) and was faced with physical complaints more than one year (79%) (Table 1). Slightly more than half of the patients were referred to secondary care during the study period. In the subpopulation of referred patients, about one in three patients received a surgical intervention.

TABLE 1. Baseline characteristics of patients with hip/knee osteoarthritis, their general practitioners and general practice

Baseline characteristic			Missing values (n)
Patient characteristics (n=313)			
Demographics			
Age, years; mean (SD)	64	(10)	0
Sex, male; n (%)	120	(38)	0
Education, higher education; n (%)	37	(20)	126
Employed, paid work; n (%)	96	(31)	1
Household composition, with partner; n (%)	229	(73)	1
Health insurance, with additional coverage; n (%)	282	(91)	2
Patients' urbanity, rural; n (%)	194	(62)	1
Health status			
Overweight, Body Mass Index >25kg/m^2; n (%)	218	(71)	4
Number comorbidities range (0-15); median (IQR)	2	(1-3)	0
Self-efficacy (Dutch General Self Efficacy Scale) *; mean (SD)	31	(5)	8
Active pain coping (Pain Coping Inventory List) †; mean (SD)	26	(6)	8
Disease characteristics			
Location of osteoarthritis			
Hip; n (%)	159	(51)	0
Knee; n (%)	246	(79)	0
Number of affected joints (range); median (IQR)	1	(1-3)	0
Duration of complaints, > 1 year; n (%)	247	(79)	1
WOMAC pain ‡; mean (SD)	62	(22)	8
WOMAC functioning ‡; mean (SD)	64	(21)	12
GP-characteristics (n=70)			
Age, years; mean (SD)	49	(9)	4
Sex, male; n (%)	51	(73)	0
Experience as GP, years; median (IQR)	17	(10-25)	4
Special interest in musculoskeletal disorders, yes; n (%)	6	(10)	12
Practice nurse involved in osteoarthritis managemen, yest; n (%)	13	(22)	12
Structural collaboration with other discipline(s), yes; n (%)	20	(34)	12
General practice characteristics (n=38)			
Practice type, solo; n (%)	6	(17)	3
Practice urbanity, rural; n (%)	23	(61)	0

Abbreviations: n=Number, SD=Standard Deviation, IQR=Interquartile Range, WOMAC=Western Ontario McMaster University Index of Osteoarthritis, GP=General Practitioner

* Higher scores reflect higher self-efficacy (ranging from 10 to 40); † Higher score indicates more use of an active coping style (ranging from 12 to 48); ‡ Standardized scores were used where higher scores reflect better health status (ranging from 0 to 100)

Non-referred versus referred patients

In Table 2, patient demographics, health status, disease characteristics and the content of previously utilized care were shown, both in non-referred patients and patients who were referred to secondary care due to their hip/knee OA. Non-referred patients reported less OA-affected joints and less comorbidities, indicated less pain and fewer limitations in activities compared to referred patients (WOMAC-scores). Moreover, non-referred patients showed a less active coping style and were treated less extensively by recommended non-surgical treatment modalities compared to patients referred to secondary care (Table 2).

TABLE 2. Patient-related characteristics and the content of care in patients with hip/knee osteoarthrtis, separate for non-referred (n=135) and referred (n=154) patients (including surgically treated population) *

	Non-referred to secondary care (n=135)		Referred to secondary care (n=154)		p-value
Demographics					
Age, years; mean (SD)	64	(11)	63	(10)	.25
Sex, male; number (%)	56	(41)	54	(35)	.26
Education, higher education; number (%)	15	(17)	22	(22)	.42
Employed, paid work; number (%)	38	(28)	50	(33)	.41
Health insurance, additional coverage physical therapy; number (%)	119	(89)	142	(93)	.24
Household composition, with partner; number (%)	101	(75)	117	(76)	.91
Patients' urbanity, rural; number (%)	85	(63)	97	(63)	.94
Health status					
Overweight, Body Mass Index >25kg/m^2; number (%)	87	(65)	111	(73)	.16
Comorbidities, number; median (Interquartile Range)	1	(0-2)	2	(1-3)	<.01
Self efficacy , Dutch General Self-efficacy Scale §; mean (SD)	31	(5)	31	(5)	.58
Active pain coping, Pain Coping Inventory list †; mean (SD)	25	(6)	27	(5)	.02
Disease characteristics					
Location of osteoarthritis					
Hip; number (%)	72	(53)	77	(50)	.58
Knee; number (%)	98	(73)	127	(82)	.04
Affected joints, number; median (Interquartile Range)	1	(1-3)	2	(1-3)	.02
Duration of complaints, > 1 year; number (%)	98	(73)	129	(84)	.02
WOMAC pain ‡; mean (SD)	70	(20)	55	(22)	<.01
WOMAC functioning ‡; mean (SD)	73	(19)	57	(20)	<.01
Content of previously utilized care, yes; number (%)					
Education	97	(72)	136	(91)	<.01
Lifestyle advise	86	(64)	117	(79)	<.01
Dietary therapy (if overweighted)	7	(8)	18	(17)	.06
Exercise therapy	62	(46)	115	(77)	<.01
Acetaminophen	98	(73)	137	(90)	<.01
Glucosaminen	44	(33)	49	(34)	.90
NSAIDs	56	(42)	89	(62)	<.01
Tramadol	5	(4)	35	(25)	<.01
Intra-articular corticosteroid injection	8	(6)	51	(35)	<.01
Radiological assessment	61	(45)	141	(94)	<.01

Abbreviations: SD=Standard Deviation, WOMAC=Western Ontario McMaster University Index of Osteoarthritis, NSAID=Non-Steroidal Anti-Inflammatory Drug

* In 24 patients it was unknown whether or not a referral to secondary care has happened; § Higher scores reflect higher self-efficacy (ranging from 10 to 40); † Higher score indicates more use of an active coping style (ranging from 12 to 48); ‡ Standardized scores were used where higher scores reflect better health status (ranging from 0 to 100)

About one-third (34%) of the population who had been referred to secondary care, received a surgical procedure, which represents 18% of the total population. Frequently, the surgical interventions concerned TJRs. Surgically treated patients were older, were less often employed, showed a more active coping style and reported less OA-affected joints than non-surgically treated patients. Acetaminophen, NSAIDs and exercise therapy had been more often applied in patients who received a surgical procedure compared to non-surgically treated referred patients. In contrast, glucosamine was less often used by surgically treated patients than by patients who continued non-surgical care (Table 3).

TABLE 3. Patient-related characteristics and the content of care in patients with hip/knee osteoarthrtis who were referred to secondary care

	Referred to secondary care (n=142)[a]				
	No surgical procedure (n=93)		Surgical procedure (n=49)		p-value
Demographics					
Age, years; mean (SD)	61	(11)	65	(7)	.02
Sex, male; number (%)	30	(32)	20	(41)	.31
Education, higher education; number (%)	15	(24)	7	(18)	.50
Employed, paid work; number (%)	34	(37)	10	(20)	.04
Health insurance, additional coverage for physical therapy; number (%)	85	(91)	45	(94)	.62
Household composition, with partner; number (%)	68	(73)	42	(86)	.09
Patients' urbanity, rural; number (%)	56	(60)	37	(76)	.07
Health status					
Overweight, Body Mass Index >25kg/m^2; number (%)	70	(77)	33	(67)	.22
Comorbidities, number; median (Interquartile Range)	2	(1-3)	1	(1-3)	.35
Self efficacy , Dutch General Self-efficacy Scale §; mean (SD)	31	(6)	31	(5)	.68
Active pain coping, Pain Coping Inventory list †; mean (SD)	26	(5)	28	(5)	.02
Disease characteristics					
Location of osteoarthritis					
Hip; number (%)	42	(45)	27	(55)	.26
Knee; number (%)	77	(83)	39	(80)	.64
Affected joints, number; median (Interquartile Range)	2	(1-4)	1	(0-3)	.02
Duration of complaints, > 1 year; number (%)	79	(85)	40	(83)	.80
WOMAC pain ‡; mean (SD)	57	(23)	53	(19)	.34
WOMAC functioning ‡; mean (SD)	59	(22)	54	(16)	.17
Content of previously utilized care, yes; number (%)					
Education	82	(88)	46	(94)	.28
Lifestyle advise	72	(77)	38	(78)	.99
Dietary therapy (if overweighted)	12	(17)	5	(16)	.85
Exercise therapy	62	(67)	45	(92)	<.01
Acetaminophen	78	(84)	48	(98)	.01
Glucosaminen	35	(38)	9	(19)	.02
NSAIDs	49	(53)	37	(77)	<.01
Tramadol	20	(22)	13	(27)	.48
Intra-articular corticosteroid injection	32	(34)	15	(31)	.71
Radiological assessment	84	(90)	48	(98)	.09

Abbreviations: SD=Standard Deviation, WOMAC=Western Ontario McMaster University Index of Osteoarthritis, NSAID=Non-Steroidal Anti-Inflammatory Drug.

[a] In 12 patients, it was unknown whether the referral resulted in a surgical procedure / continuation of non-surgical care

§ Higher scores reflect higher self-efficacy (ranging from 10 to 40); † Higher score indicates more use of an active coping style (ranging from 12 to 48); ‡ Standardized scores were used where higher scores reflect better health status (ranging from 0 to 100)

Factors associated with the provision of care

Thirteen factors were identified which were associated with at least one dependent variable (Table 4). Most of these factors were related to the patient and to the content of previously utilized care. No GP-related factors and only one general practice related factor were part of the final models. Due to collinearity, the variable 'experience years as GP' was removed before starting logistic multilevel analyses.

Treatment limited to primary care (step 1, step 2 SCS)

The analyses showed that a limitation to treatment in primary care was associated with fewer limitations in physical functioning (p=<.01) and with no-use of exercise therapy (p=.03), no-use of intra-articular injections (p=<.01) and absence of radiological assessments (p=<.01). Moreover, a positive trend was indicated with respect to being treated in a solo practice (p=.06). In total, more than 99.9% of the variance was located at the level of the patient.

Continuation of non-surgical treatment after referral to secondary care (step 3 SCS)

Eight variables at patient level were added to the final model determining factors related to the continuation of non-surgical care after referral to secondary care. In the subpopulation of referred patients, having a paid job (p=.04), more OA-affected joints (p=.04), no-use of exercise therapy (p=<.01) and no-use of NSAIDs (p=.03) were associated with continuing non-surgical treatment.

Application of surgical procedure

The final model fitted to identify factors associated with the application of a surgical procedure comprised six variables. Only one factor was indicated to be statistically significantly associated with a surgical procedure. The application of a surgical procedure was more likely after the use of exercise therapy (p<.01). Variance was mainly located at the level of the patient (89%), followed by the GP (10.3%) and the general practice (<1%).

TABLE 4. Factors related to the setting of care in patients with hip/knee osteoarthritis (logistic multilevel regression analyses)

	Non-referral in primary care population (N_{yes}=135; N_{no}=154)			Continuation of non-surgical care in referred population (N_{yes}=93; N_{no}=49)			Surgical procedure in primary care population (N_{yes}=49; N_{no}=229)		
Factors related to:	OR[a]	95% CI	p-value	OR[b]	95% CI	p-value	OR[c]	95% CI	p-value
Patient									
Predisposing component									
Active pain coping, PCI (range 12-48)†	1.01	.95 – 1.07	.79	.93	.85 – 1.01	.08	1.06	0.98 – 1.14	.15
Household composition, with partner;				.53	.12 – 1.51	.19			
Employed, paid work				2.90	1.05 – 7.82	.04			
Illness level component									
WOMAC functioning (range 0-100)‡	1.03	1.01 – 1.05	<.01	1.01	.99 – 1.04	.35	.99	0.97 – 1.01	.23
Affected joints, number (range 0-9)				2.00	1.05 – 3.82	.04			
Content of care									
Use of glucosamine				1.67	.61 – 4.60	.32	.48	.20 – 1.13	.09
Use of exercise therapy	.46	.23 – .92	.03	.19	.05 – .65	<.01	7.42	2.38 – 23.11	<.01
Use of NSAIDs				.35	.13 – .91	.03	2.19	.93 – 5.16	.07
Use of tramadol	.28	.07 – 1.08	.07						
Use of radiological assessment	.06	.03 – .16	<.01						
Use of intra-articular injections	.08	.03 – .22	<.01						
Use of acetaminophen							4.86	.56 – 42.15	.15
GP-(practice)									
Solo practice, yes	2.46	.97 – 6.26	.06						

Abbreviations: n=Number, OR=Odds Ratio, CI=Confidence Interval, PCI=Pain Coping Inventory list, WOMAC=Western Ontario McMaster University Index of Osteoarthritis, NSAID=Non-Steroidal Anti-Inflammatory Drug, GP=General Practitioner

† Higher score indicates more use of an active coping style; ‡ Standardized scores were used, higher scores reflect better health status

a Backward stepwise final model: likelihood ratio $\chi 2$ = 178.06, df = 8, p<.001; McFadden R-squared = .41;

b Backward stepwise final model: likelihood ratio $\chi 2$ = 41.12, df = 9, p<.001; McFadden R-squared = .21;

c Backward stepwise final model: likelihood ratio $\chi 2$ = 57.30, df = 7, p<.001; McFadden R-squared = .19

Discussion

The objective of this study was to identify factors related to the patient, the GP and the general practice associated with the setting of care in a population of patients with hip/knee OA after implementation of the SCS. Our study shows that in a two years follow-up period, 47% of the population visiting their GP with hip/knee OA were exclusively treated in primary care. Non-referral to secondary care seems to be stronger associated with the content of previously utilized care than with patient-demographics, disease-related factors or factors related to the GP or general practice. Based on our study, patients seem to be referred more often to secondary care after receiving exercise therapy, intra-articular injections, and radiological

assessments. This suggests that participating GPs try to act in agreement with the SCS by offering non-surgical modalities before considering surgical interventions.

The proportion of patients who underwent a surgical procedure in our study was similar to previously reported data in primary care populations[7,8]. Several studies indicated more pain and a higher level of functional limitations as important factors with respect to the decision to apply a TJR[7,11,12,27]. However, we did not find an association between receiving a surgical procedure and any disease characteristics. One difference between our study and previous studies is that we included additionally GP and general practice related factors as well as the content of previously utilized care to patient-related factors. Including these factors, the extent of health care utilization seems to be a stronger predictive factor for the application of a surgical procedure than disease characteristics. In previous research, it has been shown that a higher level of illness is accompanied by an increased health care utilization[39]. For example, in the two-year period preceding TJR, patients have been using large amounts of painkillers and more outpatient health care services[40]. This supports the principles of the SCS, suggesting TJR as final treatment option when non-surgical modalities no longer establish satisfactory results.

In our study, 34% of the patients referred to secondary care received a surgical procedure. Previous work by McHugh et al. demonstrated a surgery-rate of 50% in a referred population[11]. The latter discrepancy can possibly be explained by the nature of both populations. The McHugh study included patients newly referred to orthopaedic surgeons for TJR consideration. In contrast, in our study, patients could have been referred to both orthopaedic surgeons and rheumatologists due to many reasons, including TJR consideration and a request for a second opinion for example. Continuation of non-surgical care after a referral was hardly related to predisposing or enabling factors. One exception concerns the patients' employment status. In contrast to previous findings, we found that 'having paid employment' was significantly associated with non-surgical treatment[26]. Possibly, in view of the current labour shortage due to the financial crisis, patients prefer to prevent absenteeism rather than relieving their complaints by a surgical procedure.

Each additional joint affected with OA doubles the chance to continue non-surgical treatment after a referral to secondary care. Since previous research in patients with hip/knee OA has shown that multi-joint complaints adversely impact postoperative results[41,42], patients and/or orthopaedic surgeons possibly are reticent to turn to a surgical intervention and prefer to continue non-surgical treatment. As the incidence of multi-joint OA is expected to increase over the next years[43], it is desirable to get more insight into effective interventions in this specific population.

In general, identified factors associated with non-surgical treatment limited to primary care respectively the application of TJR in secondary care, are mainly located at the level of the patient (explaining ≥ 89% of the variance). A systematic review by O'Donnell et al. investigating

the variation in GP referral rates in the general population, reported the highest attribution to patient-characteristics as well[44]. However, it could be discussed whether the content of care is primarily related to the patient, rather than being determined by a patient's GP. Probably, in daily practice, patients agree with the proposed care by the GP, prior to its' actual application.
In our study, only one practice-related factor showed a positive trend with respect to treatment limited to primary care: being treated in a solo-practice. Previous work presented inconclusive results regarding the association between practice size and referral rate in the general population[44].

This study comprises secondary analyses of data collected by the BART project. To our knowledge, the BART project is the first project in which multi-levelled factors associated with the provision of care in patients with hip/knee OA were identified. Our results show that cohort studies are useful to get insight into health services utilization over time as long as longitudinal, multidisciplinary medical record registrations are lacking. However, this study has some limitations as well. Firstly, the content of utilized care was collected by a self-reporting tool, which could have induced an underestimation of health services utilization. Secondly, data were not available regarding some potential relevant factors, for example the radiological severity of hip/knee OA and a patient's willingness to consider TJR. These factors were indicated to be determinants for TJR in earlier work[7,27,29,30]. Thirdly, since our study sample was limited, we had to preselect the most important factors for inclusion in the final model instead of using all potential predictive factors. Despite the chosen method comprising preselection within content-matter motivated blocks using backward selection regression has been found to be a good alternative, statistical power seems to be limited to detect less strong associations. Finally, in each of the final models, the McFadden R-squared was low. As a consequence, data presented in this study could not be used to predict the care pathway of an individual patient.

In conclusion, after the implementation of the SCS in a primary care population, the performance of exercise therapy has shown to play a key role in the decision whether or not to refer for (non)surgical treatment in secondary care. Demographics, disease characteristics and health status are only slightly associated with the provision of OA care. This suggests that, in line with the SCS, GPs try to offer non-surgical modalities before appealing to surgical interventions. In future, research is desirable to determine the optimal moment of switch from primary care to secondary care, ensuring the best tailored treatment in patients with hip/knee OA.

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4

One size fits all in physiotherapy management of knee osteoarthritis? A cross-sectional, clinical vignette study

Under review: Physiotherapy

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Abstract

Objective To evaluate to what extent primary care provided physiotherapy is currently tailored to five phenotypes of knee osteoarthritis (OA), namely: the minimal joint disease' phenotype, the 'strong muscle strength' phenotype, the 'severe radiographic OA' phenotype, the 'obese' phenotype, and the 'depressive mood' phenotype respectively.

Design A descriptive, cross-sectional survey in the Netherlands.

Setting Primary care physiotherapy practices

Participants 144 Primary care physiotherapists who treated at least one patient with knee OA over the last month

Main outcome measures Predefined hypotheses regarding physiotherapists' optimal treatment strategy in five phenotypes of knee OA represented by five clinical vignettes.

Results Statistically significant differences are found regarding the content and amount of care between phenotypes of knee OA. These differences were mainly in line with our predefined hypotheses. Provided care differed from our hypotheses in the strong muscle phenotype, in which exercise therapy was provided more often than expected and the referral rate to secondary care was lower than expected. In the depressive mood phenotype, the referral rate to psychologists was higher than expected.

Conclusions Physiotherapists seem to tailor their treatment to the five phenotypes of knee OA, instead of a 'one size fits all' approach. Future research is recommended on evaluating (cost)effectiveness of stratified interventions and developing a practical screening tool for physiotherapists to facilitate stratification of patients with knee OA.

Introduction

Knee osteoarthritis (OA) is a heterogeneous, musculoskeletal disorder affecting 3.8% of the world population[1]. OA is characterized by variations in pathophysiologic etiologies[2], varying severity of clinical symptoms[3,4], different courses over time[3] and differences in responses to treatment[4]. In consequence, OA is increasingly recognized as a syndrome defined by a group of diseases or phenotypes with a common end point[5-7]. Stratification of the OA syndrome into phenotypes will probably facilitate the determination of patients which are the most likely to benefit from which treatment, inducing more personalized care and more effective and efficient use of healthcare facilities[8,9].

Knoop et al. distinguished five clinically relevant phenotypes in a large cohort of patients with knee OA[10]. This finding was replicated in another knee OA cohort[11]. The identified phenotypes were based on four clinical characteristics: radiographic severity of OA, muscle strength, body mass index, and depression. The phenotypes were named: 'minimal joint disease' phenotype, 'strong muscle strength' phenotype, 'severe radiographic OA' phenotype, 'obese' phenotype, and 'depressive mood' phenotype[10,11].

Current clinical guidelines minimally account for differences in treatment between phenotypes, but call for tailoring general treatment recommendations to individual patients[12-14]. To date, it is unknown to what extent physiotherapists respond to that call and tailor their treatment to individuals or subgroups with knee OA.

We hypothesize that the minimal joint disease phenotype could benefit from a physiotherapist-delivered, exercise program with education focusing on self-management as generally described by clinical guidelines[12-14], since this phenotype is not specifically characterized by prominent clinical features.
The strong muscle phenotype is distinguished by strong quadriceps muscles[10,11]. This phenotype mainly concerns men with a history of a knee trauma who currently demonstrate high levels of physical activity accompanied by biomechanical overload[15]. Therefore, treatment in the strong muscle phenotype is hypothesized to focus on providing education rather than exercise therapy. Educational topics regarding pain coping and preventing overloading will be of main interest. As non-surgical treatment options are limited, the number of treatment sessions will be limited and patients will be more often advised to consult secondary care compared to other phenotypes.
Degeneration of cartilage and bone is the most distinctive characteristic of the severe radiographic OA phenotype. As exercise therapy has shown to be effective regardless the severity of OA on imaging techniques[16,17], exercise therapy is hypothesized to be included. Despite the controversial relationship between radiographic severity and the need for surgical treatment, it is hypothesized that surgery will be often considered in case of non-effective exercise therapy[18-21].

Obesity is the most prominent characteristic of the obese phenotype. Therefore, weight reduction is hypothesized to be the major topic in these patients[22]. Besides dietary advises by the physiotherapist, involvement of a dietician will be considered in many cases. In addition, treatment will contain low impact, (unloading) muscle strengthening exercises[23,24] as well as exercises to improve general aerobic fitness. Patients are advised to be physically active as much as possible in their daily living.
Finally, the depressive mood phenotype distinguishes itself by the high prevalence of depression. It is hypothesized that patients will receive a combination of gradually evolved exercise therapy and an educational program focused at adopting an adequate coping style. Positive reinforcement is expected to be one of treatments' key elements. In some cases, advice for psychological care will be considered as well to treat depressive symptoms[25].

The objective of the present study is to evaluate to what extent primary care provided physiotherapy is currently tailored to the 'minimal joint disease' phenotype, the 'strong muscle strength' phenotype, the 'severe radiographic OA' phenotype, the 'obese' phenotype, and the 'depressive mood' phenotype respectively.

Methods

Design

A descriptive, cross-sectional survey was conducted among Dutch primary care physiotherapists and exercise therapists. Data were gathered between July and October 2016.

Population

Physiotherapists and exercise therapists who regularly treat patients with knee OA were invited to participate. Two recruitment strategies were used simultaneously. First, physiotherapists and exercise therapists joining a Dutch 'Rheumatology Network'[26,27] were invited to participate (June 2016). Digital reminders were sent four weeks after the initial invitation. Secondly, physiotherapists were invited through the weekly newsletter of the Royal Dutch Association of Physical Therapy and by calls on social media in October 2016. The calls comprised a compact study description and hyperlinks to the introduction page of the digital questionnaire, which provided more detailed information.
Inclusion criterion for participation in the study was involvement in treatment of at least one patient with knee OA during the last month.

Clinical vignettes

Five visual clinical vignettes representing five previously mentioned phenotypes were included in the survey questionnaire (Figure 1 & Appendix 1). Clinical vignettes offer significant advantages in studying clinical behavior of health care professionals, including high feasibility and low costs[28-30].

The content of the clinical vignettes was based on a previously described clinical vignette by Holden et al.[31]. One researcher (DB) and two clinical experts in the field of OA research (JK and WP) adapted the original vignette to five phenotype-specific vignettes.

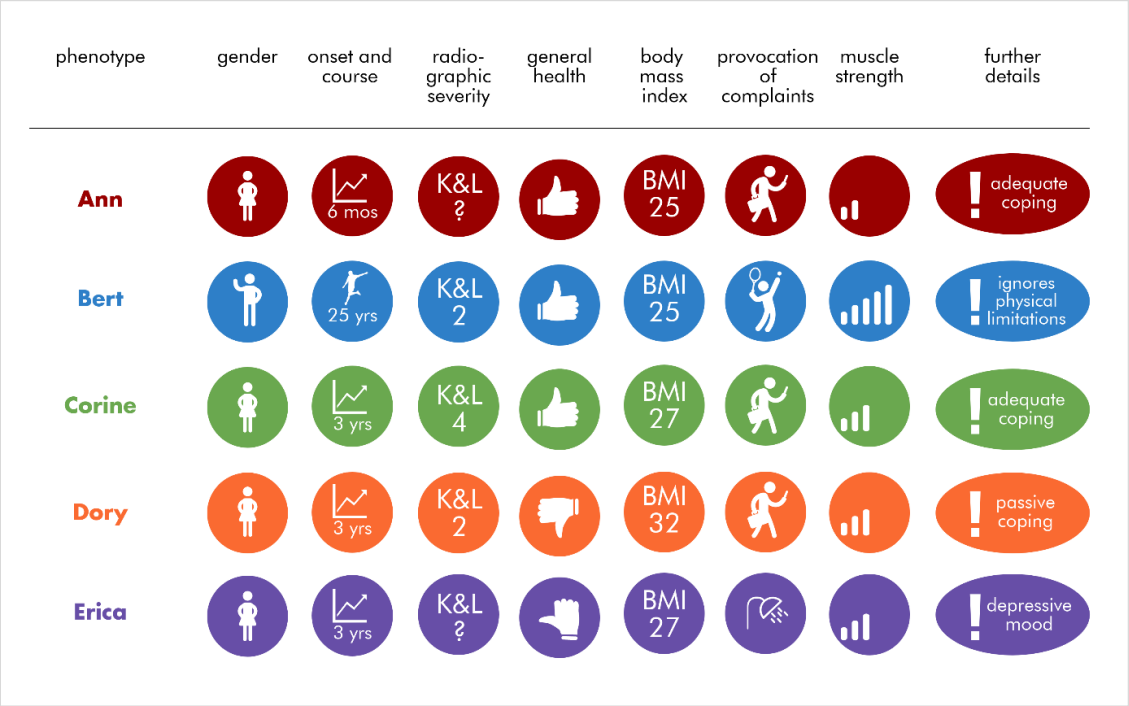

FIGURE 1. Visual presentation of five clinical phenotypes of knee osteoarthritis[10,11]
mos = months, yrs = years, K&L = Kellgren & Lawrence, BMI = Body Mass Index

Questionnaire

Participating therapists were asked to complete a series of dichotomous and multiple choice questions to get insight into the content of their treatment in different phenotypes of knee OA. The questionnaire started with two filter questions to test for eligibility on recent treatment of knee OA. Included therapists were asked to report their treatment in a patient with knee OA in general. Subsequently, the visual vignette of a patient who fits in the minimal joint disease phenotype was introduced and, again, therapists were asked to report their treatment in this specific patient. The same question was posed simultaneously regarding another four patients, representing the remaining four phenotypes. As exercise therapy and education are expected to be widespread used in physiotherapy practice, the content of those interventions was questioned in more detail. With respect to exercise therapy, participants were asked for the type of exercise therapy they would perform, for example exercises focused on aerobic fitness, local muscle strengthening, or improving activities of daily life. Regarding education, physiotherapists were asked to prioritize five topics which would be considered during a patient's treatment, for instance pain management, weight management, or the importance of pacing physical activities. Furthermore, participants were asked whether they would consider involvement of other healthcare providers in each of the five phenotypes.

Besides the content of physiotherapy treatment, questions focused on the expected number of treatment sessions and to what extent the included phenotypes cover the total population of patients with knee OA in their daily practice.

Finally, demographic questions were captured, including gender, age, clinical expertise in the field of OA, motivation to join an Rheumatology Network and practice site. Appendix 2 comprises a detailed description of the survey questionnaire.

Data analyses

Descriptive statistics were performed to describe the content and amount of physiotherapy in patients with knee OA. Subsequently, these descriptive characteristics per phenotype were used to evaluate the predefined hypotheses concerning the content and amount of care per phenotype (Table 1). A p-value of less than 0.05 was interpreted as statistically significant. Cases were excluded from analyses in case of missing data regarding >1 phenotype. Statistical analyses were executed using Stata 14.0 (StataCorp LP, College Station, TX, USA).

TABLE 1. Overview of applied statistics to test predefined hypotheses in five phenotypes of knee osteoarthritis[10,11]

Phenotype	Hypothesis	Applied statistic(s)
Minimal joint disease	Exercise program and education focusing of self-management	Descriptive statistics, Spearman's rank correlation coefficient
Strong muscle	Focus of treatment on providing education rather than exercise therapy	Descriptive statistics, Spearman's rank correlation coefficient
	Pain coping and preventing overloading are main issues in education	Descriptive statistics
	High referral rate* to secondary care compared to other phenotypes	Descriptive statistics, Kruskall Wallis for equality of proportions and a Bonferroni post-hoc analysis (2-sided)
	Limited number of treatment sessions	Descriptive statistics, Kruskall Wallis for equality of proportions and a Bonferroni post-hoc analysis (2-sided)
Severe radiographic OA	Application of exercise therapy regardless the severity of OA	Descriptive statistics, Kruskall Wallis for equality of proportions and a Bonferroni post-hoc analysis (2-sided)
	High referral rate to secondary care	Descriptive statistics, Kruskall Wallis for equality of proportions and a Bonferroni post-hoc analysis (2-sided)
Obese	Inclusion of low impact, (unloading) muscle strengthening exercises as well as exercises to improve general aerobic fitness.	Descriptive statistics
	Importance of advice to be physically active as much as possible in daily living	Descriptive statistics
	Involvement of a dietician to achieve weight reduction	Descriptive statistics, Kruskall Wallis for equality of proportions and a Bonferroni post-hoc analysis (2-sided)
Depressive mood	Inclusion of a combination of gradually evolved exercise therapy and an educational program focused at adopting an adequate coping style.	Descriptive statistics, Spearman's rank correlation coefficient
	In some cases, advice for psychological care	Descriptive statistics, Kruskall Wallis for equality of proportions and a Bonferroni post-hoc analysis (2-sided)

* A referral by a physiotherapist comprises an advice to the patient and/or his general practitioner to consider involvement of another healthcare provider

Results

In total, 225 physiotherapists accessed the digital questionnaire. Seven physiotherapists were excluded since they did not met the inclusion criterion. Demographics of these seven physiotherapists did not significantly differ from the eligible therapists. Subsequently, due to missing data, 74 cases were excluded from analyses. The remaining 144 physiotherapists were included for analyses. Fifty-six percent of these respondents were derived via Rheumatology Networks, 40% via the digital newsflash, 4% via remaining routes. Except for age, recruitment groups were comparable regarding demographics.

Population

Table 2 shows demographic data of participating physiotherapists. Forty-four percent of the respondents were male and 74% of the therapists were in the 31-60 years of age category, which was comparable to the general Dutch population of physiotherapists in primary care[32]. Seventy percent of our population were highly experienced therapists (≥15 years of experience). Ten percent of the population reported to be an expert in de field of OA.

TABLE 2. Demographics of participating physiotherapists treating patients with knee osteoarthritis (n=144)

Characteristic	Number	percentage	Missing values (number)
Gender (male)	36	(44.4)	63
Age category			64
<30 years	10	(12.5)	
31-60 years	59	(73.7)	
>60 years	11	(13.8)	
Years of experience			63
≤5 years	6	(7.4)	
6-15 years	18	(22.2)	
>15 years	57	(70.4)	
Self-reported expertise in clinical knee OA			66
(Less than) average	38	(48.7)	
More than average	32	(41.0)	
Expert in the field of OA	8	(10.3)	
Member of Arthritis Association (yes)	64	(63.4)	43
Practice site (urban)	55	(69.6)	65

Physiotherapy per phenotype of knee OA

Participating physiotherapists endorse the proposed phenotypes in their clinical practice. Overall, 21% of their population represents the 'minimal joint disease' phenotype, 15% the 'strong muscle' phenotype, 23% the 'severe radiographic OA' phenotype, 25% the 'obese' phenotype, and 15% the 'depressive mood' phenotype. Less than 2% of the patients with knee OA do not fit to any of the phenotypes.

Figure 2 shows in what percentage of each phenotype, physiotherapists would consider a specific intervention. Education and therapeutic exercises were frequently mentioned in all phenotypes. Statistically significant differences (p≤.05) were found regarding the application of most of the interventions between phenotypes, except for education, providing braces, and massage (Figure 2).

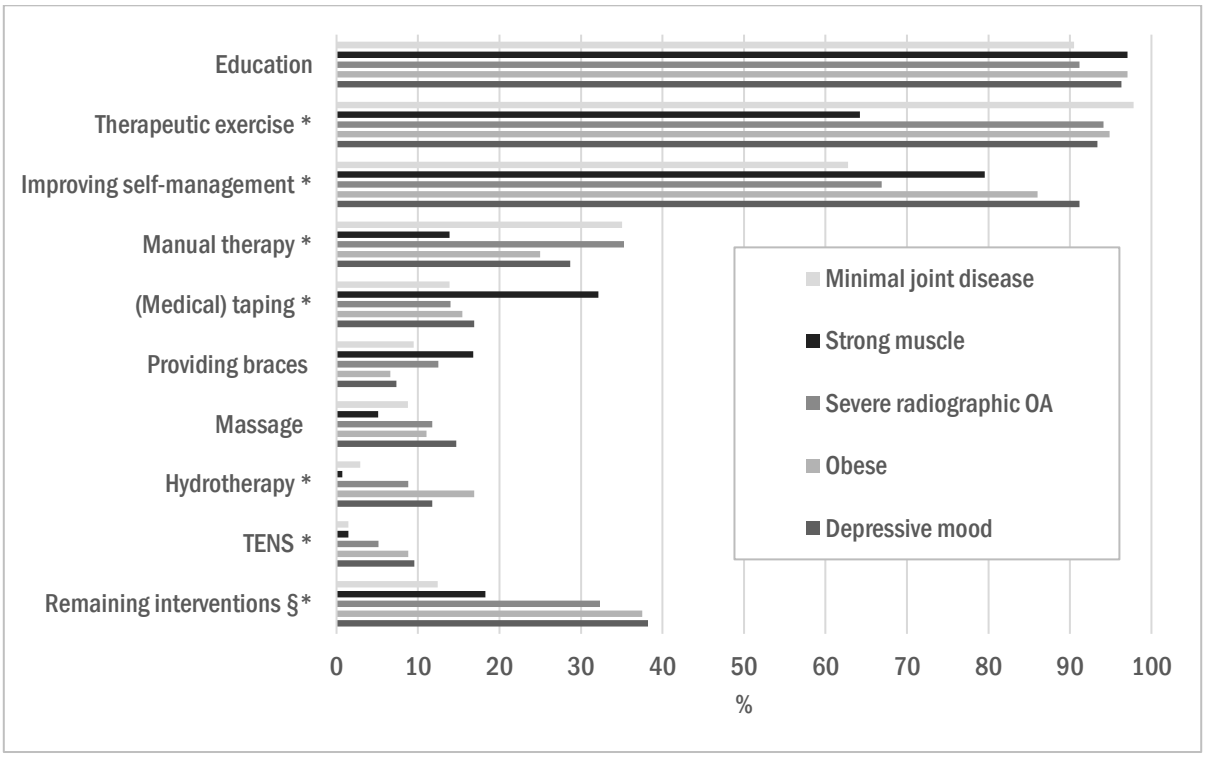

FIGURE 2. Applied interventions in patients with clinical knee osteoarthritis (OA) per phenotype
§ Remaining interventions includes electrotherapy, lasertherapy, and heat or ice
* Statistically significant difference between phenotypes (p<0.01)

Table 3 summarizes per phenotype the top-5 therapeutic exercise modalities, the top-5 topics included in patient education, and the top-5 referrals as well as the median number of considered treatment sessions per phenotype. Subsequently, these characteristics are used to evaluate the predefined hypotheses concerning the content and amount of care per phenotype of knee OA (Table 4).

Minimal joint disease phenotype

In accordance with our hypothesis, a combination of exercise therapy and education was considered in the majority of the minimal joint disease phenotype (85%) (Table 4). Respecting the content of exercise therapy, the frequent inclusion of high-loaded muscle strengthening exercises stands out. The minimal joint disease phenotype would receive less treatment sessions (median of 1-5 sessions) compared to the severe radiographic OA phenotype, the obese phenotype, and the depressive mood phenotype, (p<0.01) (Table 3).

Strong muscle phenotype

In contrast to our expectations, exercise therapy seems to play an important role in the strong muscle phenotype. Sixty percent of the physiotherapists would use a combination of exercise therapy and education, compared to education only in one third of the population (Table 4). The content of patient education was in accordance with our hypotheses and focused on pacing physical activities and improving pain coping strategies. The referral rate to secondary was lower than expected; 8% of the considered referrals concerned a referral to an orthopedic surgeon, compared to 56% in the severe radiographic OA phenotype ($p=<0.01$) and 24% in the obese phenotype ($p=0.04$). As hypothesized, physiotherapists would use significantly less treatment sessions in the strong muscle phenotype compared to the severe radiographic OA phenotype, the obese phenotype, and the depressive mood phenotype (Tables 3 and 4).

Severe radiographic OA phenotype

Eighty-nine percent of the physiotherapists would consider the use of exercise therapy in the severe radiographic OA phenotype. This application rate did not significantly differ from the remaining phenotypes, except for the strong muscle phenotype (61%, $p<0.01$) (Table 4). Furthermore, the hypothesized high referral rate to secondary care was confirmed (56%) ($p<0.01$) (Tables 3 and 4).

Obese phenotype

As hypothesized, unloaded muscle strengthening exercises and aerobic exercises were represented in the top5 of applied exercise therapy modalities and 'increasing physical activity level' was the second most mentioned topic in patient education. Furthermore, our expectation concerning involvement of a dietician was confirmed. Eighty-two percent of the obese phenotype would be advised to visit a dietician, which was significantly higher compared to the remaining phenotypes (Tables 3 and 4).

Depressive mood phenotype

Gradually evolved exercise therapy was the most considered therapeutic exercise modality in the depressive mood phenotype. In accordance with our hypothesis, this 'graded activity' would be combined with pain coping strategies in a considerable part of the population (54%). A priori, we expected that psychological care would be considered in 'some' cases. However, participating physiotherapists reported to consider a referral to a psychologist in 56% of the depressive mood phenotype (Table 4).

TABLE 3. Overview of the content and amount of care in five phenotypes of knee OA

Phenotype		Minimal joint disease		Strong muscle		Severe radiographic OA		Obese		Depressive mood	
Exercise therapy (n=108)	Top-5 therapeutic exercises (%)	Home-exercises	82	Home-exercises	69	Home-exercises	75	Home-exercises	67	Graded activity *	69
		HL muscle strength *	76	Coordinating exercises *	60	Functional exercises	61	UL muscle strength *	57	Home-exercises	64
		Functional exercises	66	Functional exercises	53	Coordinating exercises *	56	Graded activity *	55	UL muscle strength *	58
		Coordinating exercises *	50	HL muscle strength *	36	UL muscle strength *	51	Functional exercises	54	Functional exercises	56
		Mobilising exercises *	34	Graded activity *	31	HL muscle strength *	42	Aerobic exercises *	51	Aerobic exercises *	46
Education (n=108)	Top-5 education topics (%)	Consequences of OA	55	Importance of rest *	57	Treatment options *	50	Weight reduction *	62	Increasing PA level *	57
		Onset of OA	55	Consequences of OA	52	Consequences of OA	49	Increasing PA level *	54	Psychological RF decline *	51
		Treatment options *	49	Onset of OA	52	Onset of OA	43	Contact a dietician *	51	Onset of OA	40
		Pacing PA *	35	Pacing PA *	45	Pacing PA *	36	Physical RF for decline	39	Consequences of OA	38
		Physical RF for decline	20	Decreasing PA level *	36	Physical RF for decline	29	Onset of OA	36	Pain medication	26
Referral† (n=85)	Top-5 referrals (%)	GP *	42	GP *	34	Orthopedic surgeon *	56	Dietician *	82	GP *	71
		Local sports provider *	27	Local sports provider *	33	GP *	48	GP *	69	Psychologist *	56
		Podiatrist	14	Podiatrist	12	Dietician *	22	Orthopedic surgeon *	24	GP nurse mental care *	42
		Orthopedic surgeon *	6	Orthopedic surgeon *	8	Pharmacologist *	12	Local sports provider *	18	Dietician *	36
		Pharmacologist *	4	Psychologist *	2	Local sports provider *	9	Occupational therapist *	16	Multidisciplinar team *	24
Amount of care (%) *		Intake only	12	Intake only	11	Intake only	1	Intake only	1	Intake only	1
		1-5 treatment sessions	55	1-5 treatment sessions	67	1-5 treatment sessions	17	1-5 treatment sessions	1	1-5 treatment sessions	1
		6-10 treatment sessions	27	6-10 treatment sessions	17	6-10 treatment sessions	40	6-10 treatment sessions	17	6-10 treatment sessions	17
		11-15 treatment sessions	6	11-15 treatment sessions	5	11-15 treatment sessions	32	11-15 treatment sessions	31	11-15 treatment sessions	31
		16-20 treatment sessions	0	16-20 treatment sessions	0	16-20 treatment sessions	9	16-20 treatment sessions	36	16-20 treatment sessions	33
		>20 treatment sessions	0	>20 treatment sessions	0	>20 treatment sessions	1	>20 treatment sessions	15	>20 treatment sessions	17

OA = Osteoarthritis; HL = high loaded; UL = unloaded; PA = physical activity; RF = risk factors; * $p \leq 0.01$ between phenotypes;

† A referral by a physiotherapist comprises an advice to the patient and/or his general practitioner to consider involvement of another healthcare provider

TABLE 4. Evaluation of hypotheses concerning the content and amount of care in phenotypes of knee OA

Phenotype	Hypothesis	Identified data	Evaluation hypothesis
Minimal joint disease	Exercise program and education focusing of self-management	Application of exercise AND education: 84.7% Application of exercise OR education: 9.7% Application of exercise NOR education: 5.6% Spearman's ρ .52	+
Strong muscle	Focus of treatment on providing education rather than exercise therapy	Application of education WITHOUT exercise: 32.6% Application of education AND exercise: 59.7% Application of exercise WITHOUT education: 1.4% Application of education NOR exercise: 6.3% Spearman's ρ .26	-
	Pain coping and preventing overloading are main issues in education	Importance of rest, pacing activities, and decreasing physical activity level are all top-5 education topics	+
	High referral rate† to secondary care compared to other phenotypes	Referral rate comprised 8.2%, which was significantly lower than the severe radiographic OA phenotype (56.5%; p<.01) and the obese phenotype (23.5%; p=0.04)	-
	Limited number of treatment sessions	The median number of treatment sessions was 1-5 sessions, which was significantly lower than the remaining phenotypes except for the minimal joint disease phenotype.	+
Severe radiographic disease	Application of exercise therapy regardless the severity of OA	Application in severe radiographic OA: 88.9% Application in minimal joint disease: 93.1% (p=.27) Application in strong muscle strength: 61.1% (p<.01) Application in obese: 89.6% (p=.46) Application in depressive mood: 88.2% (p=.46)	+
	High referral rate to secondary care	Referral rate comprised 56.5%, which was significantly higher than the remaining phenotypes	+
Obese	Inclusion of low impact, (unloading) muscle strengthening exercises as well as exercises to improve general aerobic fitness.	Both local, unloaded muscle strengthening exercises as well as aerobic exercises were represented in the top-5 most performed exercise therapies.	+
	Importance of advice to be physically active as much as possible in daily living	Increasing physical activity level was the second most mentioned topic in patient education	+
	Involvement of a dietician to achieve weight reduction	Referral rate comprised 82.4%, which was significantly higher than the remaining phenotypes	+
Depressive mood	Inclusion of a combination of gradually evolved exercise therapy and an educational program focused at adopting an adequate coping style.	Application of graded activity AND coping: 54.4% Application of graded activity OR coping: 17.8% Application of graded activity NOR coping: 27.8% Spearman's ρ .62	+
	In some cases, advice for psychological care will be considered	Referral rate comprised 56.5%, which was significantly higher than the remaining phenotypes	+/-

Discussion

Elaborating on the identification of five clinical phenotypes of knee OA[10,11], this study aimed to evaluate to what extent currently provided physiotherapy is tailored to five phenotypes: 'minimal joint disease', 'strong muscle strength', 'severe radiographic OA', 'obese', and 'depressive mood' respectively. Based on our results, primary care physiotherapists seem to tailor their treatment to each of the five phenotypes, instead of offering an 'one size fits all' treatment. Our hypotheses concerning the content of physiotherapy and the number of treatment sessions in each specific phenotype were mainly confirmed.

Evaluation of predefined hypotheses

Considering the minimal joint disease phenotype, physiotherapists would frequently use a combination of exercise therapy and education, implying a good fit to clinical guidelines[12-14].

In the strong muscle phenotype, we did not expect a frequent use of high-loaded muscle strength exercises, since high muscle strength is the most prominent characteristic. Maybe, physiotherapists are simply used to include muscle strength exercises in their treatment rather than considering its' added value in each individual patient. Instead of therapeutic exercises, biomechanical interventions, like knee braces and wedges soles could be beneficial in preventing high local stress in the degenerated joint compartment[2,33]. Subsequently, in case of insufficient relieve of complaints despite providing appropriate non-surgical treatment, total joint replacement has shown to be an effective final treatment option[34,35]. However, in contrast to our expectations, a minority of the physiotherapists would account for surgical treatment as the referral rate to secondary care amounted only 8%.

A much higher referral rate was found in the severe radiographic OA phenotype (56%), which was in accordance with our predefined hypothesis. As the relationship between radiographic severity and the indication for surgery is controversial[20,21], therapists could be recommended to focus on a patient's functioning rather than solely on radiographic severity.

In the obese phenotype, the considered content of physiotherapy mainly comprised weight management which was in line with our expectations. Although aerobic exercises were mentioned by 51% of the therapists, an even higher appliance rate could have been expected as this intervention specifically addresses the metabolic syndrome in patients with obesity[36]. On the other hand, Christensen et al. suggested dietary guidance to be preferable over exercise therapy in patients with obesity and knee OA, since the maintaining effect on weight is higher in dietician-supported patients than patients who exclusively received exercise therapy[24].

In the depressive mood phenotype, sixty percent of the physiotherapists would consider a referral to a psychologist, which was higher than we expected prior to the study. Besides a referral for psychological care, physiotherapists also focus on behavioral aspects themselves, for example by applying behavioral graded activity, improving a patient's coping style, and addressing psychological risk factors for functional decline. This approach supports the fundamental role of central sensitization in the depressive mood phenotype and confirms that

knee OA itself not sufficiently explains the complex symptomatology in this subgroup of knee OA[33].

Methodological considerations

First, the high number of missing values should be mentioned. Most missing values were noticed when questions involved five phenotypes simultaneously. Maybe, these questions were too complex. Second, we did not ask for a preferred sequence of eligible interventions. It was previously suggested to apply non-surgical interventions prior to a referral to secondary care[37].
A strength of this study, comprised the use of visual and colored clinical vignettes. Visual communication takes less time to interpret, colored visuals increase willingness to read by 80%, and visual information is supposed to be better remembered[38]. Although vignettes are feasible to use and are accompanied with low costs[28-30], clinical vignettes may merely reflect clinicians competences rather than actual clinical practice[39]. Fourth, the content of our vignettes were restricted to the phenotypes identified by Knoop et al and replicated by van der Esch et al.[10,11]. Although less than 2% of the participating physiotherapists suggested additional subgroups of knee OA, a recent review has identified 79 different theoretical phenotypes of knee OA[33], subdivided into six main groups. Four of our phenotypes represents one of those main groups, except for the severe radiographic OA phenotype. Finally, the mode of stratification should be criticized. In this study, we focused on stratification based on phenotypes of knee OA. However, the question arises to what extent physiotherapists are familiar with thinking in terms of phenotypes. They may achieve personalized care based on other outcomes.

Implications

Primary care physiotherapists seem to tailor their treatment to specific phenotypes of knee OA, rather than using an 'one size fits all' approach. The current study provides a first indication of which interventions are considered per phenotype; development and systematic evaluation of more detailed, stratified interventions are recommended both on clinical effectiveness as well as cost-effectiveness. This may result in phenotype specific recommendations in general clinical guidelines for knee OA.
To facilitate physiotherapists in tailoring their treatment to specific phenotypes, development of a triage screening tool could be valuable. In patients with low back pain, the STarT Back Screening Tool supports clinicians in stratifying patients into subgroups and, in consequence, optimizes treatment and treatment outcome (8,9,40). This stratification could be based on phenotypes, but also on other factors, like a patient's motivation, education level, or previous experiences.
A final remark concerns the rapid development of eHealth. Although the content of physiotherapy treatment will not necessarily change when using eHealth, its' implementation could have major consequences for the organization of a patient's treatment. Especially patients who are eligible for short term, low advanced therapy (i.e. minimal joint phenotype, strong muscle phenotype) could benefit from (partly) substitution of face-to-face care to online

care. (Cost)effectiveness of this blended approach should be examined more thoroughly prior the implementation in clinical OA care[41,42].

In conclusion, based on clinical vignettes representing five different phenotypes of knee OA, physiotherapists seem to tailor their treatment to each of the five phenotypes, instead of an 'one size fits all' treatment. Identified differences in treatment are mainly in accordance with our predefined hypotheses. Future research is recommended on evaluating (cost)effectiveness of stratified interventions and developing a practical screening tool to facilitate stratification of patients with knee OA.

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Appendix 1: Extended description of five phenotypes of knee osteoarthritis (Knoop et al. (2011), van der Esch et al. (2015))

Ann represents the 'minimal joint disease phenotype', Bert represents the 'strong muscle phenotype', Corine the 'severe radiographic osteoarthritis phenotype', Dory the 'obese phenotype', and Erica the 'depressive mood phenotype'

Appendix 2:
Survey questionnaire 'Physiotherapy in knee osteoarthritis: one size fits all?'

1. How many patients suffering from osteoarthritis do you treat monthly?
   Only by exception / 1 or 2 patients / 3 to 5 patients / 6 to 10 patients / >10 patients

2. What percentage of the total population with osteoarthritis particularly involves knee osteoarthritis?
   0% / About 25% / About 50% / About 75% / 100%

3. Which interventions do you generally use in patients with osteoarthritis of the knee? (Please mark a maximum of five interventions)
   Electrotherapy / Hydrotherapy / Assessing braces / Lasertherapy / Massage / (Medical) taping / Therapeutic exercise / Manual therapy / TENS / Heat or ice / Ultrasound / Education regarding effective self-management / Other (please specify)

Suppose that Ann visits your practice. Results of the anamnesis and physical examination were presented in the figure below.

4. Ann would like to enjoy gardening again, without a continuous painful knee. Suppose, you decide to start a physiotherapy treatment. Which interventions would you include? (Please mark a maximum of five interventions)
   Electrotherapy / Hydrotherapy / Assessing braces / Lasertherapy / Massage / (Medical) taping / Therapeutic exercise / Manual therapy / TENS / Heat or ice / Ultrasound / Education regarding effective self-management / Other (please specify)

In addition to Ann, another four patients with knee OA request for your help: Bert, Corine, Dory and Erica. Compared to Ann, those patients were of similar age, were all referred for their GP, visit a physiotherapist for the first time, are former shopkeepers and enjoy gardening. However, they also differ from each other. Next questions are about consequences of these differences regarding physiotherapy treatment of Ann, Bert, Corine, Dory and Erica.

5. Which interventions would you include in each patient's treatment? (Please mark a maximum of five interventions for each patient)
   Electrotherapy / Hydrotherapy / Assessing braces / Lasertherapy / Massage / (Medical) taping / Therapeutic exercise / Manual therapy / TENS / Heat or ice / Ultrasound / Education regarding effective self-management / Other (please specify)

6. If you decide to perform therapeutic exercises, which kind of exercise would you include in each patient's treatment? (Please prioritize your five preferred interventions for each patient)
   Home-exercises / Local high-loaded muscle strengthening exercises / Local unloaded muscle strengthening exercises / Functional therapeutic exercises / Aerobic exercises / Coordinating exercises / Mobilising exercises / Gradually evolved exercises (graded activity) / Hydrotherapy / Other (please specify)

7. If you decided to perform therapeutic exercises, how would you deliver your intervention? (Please mark which manner(s) fit(s) to each of the five phenotypes)

Individually under close supervision / Individually including performing exercises independently / By group treatment / By a consult to teach home-exercises / By written home-exercises / Under supervision of a fitness coach / By referral to a local sports provider / Other (please specify)

8. If you decided to include education, which topics would be covered? (Please mark which topics would be covered in each of the five phenotypes)
   Onset of OA / Consequences of OA / Physical risk factors for functional decline / Psychoogical risk factors for functional decline / Socio-demographic risk factors for functional decline / Treatment options in OA / Advises regarding use of braces / Advises regarding use of walking aids / Advises regarding pain medication / Advises regarding food / Advise to contact a dietician / Advise to contact the GP / Importance of weight reduction / Importance of rest / Importance of increasing physical activity level / Pacing physical activities / Preventing painful activities / Decreasing physical activity level / Other (please specify)

9. How many times would you be likely to see each of the five patients? (Please check the most appropriate box)
   Just an intake / 1-5 sessions / 6-10 sessions / 11-15 sessions / 16-20 sessions / 21-50 sessions / >50 sessions

10. To what extent influences a patient's reimbursement your choice regarding the number of delivered treatment sessions?
    Not at all / To a certain extent / Substantially / Completely

11. Which timeframe fits the best to each patient's treatment from the first to the last visit?
    <1 month / 1-2 months / 3-4 months / 5-6 months / 6-12 months / >12 months

12. To whom would you be likely to refer each of the five patients? (Please check all that apply)
    GP / Orthopedic surgeon / Rheumatologist / Psychologist / Multidisciplinary pain team / Pharmacologist / Occupational therapist / Dietician / Podiatrist / Primary care assistant practitioner mental health care / Local sports provider / Acupuncturist

This questionnaire describes five fictional patients with knee OA who could be presented in primary care physiotherapy. These patients represents different phenotypes of knee OA

13. In case of ten patients with knee OA would present themselves in your practice, how many of those patients would fit to the description of Ann, Bert, Corine, Dory and Erica. (Divide the sum of ten over the five patients, including a remaining category for patients who do not fit to any of the described phenotypes)

14. If you have indicated that a part of your population of patients with knee OA does not fit to any of the five phenotypes, could you please describe the group(s) of patients you are likely to see in your practice?

Finally, we would like to gather some demographic data.

15. I am a
    Male / female

16. My age is:
    <30 years / 30-40 years / 41-50 years / 51-60 years / >60 years

17. I operate as a:
Physiotherapist / Exercise therapist / Other (please specify)

18. Regarding this profession, my year of graduation was:
    <1970 / 1970-1980 / 1981-1990 / 1991-2000 / 2001-2010 / >2010

19. Compared to an average therapist, my level of expertise in OA is
    Lower / Similar / Higher / I am an expert in the field of OA

20. My two most important motivations to join an Arthritis Association are:
    Interest in the target group / Possibility of exchanging general knowledge regarding treatment of patients with OA / Possibility to discuss patient cases / Possibility to meet fellow therapists / Possibility to recruit new patients / Possibility to improve the practice's bargaining position with healthcare insurers / Possibility to position your practice against nearby practices

21. The practice site could be best described by:
    Rural / Suburban / Urban

5

Patient-specific self-assessment instruments for measuring physical function: a systematic review of measurement properties

Published in: J Clin Epidemiol. 2012 Jun;65(6):590-601

https://doi.org/10.1016/j.jclinepi.2011.12.005

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Abstract

Objective To identify patient-specific self-assessment instruments which measure physical function in patients with musculoskeletal disorders and to evaluate the descriptive properties as well as the psychometric qualities of these instruments.

Study Design and Setting After a systematic search, included instruments were evaluated psychometrically by the checklist 'quality criteria for measurement properties of health status instruments'

Results Twenty-three studies were included, referring to twelve instruments. Nine different versions of the Patient Specific Functional Scale (PSFS) were identified. The practical elaboration of the different versions of the PSFS varied widely. None of the instruments were tested on all psychometric quality criteria of the checklist. The PSFS described by Cleland *et al.* was most extensively investigated and obtained exclusively positive scores. Overall, construct validity, reliability and responsiveness were evaluated most frequently.

Conclusion The descriptive properties and psychometric quality of patient-specific instruments measuring physical function, are only partly investigated. The PSFS was the most investigated instrument: nine different versions have been evaluated psychometrically. The version of Cleland *et al.* was most extensively investigated, obtained exclusively positive scores following the quality criteria by Terwee *et al.* and could be recommended for clinical use therefore. Future research will be necessary to confirm the psychometric quality of patient-specific instruments measuring physical function in patients with musculoskeletal disorders.

Introduction

Musculoskeletal disorders are one of the major health care problems facing the Dutch population. Low back pain is the most prevalent disorder, with a point prevalence of 24.1% in the total population[1]. Frequently, patients with musculoskeletal disorders are faced with disability which limits them in performing activities of daily living. Disability entails high economic, societal and personal cost[2,3]. To diminish disability, non-pharmacological treatments (such as rehabilitation or physical therapy) are focussed on both a patient' physical functioning and / or his context, including his psychological and social functioning[4,5]. Considering many contextual factors that determine disability are common across musculoskeletal disorders and even relevant to any chronic health condition, especially a patient' physical functioning makes the difference between the one and the other patient with musculoskeletal disorders[5]. To assess a patients' level of physical functioning and to evaluate the effect of interventions in the clinical encounter, high quality measurements are necessary[6].

Physical functioning can be assessed in different ways. Firstly, general measurement instruments, like the MOS 36-Item Short Form Health Survey (SF-36) (physical function subscale)[7-9], are often applied. Secondly, disease-specific tools are used, for example the Neck Disability Index[10]. Both general and disease-specific tools are instruments which content is completely set, irrespective a patients' health problem, request for help or nature of complaints. Data produced by these so called 'fixed-item' tools are convenient and relatively simple to categorize and compare across patients and settings[11].

However, fixed-item tools are often difficult to interpret on an individual patient level. These tools do not consider patients' preferences and variability in performance on particular activities[12]. For example, the ability to perform gardening will be of low relevance to a patient who does not own a garden or such as the ability to climb stairs will not be relevant to a patient who always takes the elevator.

The interest in so-called patient-specific outcomes which address each patient's priorities in outcome assessment, is increasing in clinical practice and research[12,13]. In contrast to fixed-item instruments, patient-specific instruments can identify relevant issues on an individual level and allow the evaluation to focus on what is important to each patient[12]. Similar to fixed-items instruments, patient-specific instruments have limitations. The question arises to what extent the outcomes are comparable between patients, because of the individualized content. The application of statistical techniques is therefore questionable. In addition, floor effects may occur as patients will choose difficult tasks as 'most important impaired activities'[11].

Nevertheless, because of the increase of a 'patient-based concept' in health policy, individualized outcome tools will become more and more important. Several patient-specific self-assessment instruments (self-administrated and interview-based) have been developed in

patients with musculoskeletal disorders[12]. However, a complete overview including a psychometric quality assessment of available patient-specific self-assessment instruments concerning physical function is lacking.

The objective of the current study is to identify available patient-specific self-assessment instruments which measure physical function in patients with musculoskeletal disorders and to evaluate the descriptive properties as well as the psychometric qualities of these instruments.

Methods

Search strategy

An extensive search strategy was conducted in the electronic databases PubMed (1966 – December 2011), CINAHL (1982 – December 2011) and Embase (1988 - December 2011). The search strategy was built upon four elements: 1. outcome assessment; 2. patient-specific character of outcome assessment; 3. outcome dimension physical function and 4. psychometric qualities. The search strategy was formulated in PubMed and adapted for use in other databases (see appendix 1). Additionally, reference lists of all relevant articles were screened to include potential articles.

Selection criteria

The following inclusion criteria were used:

1. The instrument is a questionnaire, a rating scale or a (semi-structured) interview; *2*. The instrument minimally measures the dimension 'physical function'; *3*. The instrument is applied to patients with musculoskeletal disorders; *4*. The instrument has a patient-specific character; *5*. Investigating the measurement properties of the instrument was the main aim of the study; *6*. Publications describing different versions of the same test with different items were both included;
7. For practical reasons, only articles published in English, German, French or Dutch were considered for inclusion; *8*. Only full-length published articles were included.

An article was excluded if: *1*. The instrument was a performance based test; *2*. The instrument was a different language version of an original instrument.

Study selection procedure

The study selection process was performed in two stages. The first selection on titles and subsequently on abstracts, was independently performed by two reviewers (JaB, PaH). The second step comprised reviewing full-text articles against the mentioned inclusion criteria. Disagreements concerning selection and inclusion of studies were resolved by discussion. A third reviewer (MfP) was consulted in case of persisting disagreement.

Data extraction

Study characteristics (authors, title, year of publication) and descriptive characteristics of the instrument were extracted from the selected articles, including name of the instrument, target population, size of the population in which the instrument was applied, purpose of the instrument, outcome domain(s), referral to a specific time period, mode of administration (self-administered or interview based), mode of selecting items, number of scales, number of items per scale, response options, range of scores and time to administer.

Psychometric quality assessment

Psychometric quality was determined using the standardized checklist 'quality criteria for measurement properties of health status questionnaires'[14] (see appendix 2). This checklist, developed by Terwee *et al.*, is based upon the criteria of the 'Scientific Advisory Committee (SAC) of the Medical Outcomes Trust[15]'. In contrast to the SAC-list, the list of Terwee *et al.* mentions explicit criteria for what constitutes good measurement properties. All measurement properties were rated as '+' (positive), '?' (doubtful), '-' (negative) or '0' (no information available). The following measurement properties were evaluated:

Content validity. Content validity examines the extent to which the domain of interest is comprehensively represented by the items in the instrument[16]. This term was operationalized by describing the measurement aim of the instrument, the target population, the measurement concept, the way of item selection and the interpretability of the items[17,18].

Internal consistency. Internal consistency is a measure of the extent to which items in a instrument (sub)scale are correlated, thus measuring the same construct. Factor analysis should have been applied to determine whether the items of a scale measure the same construct. In addition, Cronbach's alpha should have been calculated as a measure of internal consistency. An alpha of ≥.70 was considered acceptable[19].

Criterion validity. Criterion validity refers to the extent to which scores on a particular instrument are related to a gold standard. Positive evaluations were given when the gold standard was convincingly described as a real gold standard and if the correlation with the gold standard was at least .70.

Construct validity. Construct validity is a measure of the extent of which scores on a particular instrument relate to other measures in a manner that is consistent with theoretically derived hypotheses concerning the concepts that are being measured[17,18]. Construct validity was considered adequate if specific hypotheses were defined regarding the relationships with other measures of physical function and if ≥75% of these hypotheses were confirmed.

Reproducibility. Reproducibility concerns the amount of which repeated measurements in stable persons provide similar results. Reproducibility can be divided into two aspects:

reliability and absolute agreement. Reliability refers to the extent to which patients can be distinguished from each other, despite measurement errors (relative measurement error). Intraclass Correlation Coefficient (ICC) (continuous data) or weighted Cohen's Kappa (discrete data) were regarded as adequate measures[18]. A value of .70 was used as a minimum standard[19].
Agreement describes the extent to which the scores on repeated measures are similar to each other (absolute measurement error). Bland & Altman Limits of Agreement (LOA) and the smallest detectable change (SDC) were considered adequate measures of agreement[19-22]. A positive rating was assigned if the minimal important change (MIC) was outside the LOA or if the SDC was smaller than the MIC[14].

Responsiveness. Responsiveness was defined as the ability of an instrument to detect clinically important changes over time in the concept to be measured[23-25]. Responsiveness could be determined in many different ways[14]. However, considering responsiveness as a measure of longitudinal validity, responsiveness is independent of the treatment effect. It was considered adequate if the SDC was smaller than the MIC, if the responsiveness ratio (RR) was ≥1.96[26] or if the area under the 'receiver operating characteristics' (ROC) curve was ≥.70[23].

Floor and ceiling effects. Floor and ceiling effects were considered to be present if more than 15% of the respondents achieved the lowest or highest possible score, respectively[27]. A positive rating was assigned if floor and ceiling effects were absent.

Interpretability. Interpretability is defined as the extent to which one can assign qualitative meaning to quantitative scores[28]. To assess interpretability, means and standard deviations (SD) of relevant groups should have been presented. In addition, the MIC should have been defined. Interpretability was scored positively if mean scores and SD were presented of at least four subgroups of patients and if the MIC was defined.

Psychometric quality assessment was conducted by two reviewers independently (JaB, MfP). When disagreement was found between the two reviewers, the measurement quality which was subject of disagreement, was discussed. A third reviewer (CV) was consulted in case of persisting disagreement.

Overall quality

To obtain an overall score for psychometric quality of the identified instruments, the number of positive ratings out of the total rated items for each instrument was counted.

Results

Study selection procedure

The literature search identified 1617 unique articles. After the selection procedure, 23 studies were included, referring to twelve different instruments (figure 1). The full names of the investigated instruments are presented in Table 1. The percentage of agreement between the two reviewers amounted 88% after stage one and 75% after stage two of the selection procedure.

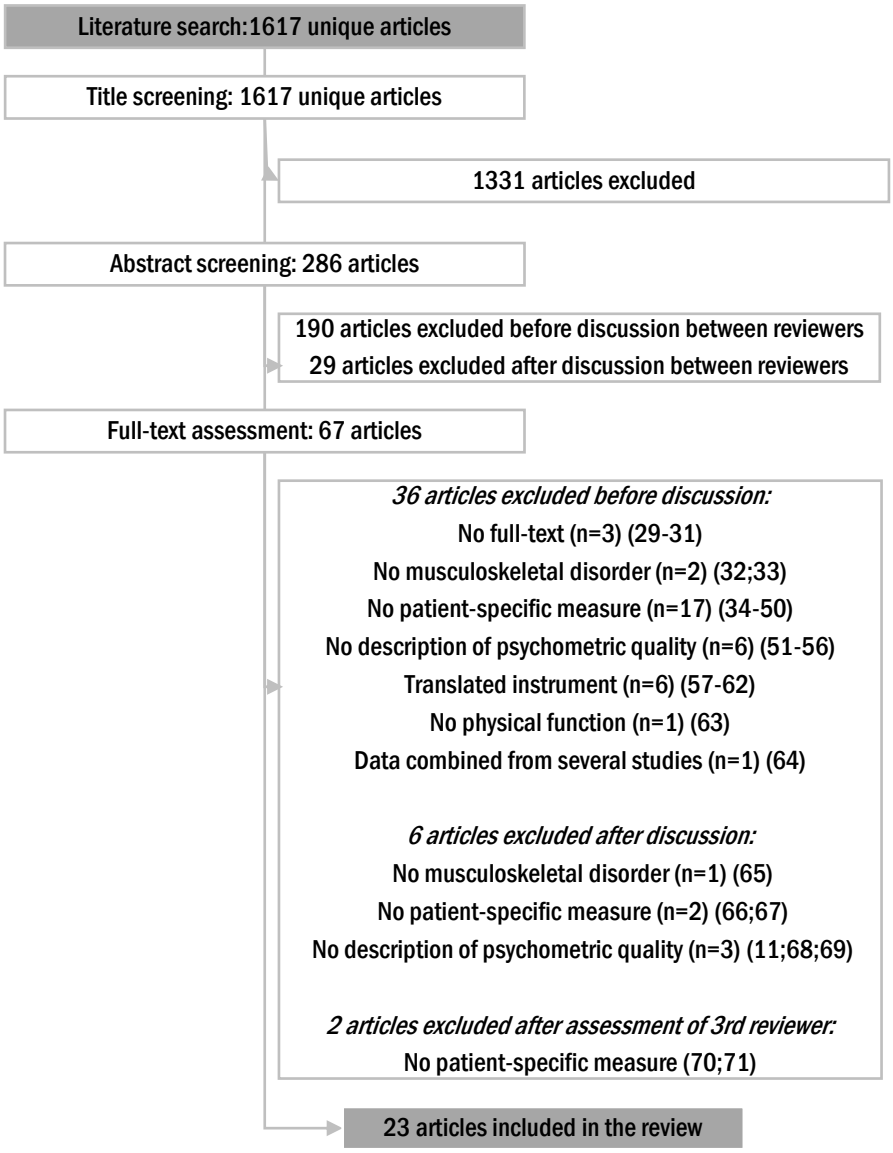

FIGURE 1. Selection procedure of a systematic review on patient-specific instruments measuring physical functioning

TABLE 1. Full names of the included instruments

Abbreviation	Full name
COPM	Canadian Occupational Performance Measure
I-HAQ-DI	Individualized Health Assessment Questionnaire Disability Index
IMAS	Individualized Milliken Activities of Daily Living Scale
I-PSI	Interviewer-administrated Patient-Specific Index
I-WOMAC	Individualized Western Ontario and McMaster Universities Osteoarthritis Index
MACTAR	McMaster Toronto Arthritis Patient Preference Disability Questionnaire
PSA	Patient-Specific Approach
PSAQ	Patient-Specific Activity Questionnaire
PS-DASH	Patient-Specific Disabilities of the Arm, Shoulder and Hand questionnaire
PSFS	Patient-Specific Functional Scale
SMCS	Severity of the main complaints scale
S-PSI	Self-reported Patient-Specific Index

Description of the instruments

Three instruments, derived from eleven articles, were found which represented minor variations of the same construct measured, namely: patients rate their most important disabilities and evaluate these disabilities over time. The most common example to measure this construct is the Patient-Specific Functional Scale (PSFS). Nine different versions of the PSFS were included in this review[72-80]. These versions differed in target population, mode of administration (interview based versus self-administrated) and scoring method. The Severity of the Main Complaints Scale (SMCS)[81] measures the same construct, as well as the McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR) does. However, the MACTAR additionally investigates patients' general, emotional and social health status[82,83].

More extended versions of the PSFS rate, beside the most important impaired activities, the severity of these impairments and / or the frequency of the impaired activities in daily life. Hereby, two measurement tools offer patients the possibility to define their most important impaired activities[84,85]; four measurement tools permit patients to choose impaired activities out of a pre-defined list[12;86-88] and also four measurement tools score severity and importance of all activities named in a pre-defined list[13,89-91].

Three studies described instruments which were derived from existing instruments: the Patient-specific Arm, Shoulder and Hand questionnaire (PS-DASH)[90], the Individualized Health Assessment Questionnaire Disability Index (I-HAQ-DI)[12] and the Individualized Western Ontario and McMaster Universities Osteoarthritis Index (I-WOMAC)[88]. The original DASH, HAQ and WOMAC are extensively psychometrically evaluated and widely used in clinical practice.

The majority of the identified instruments are used to evaluate changes over time [13,72,73,75-78,81,84-91]. Only the PSFS described by Westaway and colleagues and the I-HAQ-DI have a discriminative purpose[12,79].

All descriptive characteristics of the included measurement tools are presented in Table 2.

TABLE 2. Description of the included patient-specific instruments

Measurement tool	Purpose	Target population	Size*	Outcome domain(s)	Mode of administration	Mode of item selection	No. of scales	Number of items per scale	Response options	Range of scores	Time to administer
COPM [84;92]	Evaluative	Various musculo-skeletal disorders (small part neuro-muscular disorders)	237	Physical functioning (performance)	Interview-based	Patient	2	Unlimited	0-10	0-100	30-45 minutes
I-HAQ-DI [12]	Discrimi-native	Rheumatoid arthritis	370	Physical functioning (capacity)	Self-administrated	Investigator + Patient	2	5	0-3	0-45	?
IMAS [89]	Evaluative	Post-surgical traumata upper extremity	45	Physical functioning (capacity & performance)	Self-administrated	Patient	6	Meal: 8 Hygiene: 9 Dressing: 8 Manipulation: 9 Cleaning: 7 Else: 6	5 + 3	47-235	10 minutes
I-PSI [13]	Evaluative	Total Hip Replacement	74	Physical functioning (capacity & performance)	Self-administrated	Investigator + Patient	4	6, 7, 15, 28	7	0-100 percen-tile score	16 ± 5.5 minutes
I-WOMAC [88]	Evaluative	Hip / knee osteoarthritis	1218	Physical functioning (performance)	Self-administrated	Investigator + Patient	1	5	0-100	0-500	?
MACTAR [82,83]	Evaluative	Rheumatoid arthritis, Chronic low back pain	155 100	Physical functioning (performance) Health status	Interview-based	Patient	2	Trans: 0-10 Status: 5-9	1-7	11-47	15 minutes
PSA by Beurskens [86]	Evaluative	Low back pain	150	Physical functioning (performance)	Self-administrated	Patient	1	3	0-100	0-300	?
PSA by Rollman [85]	Evaluative	Temporo-mandibular disorders	132	Physical functioning (performance)	Self-administrated	Patient	1	1	0-100	0-100	?

Psychometric quality assessment

Psychometric properties of the included patient-specific instruments are presented in Table 3. None of these instruments has been tested on all psychometric quality criteria of the checklist. One instrument has been tested positively on four items[73], nine on two items [13,72,78-80,84,85,87,91,92], five on one item[74,77,81,82,88] and six instruments has not been evaluated positively on any of the items[12,75,76,86,89,90].

Content validity. None of the instruments scored positively on content validity, unless the measurement aim, the concept being measured and the target population were mostly described well. Content validity was often assessed as 'unknown', because it was unclear whether both the patient and an investigator or an expert were involved in item selection.

Internal consistency. Two instruments (Individualized Western Ontario and McMaster Universities Osteoarthritis Index (I-WOMAC) and I-HAQ-DI)[12,88] were assessed on internal consistency. Although Cronbach's alpha was .93 and .87 respectively, internal consistency was scored as 'doubtful', because confirmatory factor analysis was not performed.

Criterion validity. The self-reported version of the Patient Specific Index (S-PSI) was positively related to the interview-based version of the Patient Specific Index (I-PSI) (Pearson product moment correlation (r) = .78) and therefore obtained a positive score on criterion validity[91]. The Individualized Milliken Activities of Daily Living Scale (IMAS) instrument was not related to a convincible gold standard and was scored as 'doubtful'[89]. Criterion validity was not assessed for the remaining instruments.

Construct validity. Ten studies presented specific hypotheses regarding the strength and direction of expected correlations with other measurement tools which are supposed to measure physical function[13,72-74,78-80,82,84,90]. Eight out of these ten studies obtained a positive score. Two studies obtained a negative score, because less than 75% of the hypotheses was confirmed[79,90]. The Individualized Western Ontario and McMaster Universities Osteoarthritis Index (I-WOMAC) and the I-HAQ-DI were assessed on construct validity without hypotheses-testing, but with comparison to other the original instrument[12,88]. In nine studies, construct validity was not assessed.

Reproducibility – reliability. The PSFS described by Chatman, Cleland, Stratford and Westaway, as well the I-WOMAC, the I-PSI, the S-PSI and the Patient Specific Approach (PSA) described by Rollman seem to be reliable instruments to assess patient-specific physical function (.72 ≤ ICC ≤ .92)[13,72,73,78,79,85,88,91]. The PSFS described by Young showed an ICC of .17 and was rated negatively as a consequence[80]. One study used Pearson correlations to express reliability (r =0.91) and was therefore scored as 'doubtful'[89].

Reproducibility – agreement. Two instruments obtained positive scores on agreement[73,79]. In both cases, the SDC was smaller than the MIC. The PSFS by Stratford *et al.*[78] presented a Standard Error of Measurement (SEM) of .41, but did not define a MIC and subsequently obtained a 'doubtful' score.

Responsiveness. Information on responsiveness lacked in four studies[74,89-91]. The PSFS by Cleland indicated an AUC of .99, whereas the PSFS by Stewart and by Young indicated both an AUC of .71[73,77,78]. The Canadian Occupational Performance Measure (COPM) showed an AUC of .79, the SMCS showed an AUC of .82, the Patient-Specific Activity Questionnaire (PSAQ) of .75 and the PSA described by Rollman presented an AUC of .91[85-87]. An AUC ≥.70 is required for a positive score. The PSFS by Pengel *et al.* was also scored positively, based on a Guyatt Responsiveness Ratio of 2.1[76]. Conform the criteria of Terwee *et al.*, the remaining studies used an inadequate design to assess responsiveness, such as a sensitivity-to-change coefficient, the standardized response mean and the standard error.

Floor and ceiling effects. The PSAQ and the PSFS by Chatman *et al.* were evaluated with respect to floor and ceiling effects. The PSAQ scored positively on this item, because only six percent of the respondents had the lowest possible score[87]. Chatman *et al.* did not indicate a specific percentage[72] and was therefore assessed as 'doubtful'.

Interpretability. None of the studies met all criteria concerning interpretability. Because mean scores and standard deviations of at least four subgroups lacked, as well information about the MIC, interpretability was scored as 'no information available' in all studies.

TABLE 3. Psychometric quality of the included patient-specific instruments

Measurement tool	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility Agreement	Reproducibility Reliability	Responsive -ness	Floor and ceiling effects	Interpre-tability	No. of positive ratings / total no. of ratings
COPM [84;92]	0	0	0	+	0	0	+	0	0	2 / 2
I-HAQ-DI [12]	0	?	0	?	0	0	?	0	0	0 / 3
IMAS [89]	0	0	?	0	0	?	0	0	0	0 / 2
I-PSI [13]	0	0	0	+	0	+	?	0	0	2 / 3
I-WOMAC [88]	0	?	0	?	0	+	?	0	0	1 / 4
MACTAR [82;83]	?	0	0	+	0	0	?	0	0	1 / 3
PSA by Beurskens [86]	0	0	0	0	0	0	?	0	0	0 / 1
PSA by Rollman [85]	0	0	0	0	0	+	+	0	0	2 / 2
PSAQ [87]	0	0	0	0	0	0	+	+	0	2 / 2
PS-DASH [90]	0	0	0	-	0	0	0	0	0	0 / 1
PSFS by Chatman [72]	0	0	0	+	0	+	?	?	0	2 / 4
PSFS by Cleland [73]	0	0	0	+	+	+	+	0	0	4 / 4
PSFS by Gross [74]	0	0	0	+	0	0	0	0	0	1 / 1

Discussion

Twenty-three studies referring to twelve different instruments which investigated psychometric properties of patient-specific instruments measuring physical function in patients with musculoskeletal disorders were identified. The PSFS is the most described tool, with nine different variations. Extended versions of the PSFS were developed to additionally prioritize the patient-mentioned impaired activities. In none of the instruments all measurement properties proposed by Terwee *et al.* have been evaluated[14]. The PSFS described by Cleland *et al.*[73] achieved the highest score with four positively scored items. The PSAQ, the PSFS's by Cleland, Gross and Stewart, the SMCS, the S-PSI, the COPM and the PSA described by Rollman obtained positive scores on all measurement properties which have been evaluated[73,74,77,81,84,85,87,91,92].

One of the treatment goals in patients with musculoskeletal disorders who are disabled in performing activities of daily living, is to improve physical functioning. Assessing impaired activities and evaluating them over time is an adequate method to meet this goal. Nevertheless, the practical elaboration of this method varies across the different instruments. Some instruments only identify impaired activities and rank them with respect to severity[72-76,78-82,85], whereas other instruments additionally investigate the importance of the performance on the impaired activities[12,84,88,90] or the frequency of the impaired activities in daily life[86,87].

The differences in practical elaboration become even more clear in the variations between different versions of the PSFS. Nine identified studies comprised different versions of the PSFS[72-80]. Although all these instruments are designated as 'PSFSs', the scoring method and mode of administration vary between the measurement tools. This hampers comparison between different patients or conditions.

The method of identifying impaired activities differed between the identified instruments. Most instruments allow patients to formulate their own impaired activities. On the other hand, the SMCS, PSAQ, PS-DASH, IMAS, I-WOMAC, I-HAQ, I-PSI, S-PSI and MACTAR use predefined lists of potential activities[12,13,81-83,87-91]. The advantage of the application of predefined lists is the facilitated possibility for comparison with and between different populations and settings. Furthermore, change over time can be indicated easier in disabilities with potential for improvement. On the contrary, the application of predefined lists entails the risk of missing important activities[11].

Psychometric quality was extracted using a checklist developed by Terwee *et al.*[14]. In total, 189 items were assessed. One instrument achieved four out of eight positive scores[73]; six instruments noted no positive score[12,75,76,86,89,90]. Hereby, the overall psychometric quality of patient-specific instruments which measure physical function seems to be low. However, only three items obtained an insufficient score. The vast majority (75%) has been assessed as 'no

information available'. The relative short existence of patient-specific measures might explain this phenomenon. Nevertheless, despite the scarcity of psychometric data concerning patient-specific instruments, construct validity, reliability as well as responsiveness were investigated in more than half of the studies. Construct validity was positively assessed in eight out of twelve studies in which this quality was evaluated[13,72-74,78,80,82,84]. It can be concluded that patient-specific instruments seem to measure the same construct as disease-specific or generic physical function-tools. Eight instruments appeared to be reliable[13,72,73,78,79,85,88,91]. However, in case of evaluative tools, responsiveness is possibly a more appropriate property than reliability. The most adequate approach for evaluating responsiveness is still unclear[25]. Therefore, it is not surprising that we found many different ways in which responsiveness had been determined. Conform the criteria of Terwee *et al.*[14], eight studies used an adequate method (ROC-curve or Guyatts RR)[73,76,77,80,81,85,87,92]. Nine studies used inadequate methods, like the SRM and the ES. However, the SRM and ES are widely administered in psychometric research to assess responsiveness. Therefore, the question arises whether this measurement property is not judged too strictly.
Floor and ceiling effects have been poorly investigated yet. However, patients may indicate very difficult activities as their most impaired activities and, as a consequence, rate these activities with the lowest possible score. The likelihood of improvement of these impossible activities is small, even as the improvement in rating[11]. Therefore, more solid research on floor and ceiling effects of patient-specific instruments is needed.

Some limitations of this systematic review should be acknowledged. First, patient-specific instruments are developed to enable clinicians to measure changes in activities which really matter to individual patients. However, to determine the psychometric quality of patient-specific instruments, evaluation should occur in clinical practice in addition to evaluation in population studies.' Moreover, this review was limited to studies with a primary goal to determine psychometric qualities; studies in which several measurement tools were applied to detect differences in physical function might provide complementary evidence concerning measurement properties. Third, the checklist developed by Terwee *et al.* is not a gold standard to determine psychometric quality of a instrument. It is just a tool to check whether the properties are clear and systematically presented. Thereby, the criteria to obtain a positive score are very stringent sometimes. For example, content validity is exclusively supposed to be positive if both the measurement aim, the target population, the concepts that are being measured, the item selection and the involvement in item selection were sufficiently described. Missing just one of these criteria induce a 'doubtful' score. A final remark concerning the checklist of Terwee *et al.* is the unavailability to determine the overall best instrument.
Nevertheless, based on the current evidence, the PSFS described by Cleland *et al.*[73] could be recommended to use in clinical practice to monitor a patients' progress in a patient-specific way. This instrument has been evaluated most comprehensively and obtained just positive scores. In future, more studies, performed in clinical practice, are needed to confirm the psychometric quality of patient-specific instruments in general and the PSFS described by Cleland in particular.

In conclusion, although twelve instruments have been developed to measure patient-specific function in patients with musculoskeletal disorders, the descriptive properties and psychometric quality of these instruments are only partly investigated. The PSFS is the most investigated instrument: nine different versions have been evaluated psychometrically. The version of Cleland *et al.*[73] was most extensively investigated, obtained exclusively positive scores following the quality criteria by Terwee *et al.*[14] and could be recommended for clinical use therefore. Future research will be necessary to confirm the psychometric quality of patient-specific instruments measuring physical function in patients with musculoskeletal disorders.

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Appendix 1: Search strategy Pubmed (1966 through December 2011)

Outcome assessment (health care) (MeSH) OR Questionnaires (MeSH) OR Assessment Measure* OR Scale* OR Test* OR Instrument* OR Index OR Indices OR "Measurement scale" OR "Rating scale" OR "Self reported scale" OR "Self reported questionnaire" OR "Self administrated questionnaire"

AND

"Patient-centered care" (MeSH) OR Individualized OR "Individualized outcome" OR "Individualized scale" OR "Client centered" OR "Patient based" OR "Patient specific" OR "Patient specific measures" OR "Patient preference" OR "Patient reported" OR "Self reported"

AND

"Activities of Daily Living" (MeSH) OR "Mobility limitation" (MeSH) OR "Motor activity" (MeSH) OR Functional* OR "Functional index" OR "Functional stat*" OR "Functional ability" OR "Functional disability" OR Ability OR Disability OR "Physical ability" OR "Physical disability" OR "Physical function" OR "Physical functioning" OR "Physical performance" OR "Performing activities" OR "Limited activities" OR "Functional limitation" OR "Activity limitation"

AND

"Reproducibility of results" (MeSH) OR Psychometrics OR Psychometric* OR "Psychometric evaluation" OR "Psychometric properties" OR "Psychometric analysis" OR "Psychometric characteristics" OR "Psychometric assessment" OR "Measurement properties" OR Valid* OR Reliability OR Reliable OR Reproducibility OR Reproducible OR Responsive* OR Sensitivity OR Sensitive OR Agreement OR "Internal consistency"

Search date: 6th December 2011
Limits: none
Hits: 161

Appendix 2: Checklist 'Quality criteria for measurement properties of health status questionnaires' (Terwee et al. (2007))

	Property	Definition		Quality criteria[a,b]
1	Content validity	The extent to which the domain of interest is comprehensively sampled by the items in the questionnaire	+	A clear description is provided of the measurement aim, the target population, the concepts that are being measured, and the item selection AND target population and (investigators OR experts) were involved in item selection
			?	A clear description of above-mentioned aspects is lacking OR only target population involved OR doubtful design or method
			-	No target population involvement
			0	No information found on target population involvement.
2	Internal consistency	The extent to which items in a (sub)scale are intercorrelated, thus measuring the same construct	+	Factor analyses performed on adequate sample size (7 * # items and >100) AND Cronbach's alpha(s) calculated per dimension AND Cronbach's alpha(s) between 0.70 and 0.95;
			?	No factor analysis OR doubtful design or method;
			-	Cronbach's alpha(s) <0.70 or >0.95, despite adequate design and method;
			0	No information found on internal consistency.
3	Criterion validity	The extent to which scores on a particular questionnaire relate to a gold standard	+	Convincing arguments that gold standard is ''gold'' AND correlation with gold standard ≥0.70;
			?	No convincing arguments that gold standard is ''gold'' OR doubtful design or method;
			-	Correlation with gold standard <0.70, despite adequate design and method;
			0	No information found on criterion validity.
4	Construct validity	The extent to which scores on a particular questionnaire relate to other measures in a manner that is consistent with theoretically derived hypotheses concerning the concepts that are being measured	+	Specific hypotheses were formulated AND at least 75% of the results are in accordance with these hypotheses;
			?	Doubtful design or method (e.g., no hypotheses);
			-	Less than 75% of hypotheses were confirmed, despite adequate design and methods;
			0	No information found on construct validity.
5	Reproducibility			
	Agreement	The extent to which the scores on repeated measures are close to each other (absolute measurement error)	+	MIC ≥ SDC OR MIC outside the LOA OR convincing arguments that agreement is acceptable;
			?	Doubtful design or method OR (MIC not defined AND no convincing arguments that agreement is acceptable);
			-	MIC < SDC OR MIC equals or inside LOA, despite adequate design and method;
			0	No information found on agreement.
	Reliability		+	ICC or weighted Kappa ≥ 0.70;

	Property	Definition		Quality criteria[a,b]
		The extent to which patients can be distinguished from each other, despite measurement errors (relative measurement error)	? - 0	Doubtful design or method (e.g., time interval not mentioned); ICC or weighted Kappa < 0.70, despite adequate design and method; No information found on reliability.
6	Responsive-ness	The ability of a questionnaire to detect clinically important changes over time	+ ? - 0	SDC < MIC OR MIC outside the LOA OR RR>1.96 OR AUC ≥ 0.70; Doubtful design or method; SDC or SDC ≥ MIC OR MIC equals or inside LOA OR RR≤ 1.96 OR AUC < 0.70, despite adequate design and methods; No information found on responsiveness.
7	Floor and ceiling effects	The number of respondents who achieved the lowest or highest possible score	+ ? - 0	≤ 15% of the respondents achieved the highest or lowest possible scores; Doubtful design or method; > 15% of the respondents achieved the highest or lowest possible scores, despite adequate design and methods; No information found on interpretation.
8	Interpretability	The degree to which one can assign qualitative meaning to quantitative scores	+ ? 0	Mean and SD scores presented of at least four relevant subgroups of patients and MIC defined; Doubtful design or method OR less than four subgroups OR no MIC defined No information found on interpretation.

MIC = minimal important change; SDC = smallest detectable change; LOA = limits of agreement; ICC = Intraclass correlation; SD, standard deviation.

[a] + = positive rating; ? = indeterminate rating; - = negative rating; 0 = no information available.

[b] Doubtful design or method = lacking of a clear description of the design or methods of the study, sample size smaller than 50 subjects (should be at least 50 in every (subgroup) analysis), or any important methodological weakness in the design or execution of the study.

6

Validity and responsiveness of the Dutch McMaster Toronto Arthritis patient preference questionnaire (MACTAR) in patients with hip/knee osteoarthritis

Published in: J Rheumatol. 2012 May;39(5):1064-73

https://doi.org/10.3899/jrheum.110876

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Abstract

Objective To determine the content validity, the construct validity and the responsiveness of the Dutch MACTAR in patients with osteoarthritis (OA) of the hip or knee.

Methods The MACTAR comprises two parts: a transitional part and a status part. Content validity was investigated by comparing patient-elicited activities to items on the 'Western Ontario and McMaster Universities Osteoarthritis Index' (WOMAC) and the 'Medical Outcome Survey Short Form 36' (SF-36). Construct validity was determined by correlating MACTAR outcomes with WOMAC/SF-36 outcomes. Responsiveness was investigated by correlating MACTAR, WOMAC and SF-36 change scores with Patient Global Assessment (PGA) scores and plotting a Receiver Operating Characteristics (ROC) curve.

Results Eleven percent of the 894 impaired activities identified by 192 patients were not represented in either the WOMAC or the SF-36. The correlations (r_s) investigated for the MACTAR-transitional part varied between .27 and -.40; the status part correlated moderately with the general health scale of the SF-36 (r_s=.44). MACTAR change scores correlated better with PGA than WOMAC/SF-36 change scores. The area under the ROC-curve amounted to .90.

Conclusion Our results suggest that the MACTAR exhibits moderate construct validity and good responsiveness in a population of patients with OA of the hip or knee. Furthermore, the MACTAR is potentially better able to detect changes over time in activities that are important to individual patients compared to other tools measuring physical function (WOMAC, SF-36). Therefore, clinicians could use the MACTAR to evaluate clinically relevant changes over time in patient-specific physical functioning.

Introduction

Osteoarthritis (OA) is a common chronic musculoskeletal disorder[1], which can result in moderate to severe limitations in physical functioning[2]. Limited physical functioning can lead to a diminished quality of life[3-5]. OA treatment guidelines recommend exercise therapy to reduce impairments in physical function due to OA[6,7]. Exercise therapy can thus enable individuals to better meet the demands of daily living[8-11].

A number of tools are available to clinicians to evaluate the effect of exercise therapy on physical function. General, disease-specific and patient-specific tools can be distinguished, all of which are applied as either (self-reported) questionnaires or performance-based tests. A systematic review of the psychometric quality of both questionnaires and performance-based tests in patients with OA of the hip or knee has been published recently[12,13]. The reviews recommended the application of the 'Western Ontario and McMaster Universities Osteoarthritis Index' (WOMAC) (14), the 'Medical Outcome Survey Short Form 36' (SF-36)[15-17] and multi-activity tests when evaluating physical function in patients with OA[12,13].

Standardized tools, applied to all patients in an identical manner, are recommended for the evaluation of physical functioning. Data produced by these tools may be conveniently and relatively easily categorized and compared between patients and across settings[18]. However, standardized tools are often difficult to interpret at individual level and fail to take account of individual preferences and variation in the performance of particular activities[18]. Patient-specific tools measuring physical function have been developed based on the need for a more 'patient centered' approach as set out in health care policy and to enable clinicians to measure changes in activities which really matter to individual patients[19]. In contrast with standardized tools, patient-specific instruments can identify the relevant issues at individual level and allow the evaluation to focus on what is important to each individual patient[18]. Although the possibilities to compare statistical data between patients are minimal, the application of patient-specific tools may improve the validity and responsiveness for the assessment of physical function[18,19].

The 'McMaster Toronto Arthritis Patient Preference Disability Questionnaire' (MACTAR) is one example of a patient-specific scale measuring physical function[20,21] (See Appendix 1). The objective of the MACTAR is to identify individual disabilities due to the disease and their relative importance to the patient, complemented by questions on general health status[20]. The MACTAR has been described as a highly responsive and valid tool for the evaluation of physical function in patients with rheumatoid arthritis[21]. A recent psychometric evaluation of the questionnaire in patients with chronic lower back pain and patients with systemic sclerosis showed moderate correlations with general and disease-specific tools which measure physical function[22,23].

To enable clinicians to use the MACTAR when evaluating physical function in patients with OA of the hip or the knee, the psychometric properties of the questionnaire in this specific population must be determined. Therefore, the objective of the present study is to determine the content validity, the construct validity and the responsiveness of the MACTAR in patients with OA of the hip or knee.

Methods

Study design

Data reported in this study were collected from a cluster randomized controlled trial of 200 patients with OA of the hip or knee over a 12-week period (maximum 18 sessions), that compared behavioral graded activity with usual care in accordance with the Dutch physical therapy guidelines[24]. The content of the interventions has been described elsewhere[24]. The Medical Ethics Committee of the VU University Medical Center, Amsterdam, The Netherlands approved the study. For the purposes of the present validation study, data on 'physical function' were used, as well as the descriptive data on the study population.

Study population

Participants were recruited between November 2001 and May 2003 through participating physical therapists and local newspapers. Dutch-speaking patients with OA of the hip or knee (based on the criteria of the American College of Rheumatology[25,26]) aged between 50 and 80 years who experienced diminished physical function were included in the study[24]. Participants who completed both baseline and follow-up (week 13) measurements were eligible for inclusion in the present psychometric evaluation.

Measurements

Demographic and clinical data

Demographic and clinical data , including age, gender, duration of symptoms, OA location and OA grade, according to Kellgren & Lawrence[27], were collected from participating patients.

Physical function

Dutch MACTAR - The objective of this interview-based measurement tool is to evaluate changes in patient-specific physical function over time. It comprises two parts. The baseline interview starts with a transitional part. In this part, a trained interviewer asks the patient to identify up to ten activities in which he / she experiences difficulties because of OA, such as activities in domestic care, professional life and social interaction. The identified activities are ranked by the patient from 1 to 10 in order of importance: '1' for the activity the patient most wishes to be able to do without pain or discomfort due to OA, '2' for the next most important activity

and so on. The top-five prioritized activities are evaluated at follow-up. The second part of the MACTAR (status) collects information on health status. Perceived overall health, as well as psychological, emotional and social well-being is measured by five questions (Likert type rating scale); when a question obtains a less than optimal score, a follow-up question probes whether this is due to OA.
At the follow-up interview (week 13), changes in physical function are investigated. Patients evaluate progress on their five most important activities as indicated in the transitional part of the baseline interview, by evaluating each activity as 'less of a problem' (3 points), 'the same' (2 points) or 'more of a problem' (1 point). Patients also rate the perceived change in their OA on a 7-point Likert scale. The status part reassesses patients' health status.

It is quite difficult to allocate a total score to the MACTAR tool, because each part measures different domains. Moreover, the transitional part and the status part employ different scoring methods. While the transitional part measures change in physical function between baseline and follow-up, the status part investigates current health status, at both baseline and follow-up. The scoring method is presented in Table 1. Because of the differences between the transitional and status parts, scores were not added together, but presented separately. The MACTAR was translated into Dutch by Verhoeven et al. and validated in a population with rheumatoid arthritis[21].

TABLE 1. Scoring method of the McMaster Toronto Arthritis patient preference questionnaire

	Transitional part	Status part
Baseline	-	Min: 5 (poor health status) Max: 25 (good health status)
Follow-up	Min: 6 (maximum deterioration) Max: 22 (maximum improvement)	Min: 5 (poor health status) Max: 25 (good health status)
Change score	The same as the follow-up score	Min: -20 (maximum deterioration) Max: +20 (maximum improvement)

Dutch WOMAC - The physical function subscale of the WOMAC contains 17 items which represent common activities in daily living[14,28]. Patients are asked how much difficulty they have had performing the activities mentioned. Each item is scored on a categorical scale, from 'no difficulty' (score 0) to 'extreme difficulty' (score 4). The total score varies from 0 (no difficulties) to 68 (extreme difficulties). Change scores on the WOMAC physical function subscale can vary between -68 (maximum improvement) to +68 (maximum deterioration). The WOMAC has been shown to be reliable and valid in patients with OA of the hip or knee[14,28] and the Dutch WOMAC permits valid international Dutch-English comparisons after differential item functioning[28].

Dutch SF-36 - The SF-36 investigates quality of life[15-17,29]. It comprises eight subscales, three of which were used in the present validation study: physical functioning, role-physical and general health. Scores on each subscale range from 0 to 100; higher scores reflect better health status. The SF-36 has been validated for patients with various diagnoses, including those with OA[30];

the Dutch language version has proved to be practical, reliable and valid for use in general population surveys[29].

Self-perceived change - At the follow-up evaluation, self-perceived change in physical function was assessed by a 'Patient Global Assessment' (PGA) score. Patients were asked to rate their overall perception of improvement since the start of the intervention on a scale ranging from '1' (vastly deteriorated) to '8' (completely recovered). PGA scores provide reliable assessments of health transition in people with musculoskeletal disorders[31].

Statistical analyses

Descriptive statistics were applied to describe the study population. PGA ratings were dichotomized as 'improved' (PGA score 5, 6, 7 or 8) versus 'not improved' (PGA score 1, 2, 3 or 4). For continuous data, independent t-tests were used to calculate differences at baseline between those patients who improved and those who did not. For categorical data, Mann-Whitney U tests were used to compare between groups.

Content validity

Content validity examines the extent to which the domain in question is comprehensively represented by the items in the questionnaire[32,33]. To determine whether the items in the MACTAR refer to relevant aspects of the construct and are relevant to the purpose of the instrument, the impaired activities mentioned by patients were compared with items on the WOMAC and the SF-36 physical functioning subscale[34].

Construct validity

There is currently no gold standard for attributes such as disability and functional status[35-38]. Therefore, construct validity rather than criterion validity was assessed. Construct validity refers to the extent to which scores on a particular instrument relate to other assessment tools in a manner that is consistent with theoretically derived hypotheses[39].

To investigate the construct validity of the MACTAR in patients with OA, change scores on the transitional part of the MACTAR were correlated with change scores on both the WOMAC and the SF-36 physical function subscales, as well as the SF-36 role-physical subscale. Furthermore, follow-up scores on the status part of the MACTAR were correlated with follow-up scores on the SF-36 general health subscale. For normally distributed data, Pearson correlation coefficients (r) were used to express these correlations[40]. Spearman's rank correlation coefficients (r_s) were applied when data were not distributed normally.

The following hypotheses were tested: *1*. The change score on the physical function subscale of the WOMAC is negatively correlated ($r_{(s)} \leq -.5$)[41]($p<.05$) with the change score on the transitional part of the MACTAR; the correlation was expected to be negative, because the WOMAC and the MACTAR use reverse scales. *2*. Change scores on the physical functioning and role-physical subscales of the SF-36 are positively correlated ($r_{(s)} \geq .5$)[41] ($p<.05$) with the change scores on the transitional part of the MACTAR, and *3*. Follow-up scores on the general

health subscale of the SF-36 are positively correlated ($r_{(s)}$ ≥.4)[41] (p<.05) with the follow-up scores on the status part of the MACTAR.

Responsiveness

Responsiveness can be assessed in many different ways. However, one can distinguish two definition groups[42]. The first group describes responsiveness as 'the ability to detect clinically important change'[42,43]. In this group, an instrument is indicated as high responsive if it is able to distinguish real change from measurement error. Hereby, responsiveness is calculated as the magnitude of a treatment effect in which the Standardized Response Mean (SRM) and Effect Size (ES) could be very useful[42,43]. The second group defines responsiveness 'as the ability to detect changes over time in the construct to be measured'[34,42]. In this case, responsiveness is independent from any treatment effect and is interpreted as longitudinal validity. It should be assessed in analogy to construct validity[34]. Therefore, predefined hypotheses concerning change scores on the MACTAR, WOMAC and SF-36 in relation to PGA-scores were tested. In the case of normally distributed change scores, parametric statistics were applied; non-parametric variants were applied for data that were not distributed normally. It was hypothesized that *1*. The correlation between change scores on the MACTAR (transitional part) and the PGA will be better than that between change scores on the PGA and the WOMAC physical function subscale, the SF-36 physical functioning subscale and the role-physical subscale respectively (p<.05). *2*. Change scores on the MACTAR (transitional part) for patients who have improved according to PGA will differ significantly (p<.05) from change scores for those who have not improved according to PGA.

Second, responsiveness was determined by plotting a Receiver Operating Characteristics (ROC) curve. The first step in its construction was to calculate sensitivity and specificity statistics for MACTAR change scores in patients identified as improved (PGA score > 4) and patients identified as non-improved (PGA score ≤ 4). Next, the true positive rate (sensitivity) was plotted in functions of the false positive rate (1-specificity) for different cut-off points. The best possible cut-off point would yield a point in the upper left corner of the ROC space, representing 100% sensitivity, 100% specificity and an 'Area Under the Curve' (AUC) of 1.0. An instrument is indicated as 'highly responsive' if the AUC is >.90, 'moderately responsive' where the AUC is between .70 and .90 and 'lowly responsive' if the AUC is between .50 and .70[44].

All analyses were performed using PASW Statistics 18.0. If patients were unable to identify at least five impaired activities on the transitional part of the MACTAR, missing activity scores were filled with a score indicating a 'no change situation' (2 points); data from patients who mentioned less than three impaired activities were excluded from the responsiveness analyses. Furthermore, in cases of just one missing follow-up item for the status part of the MACTAR, the score obtained on the equivalent question in the baseline interview was also used for the follow-up.

Following the initial analyses, a sensitivity analysis was performed on various cut-off points of the dichotomized PGA-score, the aim of which was to determine whether the chosen cut-off point was the optimal point to dichotomize.

Results

Study population

A total of 192 patients participated in both the baseline and the first follow-up assessment and were included for content and construct validity analyses. The median PGA score of these 148 females and 44 males was '5', representing 'slightly improved'. Baseline characteristics of the study population are presented in Table 2.

TABLE 2. Baseline characteristics total population and subgroups #

Characteristic	Total population (n=192)	Improved group (n=144)†	Non-improved group (n=48)†	p-value
Female sex	148 (77)	118 (82)	30 (63)	.01
Age, mean (± SD) years	64.7 (7.9)	65.5 (7.9)	62.3 (7.6)	.02
Location of OA				.58
Knee	126 (66)	96 (67)	30 (63)	
Hip	49 (26)	36 (25)	13 (27)	
Both	17 (9)	12 (8)	5 (10)	
Radiologic severity of OA*				.62
No features / doubtful	44 (23)	35 (24)	9 (19)	
Minimal / moderate	91 (47)	67 (47)	24 (50)	
Severe or prothese	6 (3)	5 (4)	1 (2)	
Unknown	51 (27)	37 (26)	14 (29)	
Duration of symptoms				.55
<1 year	44 (23)	36 (25)	8 (17)	
1-5 years	71 (37)	52 (36)	19 (40)	
>5 years	75 (39)	55 (38)	20 (42)	

Values are represented as number (percentage), unless otherwise indicated; * Kellgren and Lawrence score[27,47]; † Improved group = Patient Global Assessment score (PGA) > 4, non-improved group PGA ≤ 4; SD = standard deviation; OA = osteoarthritis;

Outcomes

Table 3 shows absolute scores on the MACTAR, WOMAC, SF-36 and PGA at baseline and follow-up for both the total population and improved / non-improved patients. At baseline, there were no differences on any of the outcome measures between patients who indicated that they had improved and patients who indicated that they had not improved. At follow-up, MACTAR scores (both transitional and status parts), WOMAC physical function scores and SF-36 physical functioning scores differed significantly between improved and non-improved patients. The measurement variation was higher in the WOMAC and SF-36 compared with the MACTAR, at both baseline and follow-up (Table 3).

TABLE 3. Baseline, follow-up and changes scores on the outcome measures (mean ± sd)

Outcome measure	Total population (n=192)	Improved group (n=144)	Non-improved group (n=48)	p-value
MACTAR – transitional				
Follow-up	16.6 (2.8)	17.6 (2.0)	13.6 (2.6)	<.01
MACTAR – status				
Baseline	19.3 (4.0)	19.3 (4.1)	19.1 (3.9)	.76
Follow-up	20.5 (3.6)	20.8 (3.4)	19.4 (3.8)	.03
Change score	1.2 (4.3)	1.5 (4.2)	0.1 (4.5)	.05
WOMAC – physical function				
Baseline	28.6 (11.0)	28.3 (10.9)	29.8 (11.3)	.42
Follow-up	23.0 (11.4)	21.3 (10.6)	27.9 (12.1)	<.01
Change score	-5.6 (8.9)	-6.8 (9.0)	-1.9 (7.7)	<.01
SF-36 – physical function				
Baseline	48.7 (20.1)	49.1 (19.5)	47.6 (22.1)	.68
Follow-up	56.0 (21.7)	58.0 (21.2)	50.1 (22.1)	.03
Change score	7.6 (17.6)	9.4 (18.5)	2.0 (12.9)	.01
SF-36 – role physical subscale				
Baseline	42.5 (41.1)	41.2 (41.0)	46.1 (41.5)	.48
Follow-up	55.9 (42.0)	59.1 (41.5)	46.1 (42.5)	.07
Change score	14.7 (46.0)	19.2 (48.3)	1.1 (35.3)	.02
SF-36 – general health				
Baseline	50.8 (19.4)	51.8 (19.7)	47.9 (18.8)	.24
Follow-up	48.9 (16.5)	50.0 (17.2)	45.7 (14.1)	.13
Change score	-2.1 (17.3)	-2.1 (17.1)	-2.1 (17.9)	>.99
PGA (median (range))	5 (6)	6 (3)	4 (2)	-

MACTAR = McMaster Toronto Arthritis patient preference questionnaire; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; SF-36 = Medical Outcome Survey Short Form 36; PGA = Patient Global Assessment

Content validity

The study population (n=192) identified a total of 894 impaired activities, which indicates a mean of 4.6 impaired activities per patient. Seventy-one patients (37%) were unable to identify at least five impaired activities; one patient could name only one impaired activity; 10 patients identified two impaired activities; and 33 patients were able to name a maximum of three impaired activities. 'Walking' was most frequently mentioned as the most impaired activity (43%). Overall, seventy-two percent of the identified impaired activities comprised activities in the category of 'mobility'. Table 4 summarizes all the activities mentioned, ranked by category.

All items from both the WOMAC and the SF-36 physical function subscales were represented in the impaired activities list based on the MACTAR questionnaire. However, 27% of the activities mentioned by patients during the MACTAR interview were not represented in the WOMAC, and 41% were not represented in the SF-36. Eleven percent of the impaired activities mentioned were not covered either by items of the WOMAC or the SF-36: examples of which include gardening and activities related to professional life.

TABLE 4. Patient-mentioned impaired activities on the MACTAR-questionnaire

Category Activity	Mentioned as most impaired activity n (%)	Mentioned in total n (%)
Housekeeping activities †#	4 (2.3)	70 (8.5)
Vacuum cleaning, mopping, washing windows or dishes, lifting buckets, etcetera		
Leisure activities	19 (11.0)	102 (12.3)
Gardening	5 (2.9)	30 (3.6)
Remaining leisure activities (cultural activities, shopping †)	4 (2.3)	17 (2.2)
Sports (jogging, tennis, swimming, fitness, riding a horse, dancing)#	10 (5.8)	54 (6.5)
Mobility	134 (77.9)	591 (71.5)
Bicycling (including getting up/off) #	19 (11.0)	81 (9.8)
Climbing stairs †#	13 (7.6)	106 (12.8)
Driving (including getting in/out the car) †	4 (2.3)	52 (6.3)
Getting up from the floor/ a chair, getting out of bed †	10 (5.8)	53 (6.4)
Inability to stand for long †	1 (0.6)	54 (6.5)
Kneeling down, bending over, reaching down †#	12 (7.0)	77 (9.3)
Remaining mobility activities	1 (0.6)	39 (4.7)
Walking †#	74 (43.0)	129 (15.6)
Professional activities	1 (0.6)	13 (1.6)
Remaining activities	1 (0.6)	2 (0.2)
Self-care activities	7 (4.1)	82 (9.9)
Dressing (socks, underwear, trousers) †	6 (3.5)	74 (9)
Remaining self-care activities #	1 (0.6)	8 (1.0)
Sexuality	1 (0.6)	5 (0.6)
Sleeping and resting, including turning around in bed †	5 (2.9)	18 (2.2)
Social roles	-	11 (1.3)
TOTAL	172 (100)	894 (100)

MACTAR = McMaster Toronto Arthritis Patient Preference Disability Questionnaire; † item is represented in Western Ontario and McMaster Universities Osteoarthritis Index; # item is represented in Medical Outcome Survey Short Form 36

Construct validity

Correlations (r_s) between change scores on the transitional part of the MACTAR and change scores on the physical function subscales of the WOMAC and the SF-36 were -.40 (p<.01) and .27 (p<.01) respectively. Change scores on the transitional part of the MACTAR and the role-physical subscale of the SF-36 were also moderately correlated (r_s=.27 (p<.01)). Spearman's r_s between follow-up score of the MACTAR status part and the general health subscale of the SF-36 was .44 (p<.01) (Table 5).

TABLE 5. Correlation matrix change scores / follow-up score outcome measures (n=189) #

	MACTAR – transitional	WOMAC – physical function	SF-36 – physical functioning	SF-36 – role physical	MACTAR – status	SF-36 – general health
Change scores						
MACTAR- transitional part	1.00	-.40	.27	.27		
WOMAC- physical function subscale		1.00	-.36	-.30		
SF36- physical functioning subscale			1.00	.32		
SF36- role physical subscale				1.00		
Follow-up scores						
MACTAR- status part					1.00	.44
SF36- general health subscale						1.00

# Spearman's rank correlation coefficient; All correlations were significant at the .01 level
MACTAR = McMaster Toronto Arthritis Patient Preference Disability Questionnaire; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; SF36 = Medical Outcome Survey Short Form 36

Responsiveness

Data from 133 patients (82% female, mean age 64.0 ± 8.1 years) were used in the responsiveness analyses. Seventy-seven percent of these patients indicated that they had improved following treatment (PGA score >4) while 23% reported that they had not improved (PGA score ≤4). With the exception of age, the improved and non-improved group had similar baseline characteristics. Absolute change scores on physical function outcomes are presented in Table 6. Change scores for patients who indicated that they had improved differed significantly from patients who indicated that they had not improved on all outcome measures (Table 6).

Correlations between change scores on the physical function outcomes and the PGA score are also presented in Table 6. As hypothesized, change scores on the MACTAR correlate better with PGA (r_s = .69) than change scores on the WOMAC (r_s = -.39) and SF-36 (r_s = .26 and .25 respectively) (Table 6).

TABLE 6. Change scores on physical function measures and correlation coefficients (r_s) with PGA

	Absolute change score (mean (95% CI))	Correlation with PGA score**
MACTAR - transitional part*		
Total population (n=133)		.69
Improved group (n=102)	17.7 (17.3 – 18.2)	
Non-improved group (n=31)	13.7 (12.7 – 14.7)	
WOMAC - physical function*		
Total population	-6.1 (-7.7 – -4.5)	-.39
Improved group	-7.2 (-9.0 – -5.3)	
Non-improved group	-2.7 (-5.8 – 0.4)	
SF-36 - physical functioning*		
Total population	8.3 (5.2 – 11.3)	.26
Improved group	9.7 (6.0 – 13.5)	
Non-improved group	3.5 (-0.6 – 7.6)	
SF-36 - role-physical*		
Total population	14.9 (6.8 – 22.9)	.25
Improved group	19.7 (10.1 – 29.2)	
Non-improved group	-0.9 (-14.2 – 12.4)	

* Significant difference between improved and non-improved group (p<.05); ** Significant at p<.05 level, unless otherwise indicated. PGA = Patient Global Assessment; MACTAR = McMaster Toronto Arthritis Patient Preference Disability Questionnaire; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; SF-36 = Medical Outcome Survey Short Form 36

Figure 1 presents a ROC-curve of the change scores for the MACTAR (transitional part), in which the sensitivity of the MACTAR amounted to its 1-specificity. The AUC was .90 (95% CI .89 - .96) with a standard error of .03.

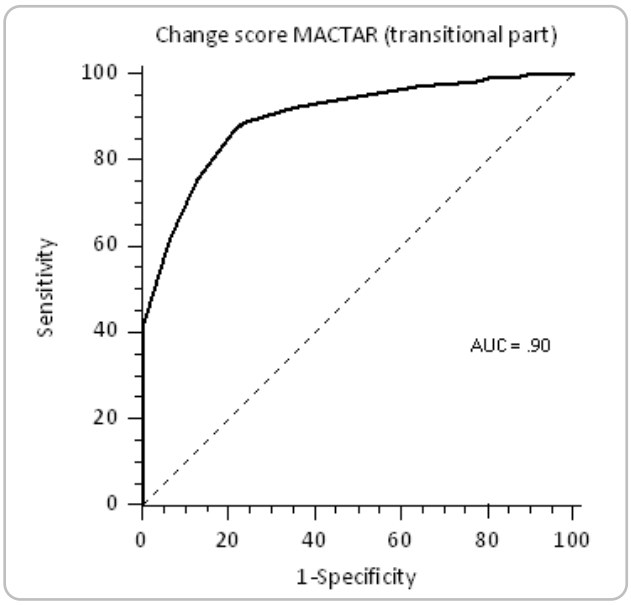

FIGURE 1. Receiver Operating Characteristics curve of the change score on the McMaster Toronto Arthritis Patient Preference questionnaire (MACTAR) (transitional part); AUC = Area Under the Curve

The sensitivity analysis showed that the cut-off point for the PGA-score dichotomization (>4), was chosen correctly. Higher and lower cut-off points resulted in less optimal responsiveness values.

Discussion

The aim of the present study was to investigate the content validity, the construct validity and the responsiveness of the MACTAR in patients with OA of the hip or knee.

The content validity of the MACTAR seems to be good. Specifically, the majority of the impaired activities identified correlate with items on the WOMAC and / or SF-36, which also aim to assess physical function. However, the MACTAR fits better with the WOMAC questionnaire than the SF-36. This is not surprising, since the WOMAC is aimed specifically at patients with osteoarthritis, whereas the SF-36 is of a more general nature. Data for 11% of the activities identified are gathered only by the MACTAR and are not represented in either the WOMAC or the SF-36. These comprised activities in the areas of leisure, professional life and social interaction. Indeed, participation in these fields varies widely between individuals. Disease-specific and general instruments do not take account of individual limitations, but patient-specific measures such as the MACTAR allow clinicians to evaluate physical functioning at individual level.
The majority of the activities identified by the MACTAR questionnaire comprised activities in the 'mobility' domain, which corresponds with the majority of activities in daily life. Recent validation studies on the MACTAR questionnaire in patients with chronic low back pain and rheumatoid arthritis showed comparable results[21,23]. The most frequently mentioned impaired activity in patients with chronic low back pain was 'taking part in sports activities[23]; in patients with hip/knee OA 'walking' was the most commonly cited impaired activity.

Although the content validity of the MACTAR seems to be good in patients with OA, the construct validity is less convincing. Moderate associations between the transitional part of the MACTAR and presumed comparable outcomes ($r_s \leq .40$) might be explained by an unbalanced distribution of impaired activities across the various activity-categories. Specifically, the 'mobility' category comprised almost 72% of all reported impaired activities, whereas the mobility domain in the WOMAC contains only 58% and in the SF-36, 60% of the total questionnaire. Thus, the transitional part of the MACTAR covers one specific part of the physical function domain extensively, whereas disease-specific and general tools account for a broader spectrum of this domain. Another explanation for the moderate construct validity could be the narrow variance around the mean on the MACTAR, compared with a wide variance in WOMAC and SF-36 scores. The variance is caused by patients who tend to assign the same disability score to very different impaired activities. The difference in variance impedes a comparison between a patient-specific instrument on the one hand and a disease specific / generic instrument on the other.
As hypothesized, the status part of the MACTAR was moderately correlated with the general health subscale of the SF-36 (r_s=.44). Previous studies identified comparable correlation coefficients between the MACTAR and other physical function measures. Sanchez *et al.* found a correlation (r_s) of .40 between the MACTAR and the Quebec Back Pain Disability Scale[37] in

patients with chronic low back pain[23] and a correlation (r_s) of .38 (p=.002) was found between the MACTAR and the Health Assessment Questionnaire (HAQ)[45] in patients with systemic sclerosis[22]. Verhoeven *et al.*[21] showed a correlation coefficient (r) of .73 (p<.0003) between the MACTAR and the HAQ in patients with rheumatoid arthritis.

The MACTAR was developed to evaluate patient-specific physical function over time. With this goal in mind, responsiveness is the most important psychometric property. For that reason, we evaluated the responsiveness of the questionnaire. As hypothesized, change scores for the MACTAR correlated better with the PGA score than change scores on the WOMAC and SF-36 do, leading to the conclusion that the MACTAR is better able to detect changes over time in patients with hip / knee OA than the WOMAC or SF-36. It has also been demonstrated that the MACTAR is capable of distinguishing patients who reported an improvement from those patients who reported no improvement. An AUC of .90 confirms the high responsiveness of the MACTAR in patients with hip / knee OA. Verhoeven *et al.*[21] also investigated the responsiveness of the MACTAR, concluding that it showed a high degree of responsiveness, based on a SRM of 3.5. However, a SRM is not an appropriate measure of assessing responsiveness as the ability to detect changes over time in the construct to be measured, but can be used to detect clinically important change[34;42].

One limitation of our study is the use of PGA scores as an external criterion to distinguish patients who improved from those who did not. Guyatt *et al.*[46] showed that patients are unduly influenced by their current health status when they complete transition ratings such as PGA scores. Moreover, the reproducibility of a single-item transitional scale is probably lower than for a more extended measurement tool[47]. Finally, 'a little better' is not, as a matter of course, equivalent to an 'important change[48]. However, better external criteria to discriminate between improved and non-improved patients have not yet been elaborated.
Although the MACTAR appears to have some advantages over the WOMAC and the SF-36 in assessing physical function in individual patients, it also has some limitations. The need for a trained interviewer to apply the MACTAR, as well as its complicated scoring method may reduce the likelihood that the MACTAR will become the instrument of first choice in clinical practice. Furthermore, patient-specific measures, including the MACTAR, do not take account of shifts in patient priorities that can occur over time in cases of change in disease status. Therefore, further studies should take account of the application of patient specific measures at long-term follow-up.

In conclusion, our results suggest that the MACTAR exhibits moderate construct validity and good responsiveness in a population of patients with OA of the hip or knee. Furthermore, the MACTAR is potentially better able to detect changes over time in activities that are important to individual patients compared to other tools measuring physical function (WOMAC, SF-36). Therefore, clinicians could use the MACTAR to evaluate clinically relevant changes over time in patient-specific physical functioning.

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Appendix 1: McMaster Toronto Arthritis patient preference questionnaire (MACTAR)

Baseline interview

Interviewers note:
Read the questions and response categories provided. Tick the response given.

*1a. How would you say your overall health has been during the **last 2 weeks**?*
You think of it as
- ❒3 *very good*
- ❒2 *pretty good*
- ❒1 *not too good*

2. Osteoarthritis may cause restrictions in several areas of your daily life. For different people the impact of osteoarthritis is also different. We will ask you to name activities in which you experience difficulties because of your osteoarthritis. What matters here, is what your personal experience has been. Please, think of what became a problem, now that you have osteoarthritis.

Interviewers note:
In order to elicit a comprehensive list of activities: First, give the patient opportunity to react spontaneously. Then read the probes. Record the exact phrases of the patient on the line hereunder.

To support you in naming any problems caused by osteoarthritis, I will read you a number of areas of your daily life that might be affected.

Does your osteoarthritis limit:
- *any (other) activities around the house such as cooking, housework etc.?*
- *any activity related to dressing such as buttoning, pulling a sweater over your heat etc.?*
- *any (other) activities at your work (outside the home), drive a care or other transportation?*
- *any (other) leisure activities. Either sport such as bowling, swimming, golf, etc. or non-sports such as needlework, woodwork etc.?*
- *any (other) social activities. Such as visiting, plying cards, going to church, etc.?*
- *sexuality?*

Are there changes in the relationship with your family?
If you live together with a hushand / wife / partner, are there changes in the relation with him / her?
If you have children living at home, are there changes in your relationship with them?

…… └──┘
The line above is printed 10 times

Interviewers note:
To rank the activities in order of importance to the patient, ask the following questions:

Which of these activities would you most like to be able to do without pain or discomfort of our osteoarthritis?
Show and read the list to the patient. Write '1' next to the activity the patient chose.
After (read activity 1), which activity would you next most like to be able to do without pain or discomfort of your osteoarthritis?
Show and read the list to the patient, with exception of the activity with priority 1.
Write '2' next to the activity the patient chose.
After (read activity 1 and 2), which activity would you next most like to be able to do without pain or discomfort of your osteoarthritis?
Show and read the list to the patient, with exception of the activity with priority 1 and 2.
Write '3' next to the activity the patient chose.

Continue like this, until all activities are ranked. The 5 with the highest priority will return in the follow-up interview.

3a. In general, how satisfying do you find the way you spend your life?
Over the last week you think of it as:
- ❒3 *completely satisfying* →*go to Q4a*
- ❒2 *pretty satisfying*
- ❒1 *not very satisfying*

3b. Is your life not completely satisfying because of your osteoarthritis? ❒0 *yes* ❒1 *no*

4a. *How would you say your overall physical functioning has been?*
Over the last week you think of it as:
- ❒5 *good* →*go to Q5a*
- ❒4 *fair to good*
- ❒3 *fair*
- ❒2 *fair to poor*
- ❒1 *poor*

4b. Is your physical function not as good as is might be because of your osteoarthritis? ❒0 *yes* ❒1 *no*

5a. How would you say your overall social functioning has been?
Over the last week you think of it as:
- ❒5 *good* →*go to Q6a*
- ❒4 *fair to good*
- ❒3 *fair*
- ❒2 *fair to poor*
- ❒1 *poor*

5b. Is your social functioning not as good as is might be because of your osteoarthritis? ❒0 yes ❒1 no

6a. How would you say your overall emotional functioning has been?
Over the last week you think of it as:

- ❒5 *good* →*stop here*
- ❒4 *fair to good*
- ❒3 *fair*
- ❒2 *fair to poor*
- ❒1 *poor*

6b. Is your emotional functioning not as good as is might be because of your osteoarthritis? ❒0 *yes* ❒1 *no*

Follow-up interview

1a. How would you say your overall health has been during the ***last 2 weeks****?*
You think of it as

- ❒3 *very good*
- ❒2 *pretty good*
- ❒1 *not too good*

1b. Have you noticed any change in your osteoarthritis since we talked during the first interview?

- ❒ *yes*
- ❒ *no → 'no change' at Q1d, go to Q2a*

1c. Please describe how your osteoarthritis has changed?

……
……

1d. When you think of your osteoarthritis during the ***two weeks before*** *the first interview, how much better or worse overall has your osteoarthritis become?*

- ❒7 *a great deal better*
- ❒6 *moderately better*
- ❒5 *slightly better*
- ❒4 *no change*
- ❒3 *slightly worse*
- ❒2 *moderately worse*
- ❒1 *a great deal worse*

You may remember the first time we spoke. You told me which activities were at that time problems due to your arthritis. I will ask you again about the five most important.

2a. Since the first interview, have you noticed any change in your ability to (activity 1)?

- ❒3 *less of a problem*
- ❒2 *the same*
- ❒1 *more of a problem*

2b. Since the first interview, have you noticed any change in your ability to (activity 2)?

- ❒3 *less of a problem*
- ❒2 *the same*
- ❒1 *more of a problem*

2c. Since the first interview, have you noticed any change in your ability to (activity 3)?

- ☐3 *less of a problem*
- ☐2 *the same*
- ☐1 *more of a problem*

2d. Since the first interview, have you noticed any change in your ability to (activity 4)?

- ☐3 *less of a problem*
- ☐2 *the same*
- ☐1 *more of a problem*

2e. Since the first interview, have you noticed any change in your ability to (activity 5)?

- ☐3 *less of a problem*
- ☐2 *the same*
- ☐1 *more of a problem*

Questions 3a to 6b are equal to the equally numbered questions in the baseline interview.

7

General discussion

Personalized treatment is recognized as one of the solutions to face the complex and continuously expanding healthcare demand of patients with (multiple) chronic conditions[1]. It is one of the key elements of the renewed view on health, introduced by Huber et al.: patients are challenged to manage their health themselves and to adapt to new situations[2]. Clinicians are supposed to strengthen a patient's functioning, flexibility, and self-control. Personalized treatment is often presented as a 'new phenomenon' in healthcare. However, in 1997, Wright et al. already presented a paper which was subtitled: '*… asking patients what they want*' [3]. This paper demonstrates that personalized care has caught attention for 20 years and over. Therefore, it could be expected that aspects of personalized care are already widespread used in clinical practice.

In this thesis, we especially focused on personalized treatment in patients with osteoarthritis (OA) of the hip and the knee. Due to its' heterogeneity, OA would be particularly appropriate for personalized treatment. The results of the studies captured in Chapter 2 to Chapter 6 of this thesis show that personalized treatment is indeed widely applied in current clinical practice of OA care. Nevertheless, there is still room for improvement. In this final chapter, we will reflect on the results presented in the previous chapters and will provide recommendations for clinical practice, policy and future research. We focus on two aspects of personalized care specifically: timing of care and focus of care.

Timing of care

Clinicians are challenged to phase interventions over time and reduce inappropriate use of advanced care[4]. Thereby, phasing treatment could offer benefits both in clinical perspective as well as financial perspective. The recently developed Stepped-Care-Strategy (SCS) phases non-surgical care in three steps[5]. The first step comprises the optimization of patients' self-care in primary care by education, lifestyle advices, and the prescription of acetaminophen. In step 2, (topical) NSAIDs are added or a referral for allied health care (exercise therapy, dietary therapy) will be considered (step 2). Finally, step 3 comprises the use of TENS and intra-articular corticosteroid injections or a referral for interprofessional evaluation in secondary care. Interventions belonging to subsequent steps should only be considered in patients with persisting complaints, despite the use of all recommended interventions from the lower step or steps. Although the SCS has not yet been widely implemented in clinical practice, Dutch general practitioners already seem to phase their interventions over time. They apply less advanced interventions, like lifestyle advices and the prescription of NSAIDs (step-1,2), more often than for instance exercise therapy or a referral for Total Joint Replacement (TJR) (step-2,3) (**Chapter 2**). Thus, their usual sequence of care seems to be mainly in accordance with the SCS. However, appropriate timing of care could still be improved. This improvement mainly concerns the appropriate timing of a referral to secondary care (**Chapter 2 & 3)**. Several results from this thesis endorse an overuse of orthopedic care and, in consequence,

an underuse of non-surgical care in patients with hip/knee OA. We will subsequently address three results which illustrate that the timing of care is not appropriate yet: *1*. the insufficient use of all recommended stepped-care interventions, *2*. the insufficient use of physical therapy, and *3*. the underutilization of non-surgical treatment in secondary care.

Insufficient use of all recommended interventions

According to the SCS, a patient should be referred to secondary care (step-3) in case of persisting complaints despite the use of *all recommended* interventions from the lower step or steps[5]. Our retrospective study on currently provided care showed that less than 3% of the patients referred to secondary care did receive all step-1 and step-2 interventions of the SCS (**Chapter 2**). Recently, Hofstede et al. confirmed the low use of all recommended interventions in hip/knee OA[6]. In their study, an amount of 6% actually received all recommended interventions of the SCS prior to surgery. In both studies, clinicians were unaware of the SCS. A study by Smink et al., which has been performed after implementation of the SCS, showed that the SCS potentially increases the use of recommended non-surgical interventions[7]. In their study, 28% of the patients received all interventions from previous steps prior to a referral to secondary care. Hence, still the majority of patients referred to secondary care did not receive all interventions captured in step-1 and step-2. Probably, a great deal of effort is requested to achieve nationwide implementation of the SCS.

However, it could also be questioned whether the SCS is currently feasible to apply in clinical practice. By way of illustration, the SCS does not yet take into account the 'Direct Access Regulation' to physical therapy[8,9]. Direct access allows patients to directly contact a physical therapist (step-2) without a visit at a general practice (step-1). In consequence, patients using direct access potentially will not receive adequate pain medication or appropriate lifestyle advises (step-1) as they turn directly to a physical therapist (step-2). To fit better to current clinical practice, Koenders et al. slightly modified the SCS, resulting in the 'Stepped-Care Osteoarthritis algorithm'[10]. The Stepped-Care Osteoarthritis algorithm indicates the use of physical therapy (step-2) in case of completing all recommended step-1 interventions *or* in case of severe limitations in physical functioning, operationalized by a score >4 on the Algofunctional Index[11]. Patients with minor limitations in physical functioning who visit a physical therapist by direct access, return to step-1 care performed by the GP[10] (Koenders). Further research should provide insight whether or not this modification on the SCS attributes to an improved implementation of stepped-care in patients with hip/knee OA.

Insufficient use of physical therapy

A large body of evidence supports the effectiveness of exercise therapy regarding improvement of functioning in patients with hip/knee OA[12-14]. Therefore, a referral to physical therapy is included in step-2 of the SCS. Based on the subsequent steps of the SCS, we could have expected a higher referral rate to physical therapists than to medical specialists in secondary care. However, one of our studies indicated that in current primary healthcare, referrals to physical therapists (step 2, 4%) lags behind compared to referrals to medical

specialists, like orthopedic surgeons and rheumatologists (step 3, 13%) (**Chapter 2**). The low referral rate to physical therapy could be due to the introduction of the previously mentioned Direct Access Regulation[8,9] - this may have led to patients directly visiting the physical therapist, without a referral by the GP. However, taking into account the self-referrers, physical therapy still seems to be underused in current clinical practice. Maybe, financial issues play a role as well. Until 2006, physical therapy due to hip/knee OA was fully reimbursed for each Dutch inhabitant. Since 2006, reimbursement for physical therapy was removed from standard health insurance packages. Patients increasingly have to cover their physical therapy treatment themselves, for example by voluntary, additional health insurance packages. It is conceivable that, due to financial issues, some patients have totally ignored physical therapy (step-2) or only used physical therapy to a limited extent. In consequence, these patients may not have received appropriate care. Previous research in dietetics care showed that restrictions in reimbursement resulted in a mean decrease of 16% in treatment time per patient[15]. To get insight into the impact of restrictions of reimbursement in physical therapy practice, we asked physical therapists to what extent a patient's reimbursement influences the number of treatment sessions they would provide (**Chapter 4**). Thirty-five percent of the therapists indicated that a patient's reimbursement did not influence the number of provided sessions, 41% indicated a limited influence, and the remaining 24% of the therapists reported that a patient's reimbursement determines the amount of care to a large extent. It is assumed that these results reflect a patient's opinion as well since 'reimbursement' is often discussed by the physical therapist and the patient during a treatment episode. Therefore, it seems a welcome development that from January 2018 and onward physical therapy treatment due to hip/knee OA is included for full reimbursement again by standard health insurance[16]. On the other hand, reimbursement by standard health insurance involves a compulsory deductible. This compulsory deductible might exceed the monthly fee for additional health insurance packages. Future research should provide insight to what extent readmission of physical therapy treatment in hip/knee OA in standard health insurance stimulates the use of physical therapy instead of use of secondary care facilities, and consequently attributes to an appropriate timing of care.

Underutilization of non-surgical treatment in secondary care

As mentioned previously, a considerable part of the OA population treated by GPs is referred for evaluation in secondary care. Our study in **Chapter 3** showed that 35% of those patients subsequently received a surgical intervention. This percentage was recently confirmed by a publication of the Dutch National Health Care Institute in patients with hip/knee OA[17]. Unfortunately, it is unknown whether or not orthopedic surgeons have determined the adequate use of non-surgical interventions when deciding for a surgical intervention. Based on two recently published reports, there seems room for improvement. First, the Dutch Orthopaedic Association dedicated one of its' five 'sensible choices for future care' to the implementation of stepped-care: *'No total joint replacement without adequate non-surgical treatment'*[18]. Second, in a recent publication of the Dutch National Health Care Institute

regarding 'improvements in OA care', it was stated that providing care in line with the stepped-care principle will reduce the number of total joint replacements by 15%[19].
To improve the implementation of stepped-care in both primary care and secondary care, interprofessional collaboration is needed during the entire clinical OA pathway. In view of this collaboration, the Dutch Orthopaedic Association currently revises the interprofessional guideline *'Non-surgical treatment in patients with osteoarthritis of the hip or knee'*. Collaborating partners in this revision process are for instance professional associations of physical therapists, general practitioners, rheumatologists, and patients with hip/knee OA are represented as well. In addition to recommendations regarding the use of stepped-care in OA, the guideline will include recommendations regarding roles and responsibilities of healthcare providers in the clinical OA pathway. By including these recommendations a further step towards wide implementation of stepped-care and subsequently personalized care is taken.

Focus of care

In addition to an appropriate timing of care, appropriate focus of care is also supposed to attribute to personalized treatment. In this thesis, we operationalized appropriate focus of care by *1*. treatment stratification and *2*. personalized measurement (over time).

Treatment stratification

Due to the heterogeneity of especially knee OA, it has been supposed that the knee OA population consists of different subgroups or phenotypes[20,21]. Each of those phenotypes comprises one distinguishing feature which hypothetically assumes a different treatment approach[22-25]. One of the questions which we have addressed in this thesis was to what extent physical therapists currently focus their treatment at different subgroups of knee OA rather than providing 'one size fits all' care (**Chapter 4**). The major conclusion drawn from our clinical vignette study is that physical therapists in primary care do not apply a 'one size fits all' approach. Physical therapists indicated to apply different treatment strategies in five previously identified phenotypes of knee OA. By way of illustration, patients with obesity were more likely to be referred for dietary therapy compared to the remaining phenotypes; patients with depressive symptoms are more often considered for psychological care; and patients with strong quadriceps muscles would receive the least number of exercise treatment sessions in comparison with other phenotypes.
The rationale for identifying subgroups in the knee OA population was to allow tailored treatment for specific subgroups of patients and, subsequently, the identification of more effective interventions[4]. Previous research has already shown that stratified care is both clinically effective and cost-effective in patients with low back pain[26]. At this moment, Knoop et al. are conducting a pilot study which evaluates the applicability of stratified treatment approaches in 50 patients with knee OA (In Dutch: 'Artrosebehandeling op maat'). Although stratification is promising for clinical practice, one remark should be addressed as well. One

of the risks of stratification is that clinicians are provoked to pigeonholing. As an individual patient practically never fits exclusively to one specific subgroup, stratification may will compromise a patient's individual needs rather than it will encourage personalized healthcare. Physical therapists are challenged to use stratified treatment approaches as a practical tool during their clinical reasoning process while maintaining an open mind on a patient's individual situation.

Personalized measurement

Personalizing the focus of care in patients with hip/knee OA could also be operationalized by determining patients' priorities or preferences in diagnostic and evaluative procedures. Commonly used measurement tools mainly contain fixed items, which do not account for patient-specific priorities and preferences[27]. Personalized measurement tools are able to address issues which specifically influence an individual's functioning in daily life. Since an overview of available personalized measurement tools was lacking on the domain of physical functioning, we performed a systematic review on this theme and, additionally, identified the psychometric qualities of the included personalized tools. The review in **Chapter 5** indicated twelve instruments measuring physical functioning in a personalized way. However, psychometric qualities are moderately reported yet. Construct validity, reliability and responsibility are most often assessed. One measurement tool, the Patient Specific Functional Scale (PSFS) operationalized by Cleland et al.[28] obtained exclusively positive scores on the assessed items. Therefore, it not surprising that the PSFS is currently well implemented in clinical practice of physical therapists. The next step is to integrate a personalized tool like the PSFS in the SCS to guarantee continuity and homogeneity during the total clinical pathway in hip/knee OA.

Another measurement tool which was identified by our systematic literature review, was the McMaster Toronto Arthritis patient preference questionnaire (MACTAR)[29]. The MACTAR is a patient-specific measurement tool, which aims to collect a patient's health status and to evaluate the severity of restricted activities over time by a structured interview. Since the MACTAR was exclusively validated in patients with rheumatoid arthritis[29], we have conducted a psychometric evaluation of the MACTAR in patients with hip/knee OA **(Chapter 6)**. Based on our results, it could be concluded that the MACTAR is a high responsive tool to evaluate patient-specific functioning over time. Furthermore, the MACTAR seems to provide additional insight into a patient's individual physical functioning as a considerable part of the mentioned priorities were not captured by fixed-item questionnaires used in patients with hip/knee OA.

Although personalized measurement potentially provide better insight in patients' priorities, the use of personalized-tools takes practice by both patients and clinicians. By way of illustration, a considerable part of the patients struggles with the identification of problem activities. Research by Stevens et al. has illustrated that high-literated patients who prefer an active role did not indicate any difficulties in recalling problem activities, but patients who lacked these characteristics had many difficulties to identify problem activities[30]. Clinicians are

challenged to facilitate patients in identifying their patient-specific limitations in daily life. In some patients, it may be helpful to keep distance from specific activities but rather pay attention to a patient's meaning of life. Subsequently, patients are asked to mention physical activities which hinder them in expressing their meaning of life. For instance, a patient values his physical independency in daily life. One precondition for physical independency in his daily life is the ability to walk for at least five minutes to reach his car. As he is currently able to walk for only three minutes, this patient-specific and patient-relevant limitation could be used to set personalized goals for treatment. Personalized goal setting has for a long time been recognized to be an effective way of achieving behavioral change[31].

Critical considerations

In this thesis, we studied to what extent elements of personalized care are represented in current clinical practice. In consequence, we mainly used data which have been gathered previously. For example, electronic health records of a large population treated in primary health care were used to provide insight into current primary OA care (**Chapter 2)**. Data gathered as part of the regional implementation of the SCS in clinical practice were used to determine the appropriate timing of care in hip/knee OA (**Chapter 3**). The use of previously gathered data has many advantages. For example, it guarantees the availability of a sufficient amount of data in a short time at low costs. Furthermore, the risk for selection bias is small. However, the use of previously gathered data also has its downsides. One disadvantage is the impossibility to influence the design of the study or the operationalization of outcomes. Furthermore, the use of existing data has contributed to the wide timeframe of the studies presented in this thesis. For instance, data used for the psychometric evaluation of the MACTAR (**Chapter 6)** were gathered in the context of a randomized controlled clinical trial applied in the early noughties[32]. Fortunately, demographic and clinical data of patients participating in this trial were comparable to recently published studies in primary care populations with hip/knee OA[33,34].

In one study, we used visual clinical vignettes to gather data concerning the content of physical therapy in several subgroups of knee OA (**Chapter 4**). Clinical vignettes offer significant advantages in studying clinical behavior, including high feasibility and low costs[35-37]. We specifically used colorized, visual clinical vignettes as visual communication takes less time to interpret, it increases the willingness to read by 80%, and it is supposed to be better remembered[38]. However, clinical vignettes also have a major disadvantage. They merely reflect clinicians competences rather than actual clinical practice[39]. Future research is recommended on studying clinicians' routine practice in patients with hip/knee OA in addition to a therapists' treatment intention.

We have demonstrated 'personalized care' mostly from the clinicians' point of view. In Chapter 2, 3, and 4, we have analyzed OA care in patients with hip/knee OA as reported by GPs and physical therapists, in Chapter 5 and 6 we studied psychometric qualities of personalized measurement tools to enable its' use by clinicians in daily practice. Although clinicians play an important role in performing personalized care, personalized care is initially about the individual patient. Unfortunately, the patient's point of view on personalized healthcare has been minimally addressed in this thesis. It would have been interesting to ask patients to what extent they are concerned in decision making processes during their treatment due to hip/knee OA. Shared decision making has shown to attribute to personalized healthcare in several populations including patients with hip/knee OA[40-42]. Therefore, future studies on personalized treatment are highly recommended to involve patients' perspectives as well.

Personalized treatment: what is next?

Based on the results of this thesis, several recommendations could be formulated regarding 'timing and focus' to improve personalized care in patients with hip/knee OA for clinical practice, policy, and future research. We have briefly touched some recommendations, but we pay attention to the main recommendations below.

Clinical practice

Personalized management is not an unknown phenomenon in clinical OA practice. Clinicians have shown to adapt their treatment to a certain degree to individual patients' needs, both with respect to the timing of care and focus of care. In this way, clinicians are ahead of clinical guidelines, which only minimally pay attention to personalized care. Based on their clinical expertise, they translate general recommendations contained in guidelines to personalized management for their individual patients. This confirms that clinical expertise should not be underestimated and could have an added value on evidence based treatment.

However, there is room for improvement. At this moment, the surgical rate in patients with hip/knee OA is too high. This could partly be attributed to the suboptimal use of non-surgical treatment strategies both in primary and secondary care. Improved collaboration, both between healthcare providers and with the patient, could improve the use of non-surgical treatment and, in consequence, the appropriate timing of care. In that perspective, the revision of the interprofessional guideline for *'non-surgical treatment in patients with hip/knee OA'* could be seen as a timely development. As this revised guideline embraces the stepped care approach, but additionally includes recommendations regarding clear partition of responsibilities, it seems an important development towards structural collaboration over the total clinical pathway.

Another recommendation based on this thesis concerns the use of personalized measurement. In physical therapy practice, its' use has become generally accepted. However, patient-specific priorities identified by personalized measurement tools are yet not evaluated during the total clinical pathway. Therefore, it is recommended to transfer patients' individual priorities from one clinician to another clinician, just like a patient's diagnosis is reported in case of a referral.

The final recommendation for clinical practice concerns the implementation of stratified care. Therapists have shown to be aware of different subgroups of patients with knee OA and, subsequently, are able to focus their treatment on these specific subgroups. Although stratification could be a useful tool to focus a patient's treatment, clinicians are challenged to maintain an open mind on a patient's individual situation.

Policy

Based on this thesis, two recommendations could be formulated for policy. The first recommendation concerns the nationwide implementation of a stepped care approach in OA care, both in monodisciplinary as well as interprofessional guidelines. This implementation could gain momentum, as several guidelines are currently under revision. In these revised guidelines, stepped care, including interprofessional consultations, will be one of the key elements.

The second recommendation for policy concerns the attention for funding in OA care. At this moment, at least three flows of funding are applied to OA care: 'fee for service' in physical therapy practices, 'shared savings' in general practices and 'bundled-payment' in secondary care[43]. Those financial partitions in funding hamper collaboration and increase the complexity of care. We endorse that it is not easy to look for a quick solution for this complex issue. However, in order to do justice to the functioning of individual patients with hip/knee OA, collaboration across flows of funding is necessary, including focus on patient-relevant outcomes.

Future research

One of the major 'lessons learned' from this thesis is that monitoring the total clinical pathway is necessary to enable the provision of personalized care. Collaboration across the borders of settings, across the borders of professional domains, and across the borders of funding are demanded to ensure appropriate timed care. Data from electronic medical records may be useful in future research to monitor the clinical pathway in hip/knee OA. These data reflect real data in clinical practice, and are consequently free of recall bias and selection bias. In the Netherlands, NIVEL Primary Care Database (NPCD) seems suitable to this aim, as this database holds the opportunity to link data registered by GPs, physical therapists, dieticians, and pharmacies. Based on data registered in the NPCD, both the use of non-surgical treatment strategies and its timing can be associated to treatment outcomes in hip/knee OA. At this moment, such an integrated overview of applied primary healthcare and achieved treatment outcomes is lacking in OA.

The second recommendation for future research concerns stratification in OA care. In this thesis we have indicated that physical therapists recognize five subgroups in knee OA based on clinical characteristics. Recently, Dell'Isola et al. presented a systematic review in which 76 phenotypes were described, summarized in six main sets of variables[22]. The way in which those phenotypes were identified, differed widely between the included studies of the review. Deveza et al. indicated that most phenotypes of knee OA were defined based on one single characteristic rather than combining data from different domains like clinical, imaging, and laboratory characteristics[21]. The wide variety in clinical characteristics encourages future studies on determining clinical relevant phenotypes in knee OA. Subsequently, treatment strategies could be developed for those clinically relevant subpopulations of patients as this is one of the aims of personalized treatment[4].

Stratification could also be applied in other ways in the pursuit of personalized treatment. In addition to stratified treatment strategies, stratification could be applied in its mode. In that context, the rising trend of eHealth applications should be involved in future research. During the timeframe of the studies described in the current thesis, development of eHealth technologies have shown exceptional growth. 'e-Exercise' for example combines usual physical therapy with online, personalized education and exercise modules resulting in a 'blended care' concept[44[. As e-Exercise has shown to be as effective as conventional care, further development of personalized eHealth applications is recommended. Particularly, insight should be provided into eligibility criteria to use eHealth applications: which eHealth applications fit to a specific person and for what purpose are they applied? Moreover, little is known on the implementation of personalized eHealth applications in usual clinical practice.

The final paragraph of this thesis on 'personalized care in patients with hip/knee OA' returns to the patient with hip/knee OA. This is a patient who suffers from a heterogeneous disease and is challenged to manage his health himself and to adapt to new situations[2]. Clinicians are being consulted to strengthen a patient's functioning in daily life in a personalized way. The current thesis has shown that providing personalized care is not a totally new concept in general practice, physical therapy practice, and in orthopedics. GPs, physical therapists, and orthopedic surgeons already differentiate treatment both in timing of care as well as focus of care. Improvement of personalized care might be achieved by better collaboration between healthcare providers in primary care and secondary care, implementation of personalized measurement during the total patient journey, and the use of stratification to support the process of clinical reasoning in individual patients with hip/knee OA. Furthermore, the determination of the concept 'personalized care in OA' has not been finished yet. Personalized treatment extends beyond the right timing of care and the right focus of care, which have been addressed in this thesis. Additional research on the identification of patients that are in greatest need of treatment, the identification of patients who may respond optimally to a specific intervention and an efficient use of healthcare resources is needed.

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Summary

Osteoarthritis (OA) of the hip and/or knee is a common musculoskeletal disorder, which prevalence is expected to increase considerably over the next decades. OA is a heterogeneous disease. Both the pathogenesis and the clinical presentation differ widely from patient to patient. To improve the functioning of a rising number of patients with hip/knee OA, there is a strong demand for efficient and effective treatment. Due to its' heterogeneity and the expected increasing burden of disease, OA would be particularly suitable for personalized treatment.

The general introduction of this thesis **(Chapter 1)** presents the rationale for personalized treatment in patients with hip/knee OA. Personalized treatment is recognized as one of the solutions to face the complex and continuously expanding health care demand of patients with (multiple) chronic conditions like OA. One motivation to apply personalized treatment is the identification of patients that are in greatest need of treatment. Furthermore, personalized treatment potentially enables the development of stratified interventions and efficient use of healthcare resources. Personalized treatment can be operationalized in many ways. The aim of this thesis is to explore two drivers which potentially contribute to personalized treatment in hip/knee OA 'timing of care' *(part I)* and 'focus of care' *(part II)*.

Part I: Timing of care

Timing of care concerns the phasing of interventions over time in patients with hip/knee OA, in particular non-surgical interventions in general practice, physical therapy practice, and orthopedic care. Although current clinical guidelines provide a clear insight into effective interventions, those guidelines do not yet provide a clear guidance for the sequence of interventions. This might be one explanation for the reported underutilization of non-surgical interventions in current OA care. To facilitate the use of non-surgical interventions prior to a referral to secondary care, a Stepped-Care-Strategy (SCS) has been developed by Smink et al. (2011). In the SCS, interventions are applied in three consecutive steps. Step-1 comprises stimulation of a patient's self-care. Step-2 adds more advanced interventions, like the prescription of NSAIDs and a referral for allied healthcare (exercise therapy / dietary therapy). Step-3 includes, for instance, a referral to secondary care. Patients will only receive more advanced care in case of insufficient results achieved by less advanced interventions.
The SCS has already been implemented in one region in the Netherlands. Nationwide implementation has not been finished yet. In preparation to nationwide implementation of the SCS, we provide insight into current OA care by general practitioners (GPs) and physical therapists, including the compliance to the SCS.

Research questions of **Chapter 2** are:

- What is the content of current general practice care in patients with hip/knee OA, including the compliance to the SCS?

- To what extent does the content of physical therapy practice in patients who were referred by their GP differ from self-referred patients with hip/knee OA?

To answer these questions, we retrospectively studied routinely registered data by Dutch GPs and physiotherapists in NIVEL Primary Care Database. In total, 12 118 electronic medical records of patients who were treated by GPs and/or physical therapists due to hip/knee OA were included for analyses. Results showed that Dutch GPs already phase their interventions over time: they apply less advanced interventions, like lifestyle advises and the prescription of NSAIDs (step-1,2), more often than for instance exercise therapy or a referral for total joint replacement (step-2,3). Although they mainly act in accordance with the SCS, there is room for improvement. First, GPs rarely use all interventions that are recommended within one step. Furthermore, referrals for physical therapy lag behind referrals to secondary care. The introduction of the Direct Access Regulation may have led to patients directly visiting the physical therapist, without a referral by the GP. Within the timeframe of our study, 35% of the patients with hip/knee OA used direct access. The content of physical therapy differed only slightly between GP-referred patients and patients who visited a physical therapist on their own initiative.

Chapter 3 focuses on the setting in which OA care is provided, which is closely related to the timing of care. As primary care is easily accessible, and cheaper compared to secondary care, the SCS advises to start OA management in primary care. Previous research has shown that a considerable part of the OA population is referred to secondary care. Subsequently, about one third of this referred population receives a total joint replacement. To date, little is known regarding factors which support the choice to stay in primary care, to refer for treatment in secondary care or to conduct total joint replacement surgery. These factors may include patient-characteristics, practitioner-characteristics, or practice characteristics. Insight into these factors at multiple levels would be useful to optimize nationwide implementation of the SCS in clinical practice.

Therefore, the question addressed in **Chapter 3** is:

- Which individual factors, GP-related factors and general practice related factors are associated with 1) treatment in primary care, 2) continuation of non-surgical care after a referral, and (3) surgical treatment in patients visiting their GP due to hip/knee OA?

To answer this question, we performed logistic multilevel analyses on data previously gathered in a cohort of 313 newly diagnosed patients with hip/knee OA treated by 70 GPs in 38 general practices in the Netherlands. Overall, significant factors almost exclusively concerned factors at patient level, in particular the content of previously utilized care. Treatment was limited to primary care in 47% of the patients. Patients who stayed in primary care tended to show better physical functioning (Odds Ratio (OR) 1.03). Furthermore, they less often received exercise therapy (OR 0.46) or intra-articular injections (OR 0.08), and were less often registered for

radiological assessments (OR 0.06). These results are in accordance with the SCS, which prefers the use of less advanced care prior to the use of more advanced interventions including a referral to secondary care.
Two out of three patients who have been referred to secondary care were exclusively treated by non-surgical interventions. The decision to continue non-surgical treatment after a referral was more likely in employed patients (OR 2.90). Furthermore, each additional joint affected with OA doubles the chance to continue non-surgical treatment in secondary care. As the incidence of multi-joint OA is expected to increase over the next decades, further research on this topic is justified.
No factors related to the patient, the GP nor the general practice were identified with respect to the use of surgical interventions, except the previous use of exercise therapy. The application of exercise therapy in the past offers a substantial higher probability to receive a surgical intervention (OR 7.42). This result could have been expected based on the SCS. Moreover, it strengthens the important role of orthopedic surgeons as they actually seem to consider the use of non-surgical interventions prior to decide for a surgical intervention.

Part II: Focus of care

In this thesis, focus of care has been operationalized by 'treatment stratification' and 'personalized measurement'. Treatment stratification aims to better account for different subgroups within the population with knee OA as treatment is adapted to those different subgroups. Personalized measurement aims to incorporate patients' preferences and priorities since commonly used fixed-item tools lack this possibility.

Treatment stratification

The clinical presentation of patients with hip/knee OA differs from patient to patient. Knoop et al. (2011) and van der Esch et al. (2015) have succeeded in distinguishing five clinical phenotypes of knee OA: minimal joint disease phenotype, strong muscle phenotype, severe radiologic OA phenotype, obese phenotype and depressive mood phenotype. As both the origin of complaints as well as the course of complaints differ between those phenotypes, it is supposed that each phenotype would benefit from specific management. It is unknown to what extent physical therapists currently differentiate their treatment between phenotypes of knee OA.

Therefore, the research question of **Chapter 4** is:

- To what extent is physical therapists' treatment tailored to the 'minimal joint disease' phenotype, the 'strong muscle strength' phenotype, the 'severe radiographic OA' phenotype, the 'obese' phenotype, and the 'depressive mood' phenotype in patients with knee OA?

Hypotheses were constructed for each phenotype regarding preferred treatment strategies, the referral policy, and the considered number of applied treatment sessions. To test these hypotheses, a clinical vignette study has been conducted. We composed five visual clinical vignettes which represented the previously mentioned phenotypes of knee OA. Subsequently, 144 Dutch physical therapists and exercise therapists were recruited to indicate their content and amount of treatment in each of the five clinical vignettes. Overall, physical therapists and exercise therapists seemed to tailor their management to specific phenotypes of knee OA. Statistically significant differences were found regarding the content and the amount of care between phenotypes of knee OA. These differences were mainly in accordance with our predefined hypotheses, with the exception of the strong muscle phenotype and the depressive mood phenotype. In the strong muscle phenotype, exercise therapy was provided more often than hypothesized and the referral rate to secondary care was lower than expected. In the depressive mood phenotype, the referral rate to psychologists exceeded our expectations. Further research was recommended on the development of stratified interventions in knee OA and its evaluation of (cost)effectiveness.

Personalized measurement

In addition to stratified treatment, personalized measurement could also attribute to a personalized focus of care in patients with hip/knee OA. At this moment, most tools applied in diagnostics or evaluation of limitations in physical functioning in patients with hip/knee OA are fixed-item tools. By those tools, patients' preferences and variability in performance on particular activities can not be measured. As a consequence, clinicians face the risk of missing patient-relevant priorities which could potentially be used in personalized goal-setting. To provide care with focus on each individual patient, it is desirable to consider the use of a personalized instrument in addition to a fixed-item tool. At this moment, it is unclear which personalized-measurement tools are available in patients with musculoskeletal disorders, including hip/knee OA.

Therefore, we performed a systematic review to indicate those tools **(Chapter 5)**. Subsequently, we assessed the psychometric qualities of the included instruments.

Corresponding research questions are:

- Which patient-specific self-assessment instruments are available to measure physical function in patients with musculoskeletal disorders?
- What are the descriptive properties as well as the psychometric qualities of patient-specific instruments measuring physical function in patients with musculoskeletal disorders?

A comprehensive search was conducted in several databases. Studies were included if (1) the main aim of the study was to investigate measurement properties, (2) the described instrument concerned a questionnaire, a rating scale or a (semi-structured) interview measuring at least

physical functioning in patients with musculoskeletal disorders, and (3) the instrument had a patient-specific character. We included 23 out of 1617 studies referring to twelve different instruments. The Patient-Specific Functional Scale was the most reported patient-specific measurement tool in patients with musculoskeletal disorders. In addition to a description of the included instruments, the psychometric quality of the eligible studies was assessed by the *'Quality criteria for measurement properties of health status questionnaires'*. None of the included instruments has been evaluated on all criteria of the checklist (9 criteria). Eight instruments obtained exclusively positive scores on the items which have been evaluated (maximum 4 criteria). However, the majority of quality criteria has not been evaluated yet. Therefore, more research is needed to get insight into a broader range of psychometric properties of instruments measuring physical functioning in patients with musculoskeletal disorders in a patient-specific way.

Chapter 6 directly responds to this request by evaluating the psychometric qualities of a patient-specific measurement tool, originally developed in patients with rheumatic arthritis: the Dutch McMaster Toronto Arthritis Patient Preference Questionnaire (MACTAR). The MACTAR aims to evaluate changes in patient-specific physical functioning over time by reassessing the experienced difficulties in ten self-reported activities of daily living during a semi-structured interview.

The corresponding research question was:

- What is the content validity, the construct validity and the responsiveness of the Dutch MACTAR in patients with OA of the hip or knee?

To answer this question, data were used from a previously conducted randomized controlled trial in patients with hip/knee OA. Content validity of the MACTAR was determined by comparing the mentioned activities in the MACTAR to the activities included in the Dutch 'Western Ontario and McMaster Universities Osteoarthritis Index' (WOMAC) respectively the Dutch 'Medical Outcome Survey Short Form 36' (SF-36). In total, 27% of the activities gathered by the MACTAR was not represented in the WOMAC, 41% were not represented in the SF-36, and 11% were not covered in the WOMAC nor SF-36. Construct validity was determined by testing theoretically derived hypotheses concerning correlations between change scores on the MACTAR and change scores on the WOMAC respectively the SF-36. In contrast to our expectations, we identified only moderate correlations between change scores of the MACTAR, WOMAC and SF-36 (rs=.27 - rs=.44). Responsiveness of the MACTAR was indicated to be 'good', based on an 'Area Under the Curve' of .90 and better correlations between MACTAR change scores and Patient Global Assessment (PGA) scores than correlations between WOMAC / SF-36 change scores and PGA scores. These results suggest that the MACTAR is potentially better able to detect changes over time in activities that are important to individual patients compared to other tools measuring physical functioning. Therefore, clinicians are recommended to use the MACTAR to evaluate clinically

relevant changes over time in patient-specific physical functioning in addition to existing tools in patients with hip/knee OA.

Chapter 7 comprises a general discussion on the current state of affairs on personalized management in patients with hip/knee OA. It can be concluded that aspects of personalized care are already extensively applied in current clinical OA care. GPs, physical therapists, and orthopedic surgeons differentiate their treatment both in timing of care and in focus of care. However, the determination of the concept 'personalized care' has not been completed yet, neither in research nor in healthcare policy or clinical practice. Therefore, Chapter 7 comprises several recommendations for clinical OA practice, policy, and future research to reach the ultimate goals of personalized healthcare: to treat the right patients, at the right time, with the right interventions at the lowest possible price.

Samenvatting

Artrose van de heup en/of knie is een veelvoorkomende musculoskeletale aandoening. Verwacht wordt dat in de komende decennia de prevalentie van artrose aanzienlijk zal gaan toenemen. Artrose is een heterogene aandoening. Zowel de pathogenese als de klinische presentatie varieert enorm van patiënt tot patiënt. Om het functioneren van een toenemende aantal patiënten met artrose te verbeteren, is de vraag naar effectieve en efficiënte behandeling groot. Vanwege de heterogeniteit van artrose en de verwachtte stijging in omvang, lijkt artrose bijzonder geschikt voor gepersonaliseerde behandeling.

De algemene introductie van dit proefschrift **(Hoofdstuk 1)** presenteert de rationale voor gepersonaliseerde behandeling bij patiënten met heup/knie artrose. Gepersonaliseerde behandeling wordt gezien als één van de oplossingen om het hoofd te kunnen bieden aan de complexe en steeds groter wordende zorgvraag van mensen met (meerdere) chronische aandoeningen, inclusief artrose. Één reden om gepersonaliseerde behandeling toe te passen is de identificatie van patiënten die de grootste behoefte hebben aan zorg. Daarnaast maakt gepersonaliseerde behandeling het mogelijk om gestratificeerde zorg toe te passen en efficiënt gebruik te maken van gezondheidzorgbudgetten. Gepersonaliseerde zorg kan op verschillende manieren vormgegeven worden. Het doel van dit proefschrift is het verkennen van twee drivers die in potentie bijdragen aan gepersonaliseerde behandeling van patiënten met heup/knie artrose: 'timing van zorg' *(deel 1)* en 'focus van zorg' *(deel 2)*.

Deel I: Timing van zorg

Timing van zorg heeft betrekking op de fasering van interventies over de tijd bij patiënten met heup/knie artrose. Hierbij richt dit proefschrift zich in het bijzonder op de niet-chirurgische behandeling door de huisarts, de fysiotherapeut en de orthopeed. Ondanks dat de huidige klinische richtlijnen een helder overzicht geven van effectieve interventies bij heup/knie artrose, schenken deze richtlijnen slechts zeer beperkt aandacht aan de volgorde waarin deze interventies toegepast moeten worden. Dit is misschien één van de verklaringen voor het vaak gerapporteerde ondergebruik van niet-chirurgische interventies in de huidige artrose-zorg. Om het gebruik van niet-chirurgische interventies voorafgaand aan een verwijzing naar de tweedelijns zorg te faciliteren, hebben Smink et al. een stepped-care behandelstrategie ontwikkeld (Behandelstrategie ARTrose, 2011). In deze stepped-care strategie worden interventies in drie opeenvolgende stappen aangeboden. Stap-1 omvat interventies om de zelfzorg te stimuleren. Stap-2 voegt meer geavanceerde interventies toe, zoals de prescriptie van NSAID's en een verwijzing voor paramedische zorg (fysiotherapie / diëtiek). Stap-3 bevat onder andere een verwijzing naar tweedelijns zorg. Het uitgangspunt van de stepped-care behandelstrategie is dat patiënten alléén meer geavanceerde zorg ontvangen bij het uitblijven van resultaten door minder geavanceerde interventies.

De stepped-care behandelstrategie is op dit moment geïmplementeerd in één regio in Nederland. Landelijke implementatie is nog niet afgerond. In voorbereiding op landelijke implementatie van de stepped-care behandelstrategie geven we in dit proefschrift inzicht in de huidige artrosezorg door huisartsen en fysiotherapeuten, inclusief de overeenstemming met de stepped-care behandelstrategie.

Onderzoeksvragen van **Hoofdstuk 2** zijn:

- Wat is de inhoud van de huidige zorg door huisartsen voor patiënten met heup/knie artrose, inclusief de overeenstemming met de stepped-care behandelstrategie?
- In welke mate verschilt de inhoud van fysiotherapeutische zorg tussen patiënten met heup/knie artrose die verwezen zijn door hun huisarts van patiënten die de fysiotherapeut op eigen initiatief bezoeken?

Om deze vragen te kunnen beantwoorden hebben we retrospectief data bestudeerd die routinematig verzameld zijn door Nederlandse huisartsen en fysiotherapeuten ten behoeve van 'NIVEL Zorgregistraties eerstelijn'. In totaal zijn 12 118 medisch-elektronische dossiers geïncludeerd van patiënten die behandeld zijn door hun huisarts en/of fysiotherapeut vanwege heup/knie artrose. De uitgevoerde, beschrijvende analyses laten zien dat Nederlandse huisartsen hun interventies op dit moment al faseren in de tijd: ze passen minder geavanceerde interventies zoals leefstijladviezen en de prescriptie van NSAID's (stap 1&2), vaker toe dan bijvoorbeeld een verwijzing voor fysiotherapie of een verwijzing voor gewrichtsvervanging in de tweedelijn (stap 2&3). Ondanks dat ze grotendeels handelen in overeenstemming met de stappen van de stepped-care behandelstrategie, is er ruimte voor verbetering. Ten eerste, op dit moment passen huisartsen zelden alle interventies toe die bij één stap van de stepped-care behandelstrategie horen. Daarnaast verwijzen huisartsen patiënten vaker naar een orthopeed dan naar een fysiotherapeut. De introductie van de regeling Directe Toegankelijkheid Fysiotherapie biedt patiënten de mogelijkheid om additioneel aan een verwijzing door een (huis)arts op eigen initiatief een fysiotherapeut te bezoeken. Binnen de tijdspanne van dit onderzoek maakte 35% van de patiënten met heup/knie artrose die de fysiotherapeut bezocht gebruik van deze regeling. De inhoud van de fysiotherapeutische zorg verschilde niet tussen de groep zelf-verwijzers en de groep die verwezen werd door de huisarts.

Hoofdstuk 3 focust op de setting waarin de artrose zorg wordt verleend. Deze setting hangt nauw samen met de timing van zorg. Omdat eerstelijns zorg voor iedereen toegankelijk is en de zorg in deze setting goedkoper is in vergelijking met tweedelijns zorg, adviseert de stepped-care behandeslstrategie om artrose-zorg te starten in de eerstelijn. Eerder onderzoek heeft aangetoond dat een aanzienlijk deel van de artrosepopulatie uiteindelijk verwezen wordt naar de tweedelijn. Ongeveer een derde deel van deze verwezen populatie ontvangt een gewrichtsvervangende operatie. Op dit moment is er weinig bekend over factoren die geassocieerd zijn met de keuze om de patiënt alléén in de eerstelijn te behandelen, te verwijzen voor niet-chirurgische behandeling in de tweedelijn of een gewrichtsvervangende operatie te laten ondergaan. Deze factoren kunnen zowel betrekking hebben op karakteristieken van de

patiënt, de huisarts als de huisartspraktijk. Inzicht in deze factoren op verschillende niveau's kan bruikbaar zijn bij de landelijke implementatie van de stepped-care behandelstrategie in de dagelijkse zorgpraktijk.

De vraag die in **hoofdstuk 3** centraal staat is:

- Welke individuele factoren, huisarts-gerelateerde factoren en huisartspraktijk-gerelateerde factoren zijn geassocieerd met 1) behandeling in de eerstelijns zorg, 2) niet-chirurgische behandeling in de tweedelijn en 3) chirurgische behandeling bij patiënten die hun huisarts bezoeken vanwege heup/knie artrose?

Om deze vraag te kunnen beantwoorden hebben we logistische multilevel analyses uitgevoerd op verzamelde data binnen een reeds afgeronde cohortstudie. Het cohort bestond uit 313 nieuw gediagnosticeerde patiënten met heup/knie artrose, behandeld door 70 huisartsen in 38 huisartspraktijken in Nederland. Significante factoren geassocieerd met de setting van zorg waren voornamelijk gerelateerd aan de patiënt, in het bijzonder de reeds ontvangen zorg door de patiënt. Bij 47% van de patiënten beperkte de zorg zich tot eerstelijn. Dit deel van de patiënten liet een hoger niveau van fysiek functioneren zien (Odds Ratio (OR) 1,03). Verder ontving de groep die uitsluitend behandeld werd in de eerstelijn minder vaak oefentherapie (OR 0,46) of intra-articulaire injecties (OR 0,08) and werd minder vaak een radiologische beoordeling gerapporteerd (OR 0,06). Deze resultaten stemmen overeen met de stepped-care behandelstrategie, waarin het gebruik van minder geavanceerde interventies wordt geprefereerd boven meer geavanceerde interventies, inclusief een verwijzing naar de tweedelijn.
Twee van de drie patiënten die werden verwezen naar de tweedelijn ontvingen uitsluitend niet-chirurgische interventies. Het besluit om niet-chirurgische interventies te continueren in de tweedelijn werd vaker genomen bij patiënten met een werkverband (OR 2.90). Ook werd duidelijk dat ieder extra gewricht dat aangedaan is door artrose de kans verdubbelt op continuering van niet-chirurgische behandeling. Aangezien de kans op multi-gewrichtsartrose toeneemt in de volgende decennia, is nader onderzoek op dit thema gewenst.
Onze studie heeft geen factoren gerelateerd aan de patiënt, de huisarts noch de huisartspraktijk aan het licht gebracht die geassocieerd zijn met het uitvoeren van een chirurgische interventie, behalve het gebruik van oefentherapie in het verleden. De toepassing van oefentherapie in het verleden biedt een aanzienlijk grotere kans op het ontvangen van een chirurgische interventie (OR 7.42). Dit resultaat komt overeen met de principes van de stepped-care behandelstrategie. Daarnaast bevestigt het de belangrijke rol van orthopeden in het timen van een chirurgische ingreep. Dit onderzoek toont aan dat deze professionals het gebruik van niet-chirurgische interventies overwegen voorafgaand aan het voorstellen van een chirurgische ingreep.

Deel II: Focus van zorg

In dit proefschrift is de focus van zorg geoperationaliseerd door middel van 'behandelstratificatie' en 'gepersonaliseerd meten'. Behandelstratificatie heeft als doel beter rekening te houden met verschillende subgroepen binnen de patiëntenpopulatie met knie-artrose, doordat de behandeling wordt aangepast aan deze verschillende subgroepen. Gepersonaliseerd meten het als doel het integreren van een patiënt' zijn of haar prioriteiten en voorkeuren. Veelgebruikte, zogenoemde 'fixed-item' instrumenten missen deze mogelijkheid.

Behandelstratificatie

De klinische presentatie van patiënten met heup/knie artrose verschilt van patiënt tot patiënt. Knoop et al. (2011) en van der Esch et al. (2015) zijn erin geslaagd om vijf klinische fenotypen van knie-artrose te onderscheiden: minimale gewrichtsschade, hoge spierkracht, ernstige radiologische afwijkingen, obesitas en depressieve stemming. Omdat zowel de oorzaak van de klachten als het beloop van de klachten verschilt tussen deze fenotypes, wordt verondersteld dat ieder fenotype gebaat zou zijn bij een specifieke behandeling. Het is onbekend in welke mate fysiotherapeuten op dit moment al onderscheid maken in hun behandeling tussen de vijf genoemde fenotypen van knie-artrose.

Daarom luidt de onderzoeksvraag van **Hoofdstuk 4**:

- In welke mate is de fysiotherapeutische behandeling afgestemd het 'minimale gewrichtsschade' fenotype, het 'hoge spierkracht' fenotype, het fenotype met 'ernstige radiologische afwijkingen', het 'obese' fenotype en het fenotype met een 'depressieve stemming' binnen de populatie patiënten met knie-artrose?

Voorafgaand aan het onderzoek zijn hypotheses opgesteld voor ieder fenotype in relatie tot de geprefereerde interventies, het verwijsbeleid en het aantal te geven behandelsessies. Deze hypotheses zijn getoetst via een klinische vignettudie. We hebben vijf visuele, klinische vignetten samengesteld die de reeds genoemde fenotypen vertegenwoordigden. Vervolgens zijn in Nederland 144 fysiotherapeuten en oefentherapeuten geworven om aan de hand van de vignetten hun voorgenomen behandeling inclusief de omvang van de behandeling te beschrijven. Over het algemeen lijken fysiotherapeuten en oefentherapeuten hun behandeling aan te passen aan de verschillende fenotypen van knie-artrose. Er zijn namelijk statistisch significante verschillen gevonden ten aanzien van de inhoud en omvang van zorg tussen de vijf fenotypen. Deze verschillen kwamen grotendeels overeen met onze vooraf gestelde hypotheses, met uitzondering van het sterke spierkracht fenotype en het fenotype met een depressieve stemming. Met betrekking tot het sterke spierkracht fenotype viel op dat oefentherapie veel vaker werd toegepast dan vooral gedacht en dat het aantal verwijzingen naar de tweedelijn juist lager was dan verwacht. Bij het fenotype met een depressieve stemming oversteeg het aantal verwijzingen naar psychologen onze verwachting. Nader

onderzoek wordt aanbevolen met betrekking tot de ontwikkeling van gestratificeerde interventies bij patiënten met knie-artrose, inclusief de evaluatie op (kosten)effectiviteit.

Gepersonaliseerd meten

Naast gestratificeerde behandeling kan gepersonaliseerd meten ook bijdragen aan een gepersonaliseerde focus van zorg bij patiënten met heup/knie artrose. Op dit moment worden met name fixed-item instrumenten gebruikt bij de diagnostiek en evaluatie van beperkingen in het fysiek functioneren binnen de artrose-populatie. Deze fixed-item instrumenten zijn niet in staat om voorkeuren en prioriteiten van patiënten mee te nemen. Ook variatie in uitvoering van specifieke activiteiten kunnen niet gemeten worden. Dit heeft als consequentie dat clinici patiënt-relevante activiteiten missen, die ze hadden kunnen inzetten bij gepersonaliseerde doelbepaling. Om zorg te kunnen bieden die gefocust is op de individuele patiënt is het wenselijk om het gebruik van gepersonaliseerde meetinstrumenten te overwegen in aanvulling op fixed-item instrumenten. Op dit moment is het niet duidelijk welke gepersonaliseerde meetinstrumenten beschikbaar zijn voor patiënten met musculoskeletale aandoeningen, waaronder heup/knie artrose.

Daarom hebben we een systematische literatuurstudie uitgevoerd om deze instrumenten te identificeren **(Hoofdstuk 5)**. Vervolgens hebben we de psychometrische kwaliteiten van de instrumenten bepaald.

De onderzoeksvragen waren:

- Welke gepersonaliseerde zelf-assessment instrumenten zijn beschikbaar om fysiek functioneren te meten bij patiënten met musculoskeletale aandoeningen?
- Wat zijn de kenmerken en psychometrische kwaliteiten van gepersonaliseerde meetinstrumenten die fysiek functioneren meten bij patiënten met musculoskeletale aandoeningen?

We voerden een uitgebreid literatuuronderzoek uit in verschillende databases. Studies werden geïncludeerd als: (1) het hoofddoel van de studie was het onderzoeken van psychometrische eigenschappen, (2) het beschreven instrument een vragenlijst, een beoordelingsschaal of een (semi-gestructureerd) interview was die minimaal fysiek functioneren in kaart bracht bij mensen met musculoskeletale aandoeningen en (3) het instrument een gepersonaliseerd karakter had. Uiteindelijk zijn 23 van de 1617 geïdentificeerde studies geïncludeerd, verwijzend naar twaalf verschillende instrumenten. De 'Patient-Specific Functional Scale' was het meest gerapporteerde, gepersonaliseerde meetinstrument bij patiënten met musculoskeletale aandoeningen. Naast een beschrijving van de geïncludeerde artikelen is de psychometrische kwaliteit van de studies getest door middel van de lijst *'Quality criteria for measurement properties of health status questionnaires'*. Geen van de geïncludeerde artikelen is geëvalueerd op alle criteria van de lijst (9 criteria). Acht instrumenten ontvingen wel uitsluitend positieve scores op de items die beschreven zijn, met een maximum van 4 criteria. Echter, de meerderheid van

de kwaliteitscriteria is op dit moment nog niet onderzocht. Meer onderzoek is daarom nodig om inzicht te krijgen in een breder spectrum van psychometrische kwaliteiten van instrumenten die fysiek functioneren in kaart brengen bij patiënten met musculoskeletale aandoeningen op een gepersonaliseerde wijze.

Hoofdstuk 6 geeft direct gehoor aan deze oproep door het evalueren van de psychometrische kwaliteit van een gepersonaliseerd meetinstrument, oorspronkelijk ontwikkeld voor patiënten met reumatoïde artritis. Dit instrument is de 'Dutch McMaster Toronto Arthritis Patient Preference Questionnaire' (MACTAR). De MACTAR heeft als doel om veranderingen in de tijd te evalueren op het gebied van gepersonaliseerd fysiek functioneren. Dit wordt gedaan via het herbeoordelen van ervaren problemen met maximaal tien zelf-gerapporteerde activiteiten van het dagelijks leven in een semi-gestructueerd interview.

De bijbehorende onderzoeksvraag was:

- Wat is de content validiteit, de construct validiteit en de responsiviteit van de Nederlandse versie van de MACTAR bij patiënten met artrose van de heup of de knie?

Om deze vraag te beantwoorden hebben we gebruik gemaakt van data die reeds eerder verzameld is in het kader van een gerandomiseerd, gecontroleerd onderzoek in een patiëntenpopulatie met heup/knie artrose. De content validiteit van de MACTAR is bepaald door het vergelijken van genoemde problematische activiteiten in de MACTAR met activiteiten die voorkomen in de Nederlandse versies van de 'Western Ontario and McMaster Universities Osteoarthritis Index' (WOMAC) respectievelijk de 'Medical Outcome Survey Short Form 36' (SF-36). In totaal kwam 27% van de activiteiten verzameld in de MACTAR niet voor in de WOMAC, 41% niet in de SF-36 en 11% werd niet gedekt in de WOMAC noch in de SF-36. Construct validiteit werd bepaald door het toetsen van hypotheses over de correlatie tussen veranderscores op de MACTAR met veranderscores op de WOMAC / SF-36. In tegenstelling tot onze verwachtingen vonden we uitsluitend matige correlaties tussen veranderscores op de MACTAR, WOMAC en SF-36 (r_s=.27 – r_s=.44). Responsiviteit van de MACTAR werd op basis van twee manieren als 'goed' beoordeeld. Ten eerste op basis van een 'Area Under the Curve' van .90. Ten tweede werd de goede responsiviteit van de MACTAR bevestigd door een hogere correlatie tussen de veranderscores op de MACTAR en Patient Global Assessment (PGA) scores dan de correlatie tussen de veranderscores op de WOMAC / SF-36 en de PGA scores. Deze resultaten suggereren dat de MACTAR in potentie beter in staat is om veranderingen over de tijd te detecteren in activiteiten die belangrijk zijn voor individuele patiënten dan andere instrumenten die fysiek functioneren meten. Daarom wordt aanbevolen om, naast de reeds bestaande instrumenten, de MACTAR te gebruiken in de zorgpraktijk om klinisch relevante veranderingen over de tijd te meten in gepersonaliseerd fysiek functioneren.

Hoofdstuk 7 bevat een algemene discussie over de huidige stand van zaken met betrekking tot gepersonaliseerde behandeling van patiënten met heup/knie artrose. Er kan geconcludeerd

worden dat aspecten van gepersonaliseerde zorg al uitgebreid toegepast worden in de huidige klinische artrose-zorg. Huisartsen, fysiotherapeuten en orthopeden differentiëren hun behandeling zowel in timing van zorg als focus van zorg. Echter, de ontwikkeling van het concept 'gepersonaliseerde zorg' is nog niet afgerond. Dit geldt zowel voor het onderzoek, het beleid en de klinische praktijk. Daarom bevat hoofdstuk 7 verschillende aanbevelingen voor klinische artrose-zorg, beleid en onderzoek om het ultieme doel van gepersonaliseerde zorg te kunnen bereiken: het behandelen van de juiste patiënten, op het juiste moment met de juiste interventies tegen de laagst mogelijke prijs.

Dankwoord

'Een sprokkelpromotie? Daar heb ik echt nog nooit van gehoord. Wat is dat?' Deze zinnen heb ik de afgelopen zes jaar vaak gehoord uit monden van onderzoekers, beleidsmakers en fysiotherapeuten. Voor NIVEL-lers is het een bekende constructie: je participeert in een lopend onderzoeksproject en gebruikt data die verzameld zijn binnen dit project als basis voor je proefschrift. Waar nodig 'sprokkel' je nog data bij andere projecten of je voert een aanvullend onderzoek uit om je vraagstellingen te kunnen beantwoorden. Het klinkt misschien wat armoedig, maar ik heb ervaren dat een sprokkelpromotie ook veel voordelen kent. Drie voorbeelden. (1) Géén subsidie voor drie of vier jaar waarin je je onderzoek moet opzetten, uitvoeren, analyseren én publiceren. Met drie kinderen geboren in vier jaar tijd was dat best een opgave geworden. (2) Géén totale focus op één onderwerp. Doordat ik primair werkte aan een veelzijdig project als 'NIVEL Zorgregistraties eerste lijn' heb ik me kunnen ontwikkelen op veel meer vlakken dan alleen het doen van onderzoek. (3) Géén strijd tegen de eenzaamheid van het promovendus-bestaan. Perioden van focus op het proefschrift wisselden vaak met hectische perioden rond projectdeadlines.
Natuurlijk ben ik best wel eens jaloers geweest op collega-onderzoekers die zich vol konden storten op hun vierjarige promotie-onderzoek. Ik bewonder de gedrevenheid waarmee deze mensen zich vastbijten in één onderwerp en na vier jaar hard werken hun levenswerk opleveren in een mooi boekje. Na het promotiefeestje sluiten ze een fase in hun leven af en begint een volgende fase waarin het sociale leven weer een plaats kan krijgen.

Wat dat betreft sta ik er echt wel anders in. Promoveren heeft nooit mijn leven beheerst in positieve of negatieve zin. Het was een natuurlijk onderdeel van mijn dagelijks bestaan, net als mijn gezin en sociale leven. Dat neemt niet weg dat ik het als een groot voorrecht beschouw dat ik de kans heb gekregen om via het promotie-onderzoek te doen waar ik energie van krijg: bijdragen aan de innovatie van de (beweeg)zorg ten dienste van de individuele patiënt. Gedurende het promotie-traject heb ik me kunnen ontwikkelen als onderzoeker, heb ik veel verschillende mensen leren kennen in heel verschillende rollen en organisaties en heb ik plaatsen van de wereld gezien die ik nog niet eerder gezien had. De waarde van promoveren zit voor mij dus zeker niet alleen in het uiteindelijke boekje, maar veel meer in het traject daar naartoe.

Tijdens dit traject is een groot aantal mensen belangrijk geweest, waarvan ik er een aantal in het bijzonder wil noemen.

In de eerste plaats de leden van het promotieteam. Graag had ik willen beginnen met het bedanken van Dinny de Bakker. Dinny heeft mij aangenomen als junior onderzoeker op het project LiPZ, de voorganger van NIVEL Zorgregistraties, en werd later mijn promotor. Als hoofd van de onderzoeksafdeling had hij met een groot aantal verschillende projecten en onderzoekers te maken, maar door zijn enorme geheugen én persoonlijke betrokkenheid kon hij altijd terughalen waar je mee bezig was. Een gesprek met Dinny voelde dan ook altijd vertrouwd. Helaas is Dinny op de laatste dag van 2016 overleden aan de gevolgen van kanker.

Beste Joost, heel erg bedankt dat je relatief laat in het traject toch bereid was om in te stromen in het promotieteam. Jouw enorme kennis en ervaring op het gebied van artrose, revalidatie én het doen van onderzoek hebben de laatste twee artikelen en de in- en uitleiding zeker naar een hoger niveau gebracht. Ik heb veel geleerd van je concrete feedback en vind het bewonderenswaardig dat je vrijwel altijd binnen 24 uur mijn mails beantwoordde, waar ter wereld je ook was.
Lieve Cindy, jij bent de enige die als co-auteur aan alle vijf de artikelen van dit proefschrift verbonden bent. Dat zegt eigenlijk al wel iets over onze band. Na mijn stage bij het NIVEL verontschuldigde je je dat er op dat moment geen vacature was binnen het Paramed team. Nog geen maand later belde je met het verzoek te sollicteren op een juniorfunctie binnen LiPZ. Ik ben je enorm dankbaar voor deze kans. Mede dankzij jou kwam ik terecht in een warm nest met gedreven onderzoekers dat echt als een team functioneerde. Je bent een echte verbinder, zowel als persoon binnen het team als in je rol als leidinggevende tussen onderzoek, beleid en beroepspraktijk. Je bent een voorbeeld voor me als het gaat om het enthousiasmeren van mensen, kansen zien en het combineren van werk en gezin. Dank je wel voor je betrokkenheid en support en ik vind het echt heel fijn om opnieuw lid te zijn van je onderzoeksgroep in een andere setting.
Lieve Ilse, ook jou beschouw ik als één van de belangrijkste personen van mijn loopbaan tot nu toe. Ik kan me mijn eerste dagen als LiPZ-onderzoeker nog goed herinneren. Na het rondje door het gebouw en het verwerken van minimaal 30 nieuwe namen en gezichten doken we samen achter de computer. Je liet me alle ins-en-outs van de STATA do-files zien die nodig waren om het jaarbestand voor LiPZ te genereren. Dat was wel wat anders dan het registreren van parameters van COPD-patiënten tijdens hun revalidatie… Maar door je enthousiasme en schat aan ervaring op het dossieronderzoek voelde ik me al heel snel thuis op mijn nieuwe plek. Doordat je alles top georganiseerd had, kreeg ik al snel ruimte om naast reguliere LiPZ-werkzaamheden met innovatie aan de slag te gaan. Je nam me mee naar softwareleveranciers, koepelorganisaties en het ministerie. Je hebt laten zien dat onderzoek veel meer (en leuker!) is dan het analyseren van data en schrijven van publicaties. Ook toen je rol binnen het NIVEL veranderde was je altijd bereid om even te helpen. Hoe vaak je niet gevraagd hebt of je nog iets voor me kon doen met het oog op je rol als co-promotor kan ik niet zeggen. Je was er altijd voor me. Dank je wel daarvoor! Ik heb echt wel moed moeten verzamelen om te vertellen dat ik het NIVEL ging verlaten. Gelukkig zien en appen we elkaar nog regelmatig en ik hoop ook echt dat dat zo blijft!

Met het afronden van mijn proefschrift komt er dan toch echt een einde aan mijn NIVEL-tijd. Ik ben al even weg, maar ik voel me nog altijd verbonden met deze fijne plek. Lange tijd deelde ik kamer 3.19 met Jacqueline en Margit. Wat was het een leuke tijd! Alledrie LiPZ-onderzoekers en alledrie bezig met een sprokkelpromotie. Jacqueline is al even klaar en ik hoop dat Margit ook nog gaat volgen. In mijn laatste NIVEL jaar was de samenstelling van 3.19 volop in beweging. Dat past ook wel bij een organisatie als het NIVEL en heb dat als positief ervaren. Leontien, we konden lekker sparren over babykwaaltjes en peuteravonturen, want

onze jongens zijn ongeveer even oud. Ook de andere kamergenootjes wil ik bedanken voor de gezellige tijd: Marijn, Daphne, Esther en Sabine.
Mijn eerste NIVEL-jaren maakte LiPZ onderdeel uit van het Paramed team. Dat het een hecht en echt team was, blijkt wel uit de activiteiten die we ver na het uiteenvallen van Paramed nog met z'n allen ondernomen hebben. Met als hoogtepunt toch wel de curlingworkshop in Zoetermeer. Daniël, Karin, Wil, Chantal, Cindy, Corelien, Ilse, Jacqueline, Linda, Lisa en Margit dank jullie wel voor de fijne tijd!
In 2013 werd LiPZ onderdeel van de NIVEL Zorgregistraties eerste lijn. Een heel nieuwe groep mensen die echt wel aan elkaar en elkaars' werkwijze moest wennen, maar het kernteam vormde zeker wel een mooi geheel! Robert, als programmaleider had je de moeilijke taak om een stel eigenwijze onderzoekers met verschillende achtergronden bij elkaar te brengen en er één geheel van te smeden. Logisch dat het in dat proces nog wel eens botste, maar je liet je niet uit het veld slaan. Dat waardeer ik enorm aan je. Ik ben je dankbaar voor het vertrouwen dat je me gaf als persoon en je steun voor het relatief kleine onderdeel 'fysio-/oefentherapie' in het grote geheel van de Zorgregistraties. Lando, als projectleider en verantwoordelijke voor de paramedische zorg binnen de Zorgregistraties hebben we de laatste jaren intensief samengewerkt. Je zorgvuldigheid en precisie hebben zeker bijgedragen aan de kwaliteit van onze publicaties. Je afscheidsspeech zal ik nooit vergeten. Dank je wel! Mark, Marieke, Karin en Lisa, we zaten in hetzelfde schuitje: het was onze taak om gegevens binnen te halen uit de deelnemende praktijken en via de juiste analyses iets te zeggen over zorg en gezondheid in de eerste lijn. Dat de disciplines niet gelijk waren, was niet zo belangrijk. Dank jullie wel voor de vele uurtjes LINEL-klein, LINEL-groot, website-overleg, peer-feedback en natuurlijk het spuien over allerlei randzaken.
NIVEL Zorgregistraties zou echt niet kunnen bestaan uit alleen onderzoekers. Zowel voorafgaand aan het onderzoekers-traject als aansluitend hieraan, zijn veel mensen onmisbaar. Jan Gravestein, als expert én ervaringsdeskundige op het gebied van (LiPZ)-Beweegzorg heb je me veel geleerd. Ik wist niets van datamodellen, entiteiten en csv bestanden maar al doende konden we goed met elkaar communiceren. Dank je wel voor al je werk voor LiPZ en NIVEL Zorgregistraties, je enthousiaste verhalen over je koor en je interesse voor mijn leven. Bram, jij vormde echt de schakel tussen de ICT'ers en de onderzoekers. Waar de ICT-taal mij soms echt boven de pet ging, kon jij de vertaalslag maken zodat ik toch weer aanhaakte. Onmisbaar wat mij betreft. Marcus, vele uurtjes hebben we samen achter een scherm gezeten om de websites van de Zorgregistraties en vergelijkbare projecten te vullen. Wat een gedoe soms om alles precies goed te krijgen. Jij verloor nooit je geduld en daardoor kwam het altijd goed.

Toen ik in september 2016 het NIVEL inwisselde voor de Hogeschool Utrecht, was dat inhoudelijk een grote verandering. Bij het NIVEL maakte ik onderdeel uit van een geoliede machine, bij het lectoraat was alleen de bouwtekening nog maar gemaakt. In het begin was deze vrijheid even wennen, maar het kwam goed van pas. Naast het opbouwen van een netwerk en het initieren van onderzoeksprojecten kon ik tijd besteden aan de afronding van mijn proefschrift. Corelien, je was daarin echt een droomvoorbeeld, maar je maakte me ook wel zenuwachtig. Je had alles voor je promotie zo strak geregeld naast al je andere

werkzaamheden en loopactiviteiten. Echt super knap! Ik ben heel blij dat ik eerst jouw paranimf mag zijn en dat we daarna de rollen omdraaien. Andere HU-collega's van de kenniscentrumruimte, inhoudelijk stond mijn proefschrift al wel toen ik bij de HU begon, maar in het proces heb ik veel steun van jullie gehad. De terugkerende vraag 'heb je al een datum?' heeft wel geholpen om vaart te maken. De lijst met namen is te lang om op te noemen, maar ik hoop op nog heel veel gezellige uren in onze ietwat lawaaige ruimte, mét de imiddels al traditionele dropjes op de vrijdagmiddag.

Één persoon uit de bredere onderzoeksgroep 'Fysiotherapiewetenschap', waar het lectoraat onderdeel van uitmaakt, wil ik nog in het bijzonder bedanken. Dat is Martijn. Martijn, jij was begeleider van een werkgroep bij de master Fysiotherapiewetenschap en bezig met de afronding van je promotie bij het NIVEL. Jij vormde de schakel naar mijn afstudeerstage bij het NIVEL en legde zo de basis voor mijn wetenschappelijke loopbaan. Je vertrok bij het NIVEL toen ik in dienst kwam, dus NIVEL-collega's zijn we eigenlijk nooit geweest. Hoe grappig is het dan dat we dat nu wel zijn binnen de mooie onderzoeksgroep van Cindy aan de HU/UMC.

Zoals ik aan het begin van dit dankwoord al schetste vormde dit promotie-traject een natuurlijk onderdeel van mijn dagelijks leven. Familie en vrienden weten uiteraard dat ik onderzoek doe op het thema Beweegzorg, maar niet persé dat dit deels verpakt is in een promotie-onderzoek. Het voelt dan ook een beetje vreemd om mensen te bedanken voor hun steun en betrokkenheid gedurende de afgelopen zes jaar. Ik ben hen los van dit proefschrift dankbaar voor wie ze zijn en wat ze doen.

Een paar mensen wil ik toch apart noemen. Opa en oma, voor jullie is deze promotie een heel bijzondere gebeurtenis. Het zou prachtig zijn geweest om dit moment met jullie allebei te delen, maar helaas kan oma niet naar Utrecht komen. Pap, mam, jullie hebben Michel, Ninke en mij van jongs af aan gestimuleerd om ons te ontwikkelen en door te zetten. Daar is deze promotie denk ik wel een mooi voorbeeld van. Ninke, als 'kleine zusje' heb je altijd een bijzondere plaats. Ik vind het super leuk dat ik jouw getuige mocht zijn toen je trouwde met Bram en dat jij nu een speciale rol als paranimf hebt bij mijn promotie. Lieve Guus, Koen en Stef, jullie hebben nog geen idee wat 'promoveren' is. Wat mij betreft blijft dat voorlopig ook zo. Doen wat je leuk vindt en waar je anderen mee kan helpen heeft prioriteit. Als dat uitmondt in het volgen van een studie of het doen van promotie-onderzoek is dat helemaal goed. Lieve Jaap, jij hebt uiteraard het meest meegekregen van dit hele traject. Soms voelde ik me wel een beetje schuldig als jij een keer lekker op de bank een filmpje zat te kijken terwijl ik aan het typen was aan de keukentafel. Maar 'gelukkig' hebben we het laatste jaar best veel tijd samen aan die keukentafel doorgebracht. Volgend jaar rond jij je parttime studie af, die je naast je bijna fulltime baan in de 'tropenjaren' van ons leven gestart bent. Met die tropenjaren gaan we nog even door, want we leven toe naar het hoogtepunt van het jaar: de geboorte van een nieuw lid van ons prachtige gezin!

About the author

Di-Janne Barten was born on May 13th 1985 in Wageningen, the Netherlands and moved to Opheusden, the Netherlands at the age of three years. She completed secondary school (VWO) in 2003 at the Hendrik Pierson College in Zetten. Subsequently, she joined the bachelor program Physical Therapy at the Utrecht University of Applied Sciences (2003-2007). Her senior internships, respectively at a primary care practice in Wageningen and at a hospital in Tiel, resulted in her first jobs at the domain of physical therapy. Shortly afterwards, these activities were extended by therapeutic guidance of patients suffering from Chronic Obstructive Pulmonay Disease at a primary care practice in Buren, Gelderland. Next to these jobs, she completed the pre-master and master program Clinical Health Sciences, particularly Physical Therapy Sciences at the Utrecht University Medical Center. During her internship at the Netherlands Institute for Health Services Research (NIVEL) in Utrecht, the 'contamination' with osteoarthritis-research has happened. By conducting a systematic review on psychometric properties of personalised measurement tools and validating a personalised measurement tool in patients with hip/knee osteoarthritis, a sound basis for her PhD thesis has been provided. After her graduation in 2010, she started as junior researcher at NIVEL on the long-term project 'NIVEL Primary Care Database'. By this project, she gained lots of experience with developing data-extraction modules, projectmanagement, analyzing large datasets, and writing (inter)national scientific publications both on the domain of health services research as well as physical therapy. A small part of the data gathered by this project has been used in her PhD-thesis. Additional data were gathered during a temporary assignment at St. Maartenskliniek Nijmegen, a hospital specialized in orthopaedic care. In 2016, her activities in clinical practice ended. Unfortnuately, the desired combination of applying research, performing clinical care and 'managing' a family was not feasible any longer.

Since the autumn of 2016, Di-Janne has joined the researchgroup 'Innovation of Human Movement Care' at the Utrecht Univerisity of Applied Sciences. Her research focuses on the development and implementation of innovative physical therapy pathways, especially in primary care settings, communities, and neighbourhoods. Interprofessional collaboration and co-creation with stakeholders from a citizen's or patient's perspective, are important aspects in her current research projects. In that respect, her current focus of research meets the personalized focus of her PhD thesis in patients with hip/knee osteoarthritis.

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