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Title

Guidelines for the use of diagnostic imaging in musculoskeletal (MSK) pain conditions affecting the lower back, knee and shoulder: a scoping review

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Conflicts of Interest

There are no conflicts of interest to declare for any of the authors.

Title

Guidelines for the use of diagnostic imaging in musculoskeletal (MSK) pain conditions affecting the lower back, knee, and shoulder: a scoping review

Abstract

Background

Musculoskeletal (MSK) pain is one of the most common reasons for primary care consultation, particularly pain in the lower back (LBP), knee, and shoulder. The use of diagnostic imaging for musculoskeletal pain is increasing but it is unclear whether this increase is justified based on clinical practice guideline (CPG) recommendations.

Aim

To identify and map the content of CPGs that inform the use of diagnostic imaging in those with non-traumatic LBP, knee, and shoulder pain in primary and intermediate care in the UK.

Design and Setting

A scoping review of CPGs.

Methods

This scoping review was conducted and is reported in accordance with PRISMA guidance. A broad search strategy included electronic searches of MEDLINE, CINAHL, PsychINFO and SPORTDiscus from 2009 to the 17th April 2019. This was conducted alongside a search of

guideline repositories and was combined with a snowball search of Google, relevant professional bodies and use of social media.

Results

31 relevant CPGs were included. Routine use of diagnostic imaging for those with non-traumatic LBP, knee or shoulder pain is generally discouraged in primary care or intermediate care. Diagnostic imaging should be reserved for when specific or serious pathology is suspected or where the person is not responding to initial non-surgical management and the imaging result is expected to change clinical management decisions.

Conclusion

Diagnostic imaging should not be routinely requested in primary or intermediate care for non-traumatic LBP, knee, or shoulder pain. CPGs do not justify the increasing imaging rates in the UK for musculoskeletal pain.

Keywords

- Musculoskeletal
- Lower Back Pain
- Knee Pain
- Shoulder Pain
- Clinical Practice Guidelines
- Scoping Reviews

Introduction

Musculoskeletal (MSK) pain conditions are one of the most common reasons for primary care consultation (Jordan *et al.*, 2010), with the highest prevalence for low back, shoulder and knee pain (Urwin *et al.*, 1998; Jordan *et al.*, 2010). The majority of these presentations are non-traumatic and often cannot be attributed to a specific structural or biomedical diagnosis. In turn, these are regularly allocated a non-specific label (Jordan *et al.*, 2010).

For nearly all of those presenting with lower back pain (LBP), knee or shoulder pain the recommended first-line clinical care is non-surgical (Lin *et al.*, 2019) and includes advice and education, exercise, activity modification, and pharmacological interventions. More invasive treatments such as injections or surgery are reserved for a smaller proportion of patients with either clear pathology that justifies a particular type of invasive intervention or for patients whose symptoms persist following recommended non-surgical treatment (Lin *et al.*, 2019). Whilst this 'stepped care' approach is advocated, the indications for proceeding to surgery in those that have not previously responded to non-surgical management have been challenged (Lurie *et al.*, 2015; Beard *et al.*, 2018; Sihvonen *et al.*, 2018).

The decision to request diagnostic imaging (DI) is increasing in early primary care consultations. Between 2014-2019, there has been a 16% increase in the use of radiology within the National Health Service (NHS). This level of demand has been acknowledged as a challenge within the NHS (NHS England, 2019b). A recent systematic review (SR) and meta-analysis investigated global rates of imaging for LBP over the ten-year interval from 1995 to 2015. This review estimated that 24.8% of patients with LBP that present to primary care currently will undergo DI and found that the rate of complex imaging (MRI and CT Scan) has increased by 50% for those consulting in primary care or emergency departments (Downie *et al.*, 2019). Despite this increase in investigation rate, for those presenting with acute or sub-acute LBP in primary care, no difference is seen between those who received

imaging and those who received usual care without imaging (Chou *et al.*, 2009) with regards to pain, function or quality of life at any time point up to 12-months (Chou *et al.*, 2009). Similar findings have been demonstrated for knee pain (Karel *et al.*, 2015) and shoulder pain (Bradley, Tung and Green, 2005).

In the context of a rising prevalence of imaging, the problems associated with the risk of misuse of DI are well recognised. These include a potential waste of finite healthcare resources, poorer perceived prognosis and an increased chance of undergoing surgery (Webster *et al.*, 2014; Darlow *et al.*, 2017). Furthermore, there is considerable uncertainty about how scan findings, for example ultrasound scan (USS) evidence of a rotator cuff tear (Girish *et al.*, 2011), or evidence of a prolapsed intervertebral disc on an MRI scan (Brinjikji *et al.*, 2015) correlate with patient symptoms. Despite this uncertainty and questionable added value, scan results are perceived by patients as authoritative (Cuff and Littlewood, 2018). Given that a substantial proportion of primary care consultations involve MSK pain presentations and 90% of all consultations occur within primary care (Network, 2019), there is a clear need to better understand the reasons for the increasing use of DI.

Clinical practice guidelines (CPGs) are 'statements that include recommendations intended to optimise patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options' (Graham, Mancher and Miller Wolman, 2011). They are a key source of information about the appropriate use of DI (Darlow *et al.*, 2017). The aim of this study was to identify, summarise, and identify similarities and differences between CPGs that inform UK clinical practice with respect to DI (X-ray, MRI, USS) for non-traumatic LBP, knee, and shoulder pain.

Methods

This scoping review was designed with reference to guidance described by the Joanna Briggs Institute (Peters, et al. 2015). An attempt was made to register the protocol with PROSPERO however, scoping review protocols are not currently accepted. Any deviations from the protocol are outlined below.

Eligibility Criteria

CPGs were included which:

- were either developed in the UK or intended for wider regional use that inform MSK clinical practice within UK primary or intermediate care.
- met the definition of a CPG: statements that include recommendations intended to optimise patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.
- provide recommendations on the use of DI in adults with non-traumatic LBP, knee, and shoulder pain.
- were published between 2009-2019 and accessible in the public domain.

Search Strategy & Information Sources

The full electronic search strategy can be found in **Supplementary Tables 1-22**.

A comprehensive search of key databases (MEDLINE, CINAHL complete, PsycINFO and SPORTDiscus) was undertaken from 2009 to the 17th April 2019. The full MEDLINE search strategy for LBP can be found in **Table 1**. This was complemented by a search of CPG repositories as well as a 'snowball' search of the top 50 results from a Google search and the websites of professional bodies relevant to primary care MSK practice. A request for CPGs that met the inclusion criteria was circulated through the same professional bodies as well as through the social media platform Twitter.

Insert Table 1 here

Selection of Sources of Evidence

All titles identified were screened by one reviewer (AC) and duplicates removed using Mendeley reference management software following a pilot of the selection criteria and process by authors AC and RT.

Following this initial screening, if abstracts were available, they were reviewed independently by two reviewers (AC and RT) who applied the selection criteria. Where a decision could not be made on eligibility, or if an abstract for the CPG was not available, the full CPG document was obtained.

Full CPG documents were reviewed independently by two reviewers (AC and RT) and if it was not clear whether the identified document met the criteria for definition as a CPG, then the producing organisation (or authors if there was no producing organisation identified) were contacted for further information. In cases of no response to the request for further information and following reminders, the document was excluded.

Finally, the reference list of all selected CPGs was hand searched by one reviewer (AC).

Data charting process

The relevant characteristics of the included CPGs and the key data items relevant to the review objectives were recorded in a charting table.

Data extraction was first tested, independently, by two reviewers (AC and RT) using five included CPGs. Changes were agreed upon by both reviewers and implemented including the removal of the columns titled 'development process' and 'concept e.g. imaging modality'.

One reviewer (AC) was responsible for charting the results and these were verified by a second reviewer (RT).

Critical appraisal of individual sources of evidence

An assessment of the rigour of the development process was performed through a modification of the Appraisal of Guidelines for Research and Evaluation (AGREE) II tool. All included CPGs were appraised using the third domain of the AGREE II tool 'Rigour of Development'; the AGREE II tool does not provide cut-off scores for whether a CPG is high or low quality however, previous reviews have utilised this domain as an important indicator of CPG quality. If a CPG scored $\geq 50\%$ then the CPG was deemed high quality (Lin *et al.*, 2018).

Synthesis of results

When all results were charted, a narrative synthesis was undertaken to provide an overview of recommendations. A narrative synthesis refers to the process of combining, outlining, and summarising the recommendations via a textual approach (Popay *et al.*, 2006). Through this synthesis, similarities and differences across the CPGs were identified.

Results

Selection of sources of evidence

A total of 12,775 citations were identified through the search strategies. Following the study selection process, 31 CPGs met the inclusion criteria (**Table 2**). 26 citations were excluded at full document stage and the reasons for exclusion are outlined in brief within **Figure 1**.

Insert Figure 1 here

Insert Table 2 here

CPG Origin

The majority of included CPGs were developed in the UK (n = 19), followed by development as part of a continental (European) workforce (n = 9) and international workforce development (n = 3).

Regional MSK Pain Presentations

The included CPGs were equally divided between those for a specific MSK pain presentation (n = 16) with LBP (n=5), knee (n=8) and shoulder pain (n=3) and those for a regional pain condition that has the potential to present as LBP, knee or shoulder pain (n = 15).

CPG Rigour of Development

The majority (27/31) of the included CPGs were deemed to be of high quality; the common areas of guideline development lacking rigour were balancing the benefits of recommendations alongside risks, harms or side effects; undergoing an external consultation period for stakeholder input and providing clarity on any intended updates (**Table 2**).

Recommendations on the use of diagnostic imaging in those with LBP, knee and shoulder pain.

The majority (21/31) of the included CPGs made recommendations on the use of DI within primary and intermediate care (**Supplementary Tables S23-26**).

Synthesis of Results

Low Back Pain (CKS, 2013, 2018a, 2018c; White *et al.*, 2014; Mandl *et al.*, 2015; Ward *et al.*, 2016; Compston *et al.*, 2017; McVeigh *et al.*, 2017; Remedios *et al.*, 2017; Ralston *et al.*, 2019)

Routine DI is not recommended within primary care or intermediate care, in either non-specialist (e.g. GP Practice) or specialist (e.g. Musculoskeletal Interface Clinic) settings. In the absence of suspected serious pathology, imaging is not recommended within non-specialist settings but rather should be reserved for cases in whom serious pathology is suspected. Within a specialist setting, DI should be reserved for cases for whom it is likely to change clinical management decisions.

The use of x-ray is discouraged in those with LBP unless a fracture or axial spondyloarthropathy (SpA) is suspected. Where there is a suspicion of axial SpA, if sacroiliitis is not demonstrated and suspicion remains, the recommendation is to perform an MRI of the sacroiliac joints. The National Institute for Health and Care Excellence (NICE) SpA guidelines (McVeigh *et al.*, 2017) also recommend the addition of a Whole Spine MRI however, the European League Against Rheumatism (EULAR) guidelines (Mandl *et al.*, 2015) do not recommend this.

Knee Pain (W Zhang *et al.*, 2010; Colebatch *et al.*, 2013; Fernandes *et al.*, 2013; McAlindon *et al.*, 2014; Conaghan *et al.*, 2014; Barton *et al.*, 2015; Hajioff *et al.*, 2015; Mandl *et al.*, 2015; Crossley *et al.*, 2016; CKS, 2017a; McVeigh *et al.*, 2017; Price *et al.*, 2017; Remedios *et al.*, 2017; CKS, 2018b; Garifallia Sakellariou *et al.*, 2017; Ralston *et al.*, 2019; Richette *et al.*, 2019)

The majority of CPGs relevant to knee pain focus on knee osteoarthritis (OA); those CPGs for patellofemoral pain (PFP) make no recommendations on the use of DI. Knee OA is typically considered a clinical diagnosis based on age ≥ 45 years, activity related joint pain and absence of significant morning stiffness. Routine imaging is not recommended for patients with suspected knee OA or during follow up of those with known OA.

The recommendations are to consider the use of DI to exclude alternative presentations in atypical presentations, such as suspected gout or if there is a sudden clinical deterioration. In such circumstances an x-ray is recommended as the initial investigation. If peripheral SpA or malignancy are suspected, then it is recommended to consider an USS and/or MRI.

Shoulder Pain (Hanchard *et al.*, 2011; Colebatch *et al.*, 2013; Conaghan *et al.*, 2014; DeJaco *et al.*, 2015; Hajioff *et al.*, 2015; CKS, 2017b, 2018b; McVeigh *et al.*, 2017; Remedios *et al.*, 2017; Richette *et al.*, 2019; Ralston *et al.*, 2019)

Routine imaging is not recommended for those with shoulder pain. If movement is significantly restricted, symptoms are not improving or if suspecting serious pathology then a two-view x-ray is recommended. USS and MRI are usually not recommended for those with shoulder pain unless gout or malignancy are suspected.

Similarities between CPGs

The recommendations of the CPGs included are similar. The routine use of DI for those with non-traumatic LBP, knee or shoulder pain is discouraged. In clinical circumstances where serious pathology is suspected, or where the person is not responding to initial conservative management and the imaging result is expected to change management decisions, then DI is indicated.

Differences between CPGs

The differences are concerned with modality and clinical setting. The use of x-ray in those with LBP is discouraged unless there is a clinical suspicion of a specific pathology, for

example spinal fracture. In those with knee or shoulder pain, an x-ray is encouraged as the initial investigation.

The recommendations within the guidelines are sometimes written with the care setting in mind, e.g. what should be considered within primary care (Price *et al.*, 2017); whilst others are written with the level of expertise in mind e.g. specialist settings (Ward *et al.*, 2016) as opposed to where that care episode takes place.

Discussion

Summary

The aim of this scoping review was to identify and map the content of CPGs relevant to UK clinical practice in primary and intermediate care, specifically regarding the use of DI for adults with non-traumatic LBP, knee, and shoulder pain. To date, this represents the most up to date and comprehensive review of CPGs and recommendations regarding DI within these care settings for these musculoskeletal pain presentations. The routine use of DI for those with non-traumatic LBP, knee or shoulder pain is discouraged across CPGs. DI should be reserved for where serious pathology is suspected, the person is not responding to initial conservative management or the imaging result is expected to change management decisions.

The CPGs for LBP consistently recommend against the use of x-ray unless there is a suspicion of specific pathology. This differs to the CPGs for knee or shoulder pain where the use of x-ray as a first line investigation, albeit for a minority of cases, is recommended. A possible reason for this may be that x-ray findings of peripheral joints may alter the management plan to a greater extent than in the spine. A spinal fracture is usually managed for pain-relief in the absence of neurological signs with surgical options being limited (McCarthy and Davis, 2016). In contrast, in peripheral joints an x-ray may inform the decision to refer for orthopaedic opinion for consideration of more invasive intervention such as arthroplasty.

Strengths and limitations

To date, this represents the most up to date and comprehensive review of CPGs and recommendations for use of diagnostic imaging within UK primary and intermediate care

settings. The strengths of this scoping review include conduct in accordance with good practice as recommended for the conduct of scoping reviews (Peters *et al.*, 2015) and the methods have been reported clearly, allowing for replication. Previous scoping reviews (Lowe *et al.*, 2018) have demonstrated how the use of novel social media can complement a search strategy to increase the reach and totality of a search. Using Twitter impressions can act as a measure of reach within those using Twitter as a means of Continuing Professional Development (CPD). Within the 14-days that the tweet involved within the search strategy was live, the analytics demonstrate that it was retweeted by 73 people and that 21,375 twitter uses saw the tweet. The inclusion of the tweet as part of the search strategy identified 8 additional hits that were not identified from the more traditional means of searching, two of which were included within the review. This further demonstrates that the inclusion of twitter within a search strategy offers a pragmatic, accessible and low-cost method of increasing the reach and totality of a search.

The results of this scoping review must be considered with respect to its limitations. The inclusion criteria for this review were strict in respect that only CPGs were reviewed, and only those citations that satisfied the definition of a CPG were included. This means that resources that clinicians may use to guide their clinical practice, including those that may be described as a 'guideline' without satisfying the criteria for a CPG, may have been excluded. The focus of this review was also limited to UK practice which limits the generalisation of the findings however, it must be considered that the findings are similar to a review of international guidelines (Lin *et al.*, 2019).

Comparison with existing literature

The results of this scoping review are similar to the findings of a recent SR of high-quality international CPGs (Lin *et al.*, 2019). This SR aimed to identify recommendations that were common across a wide range of MSK pain conditions, derived from CPGs. With regards to investigations, it was recommended that DI was discouraged unless serious pathology is suspected; there has been unsatisfactory response to conservative care or unexplained

progression of signs and symptoms; it is likely to change management. Within this review by Lin et al. (2019), recommendations did not focus on a particular care setting or country of practice and excluded specific diseases processes e.g. rheumatological conditions. The inclusion of regional MSK conditions within this scoping review that may present as LBP, knee or shoulder pain adds to the knowledge base as it highlights a level of consistency with regard to recommendations for the use of DI across clinical populations.

Implications for research and practice

This review included 31 CPGs that were published between 2009 and 2019. 26 hits returned by the search were excluded with 18 either due to not fulfilling the definition or criteria of a CPG (n=12) or being unable to determine whether the definition or criteria had been fulfilled (n=6). In most circumstances, this related to the absence of an initial systematic review being undertaken as part of the CPG development process.

The NICE accreditation programme appraises the processes used to develop a CPG with the aim of raising CPG development standards, ensuring high-quality processes are utilised, high-quality information disseminated to clinicians and in turn to increase the chances that the guideline is used to improve patient outcomes. The presence of the accreditation award is intended to identify the most trusted sources of CPGs that have been developed (NICE 2019). Of note was the exclusion of Kulkarni et al. (2015) which had associated NICE accreditation (Kulkarni *et al.*, 2015). The reason for exclusion was due to the systematic review upon which the CPG was supposed to be based had been undertaken in 2009, and seemingly independent of the CPG process. Therefore, whilst this means that the publication does not meet the definition of a CPG and is excluded from the review, the wider implication is that the recommendations made may not be based on the most contemporary evidence.

This raises two issues; the first questioning the utility of the NICE accreditation programme as a mark of quality and the second that this publication provides a substantial amount of the information upon which the NICE CKS for shoulder pain (Excellence, 2017) is based, which has been included within this scoping review. In turn, it not clear whether the recommendations made within the CKS are founded on the best available, contemporary evidence which may impact on clinical decisions and subsequent patient outcomes.

The recommendations within the CPGs varied regarding presentation, either by care setting or by level of expertise. Historically, primary care was considered a non-specialist setting in which an initial assessment would be undertaken and the patient referred to a specialist setting (if needed) in secondary care. In recent years, this approach to patient pathway design has changed with specialist services increasingly delivered in primary and community care settings in the UK, a change further reinforced within the NHS Long Term Plan (NHS England, 2019a). Future CPGs should consider this within the development process to aid implementation of recommendations into contemporary practice.

With the routine use of DI discouraged, it would appear that CPGs do not justify the increasing imaging rates in the UK for musculoskeletal pain. This would suggest that other factors such as clinician behaviour, or patient expectations may offer a more likely explanation and should be explored through future research.

Conclusion

The routine use of DI for those with non-traumatic LBP, knee or shoulder pain is discouraged in primary and intermediate care. DI within a primary care or intermediate care setting within UK practice should be reserved for cases where specific or serious pathology is suspected or where the person is not responding to initial non-surgical management and the imaging result is expected to change clinical management decisions.

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Table 1. Search terms – LBP (Medline)

1. (in title/abstract) MH "Practice Guidelines")
2. (in title/abstract) OR Guideline* OR consensus OR recommendations
3. (title/abstract) AND Lumb* or LBP or NSLBP or CNLSBP or non-specific or low* or back or spin* or radic* or stenosis or facet* or inf* or fracture or scoliosis or cancer* or malign* or cord or cauda or CES or spond* or OA or osteo*
4. (title/abstract) AND Imaging or diagnostic imaging or x-ray or radiograp* or ultraso* or USS or MRI or magnetic resonance imaging or computed tomography or radiolog* or CT
Limits: 2009 – to date of search, English Language, Guidelines, Consensus Development Conference, Practice Guideline

Table 2: This table provides an overview of CPGs included within the scoping review.

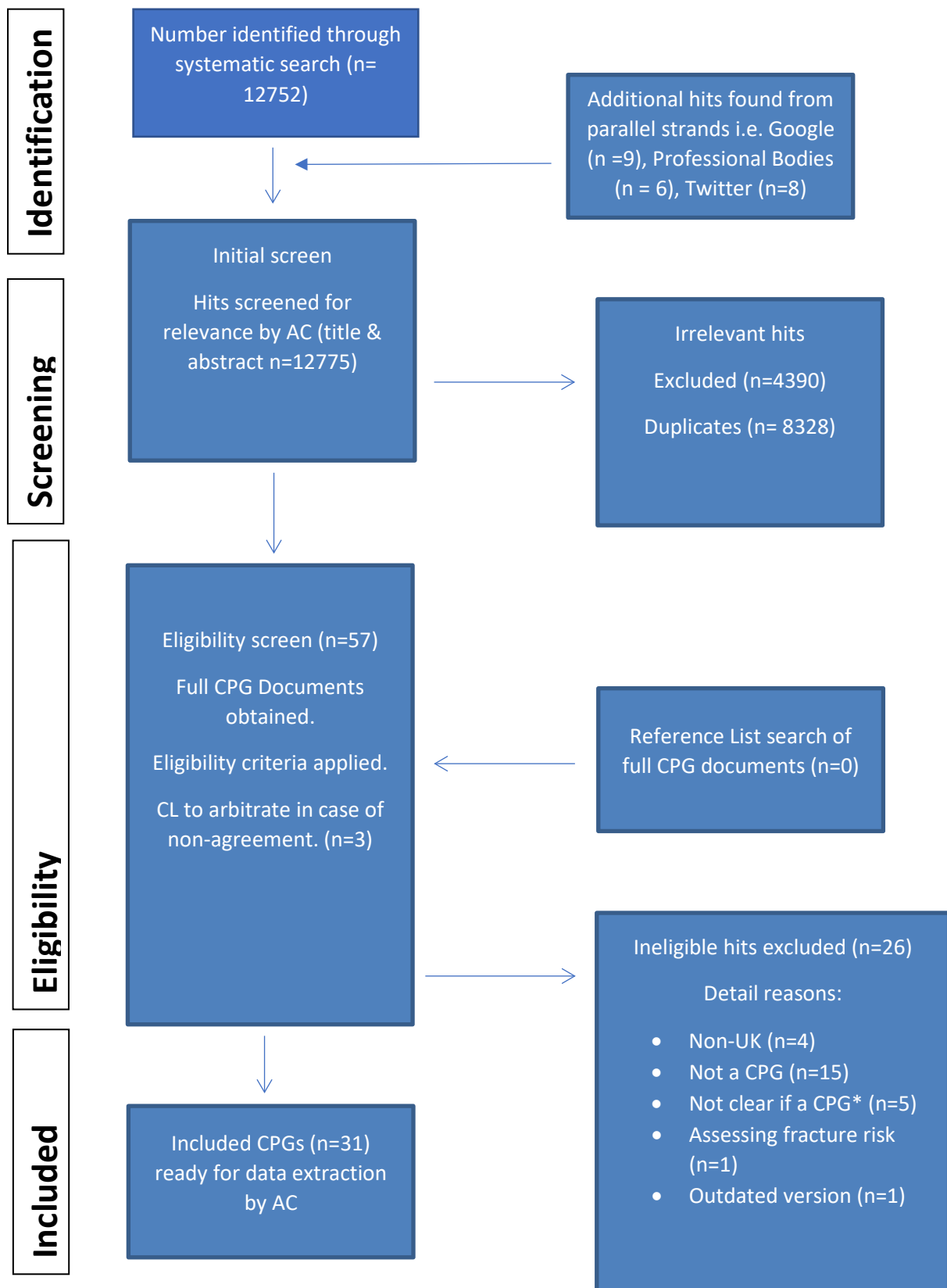
Authors	Year	Development Group e.g. NICE	Body site/regional condition	Origin	Agree II
Ward et al. (Ward <i>et al.</i> , 2016)	2016	National Institute for Health and Care Excellence (NICE)	LBP	UK	91%
NICE Clinical Knowledge Summary (CKS) – LBP (CKS, 2018a)	2018	NICE	LBP	UK	50%
NICE CKS – Sciatica (CKS, 2018c)	2018	NICE	LBP	UK	50%
NICE CKS – Ankylosing Spondylitis (AS) (CKS, 2013)	2013	NICE	LBP	UK	51.7%
White et al.(White <i>et al.</i> , 2014)	2014	NICE	LBP	UK	78.6%
Zhang et al. (Weiya Zhang <i>et al.</i> , 2010)	2010	EULAR	Knee Pain	Europe	57.1%
Price et al. (Price <i>et al.</i> , 2017)	2017	British Orthopaedic Association (BOA)	Knee Pain	UK	26.7%
Sakellariou et al. (G. Sakellariou <i>et al.</i> , 2017)	2017	EULAR	Knee Pain	Europe	64.2%
Fernandes et al. (Fernandes <i>et al.</i> , 2013)	2017	EULAR	Knee Pain	Europe	57.1%
Crossley et al. (Crossley <i>et al.</i> , 2016)	2016	Patellofemoral Pain Research Retreat	Knee Pain	International	53.5%
Barton et al. (Barton <i>et al.</i> , 2015)	2015	N/A	Knee Pain	International	57.1%
McAlindon et al.	2014	Osteoarthritis Research Society International (OARSI)	Knee Pain	International	60.7%
NICE CKS (CKS, 2017a)	2017	NICE	Knee Pain	UK	48.2%

Hanchard et al. (Hanchard <i>et al.</i> , 2011)	2011	Chartered Society of Physiotherapy (CSP)	Shoulder Pain	Frozen Shoulder	71.4%
Dejaco et al.	2015	EULAR	Polymyalgia Rheumatica (Shoulder Pain)	Europe	75%
NICE CKS (CKS, 2017b)	2017	NICE	Shoulder Pain	UK	46.4%
Compston et al. (Compston <i>et al.</i> , 2017)	2017	National Osteoporosis Guideline Group	Osteoporosis	UK	62.5%
Ralston et al. (Ralston <i>et al.</i> , 2015)	2015	Scottish International Guidelines Network (SIGN)	Osteoporosis	UK	66%
Lems et al. (Lems <i>et al.</i> , 2017)	2016	EULAR	Osteoporosis	Europe	50%
McVeigh et al. (McVeigh <i>et al.</i> , 2017)	2017	NICE	Spondyloarthropathy (SpA)	UK	80%
Mandl et al. (Mandl <i>et al.</i> , 2015)	2015	EULAR	SpA	Europe	41%
NICE CKS (CKS, 2018b)	2018	NICE	Osteoarthritis (OA)	UK	51.7%
Conaghan et al. (Conaghan <i>et al.</i> , 2014)	2014	NICE	OA	UK	83.9%
Ward et al. (Ward <i>et al.</i> , 2018)	2018	NICE	Rheumatoid Arthritis	UK	89.2%
Colebatch et al. (Colebatch <i>et al.</i> , 2013)	2013	EULAR	RA	Europe	57.1%
Richette et al. (Richette <i>et al.</i> , 2017)	2016	EULAR	Gout	Europe	55.2%
Richette et al. (Richette <i>et al.</i> , 2019)	2018	EULAR	Gout	Europe	50%
Hui et al. (Hui <i>et al.</i> , 2017)	2017	British Society of Rheumatology (BSR)	Gout	UK	53.5%
Hajioff et al. (Hajioff <i>et al.</i> , 2015)	2015	NICE	Malignancy	UK	94.6%

Ralston et al. (Ralston <i>et al.</i> , 2019)	2019	Paget's Association UK	Paget's Disease	UK	75%
Remedios et al. (Remedios <i>et al.</i> , 2017)	2017	The Royal College of Radiologists (RCR)	Miscellaneous	UK	64.2%

Abbreviations: BOA, British Orthopaedic Association; BSR, British Society of Rheumatology; CPG, Clinical Practice Guideline; CKS, Clinical Knowledge Summary; EULAR, European League Against Rheumatism; LBP, Lower back pain; NICE, National Institute for Health and Care Excellence; OARSI, Osteoarthritis Research Society International; SIGN, Scottish International Guidelines Network; RCR, The Royal College of Radiologists; UK, United Kingdom.

Figure 1. Flowchart outlining the selection process for Clinical Practice Guideline (CPG) inclusion within the scoping review of CPGs.



*Where it was not clear whether a systematic review had been conducted as part of the CPG development process (in order to meet the definition of a CPG) authors were contacted, if no reply was received, this hit was excluded.