

Anxiety and Osteoarthritis Research and Clinical Implications

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Abstract

Osteoarthritis, a widespread highly painful oftentimes incapacitating joint disease with few efficacious remedies continues to pose immense personal and societal challenges on a large scale in an aging population. In absence of any effective cure or treatment for this condition, this brief was designed to update the reader as to whether anxiety, a widespread psychological syndrome affecting many adults, remains an underestimated contributor to osteoarthritis disability. Drawn from the prevailing peer reviewed data sources in the leading electronic data bases, using the keywords *osteoarthritis* and *anxiety*, detailed are some recent research observations published predominantly between the years 2014-2018 in this regard. Although not extensive, nor amenable to any systematic analysis, the search revealed that anxiety is indeed often present among sizeable numbers of osteoarthritis cases, and its presence appears to have a multitude of negative health effects at all disease stages. Consistent with prior reports on this topic, it is concluded that the topic of anxiety, which may play a bi-directional role in influencing disease outcomes, warrants attention as a potentially clinically relevant disease predictor or outcome variable on a more consistent basis. Moreover, where present, multidisciplinary follow-ups and tailored treatments may enhance overall well-being, and prevent excess disability, regardless of joint[s] affected and their severity or status.

Background

Osteoarthritis, a highly prevalent health condition affecting many older adults commonly produces varying degrees of local joint and bone pain, as well as muscle and soft tissue pain consequent to progressive destruction of the cartilage tissue lining one or more freely moving joints, as well as its bone surfaces and surrounding tissues, along with heightened central sensitivity to pain, if the condition persists. Often heightening the risk for—or concurrently associated with other chronic health conditions [1], most notably, cardiovascular diseases and obesity, as well as varying degrees of inflammation, and considerable activity limitations, treatments for this condition continue to focus largely on pharmaceutical drugs that are often toxic with detrimental side effects, alongside the likelihood of joint replacement surgeries, which are often associated with short and long term complications, and a general failure to fully restore mobility or eliminate pain. However, while this disease clearly has several physical components, the viewpoint that osteoarthritis is predominantly a biomechanical disorder associated with aging, may be one reason why physical treatments applied in isolation do not always ameliorate the prevailing pain or disability of osteoarthritis at all successfully.

Given that a linkage between pain and anxiety is a prevalent one in the mainstream literature, along with knowledge that cognitive status or emotional states can impact health decisions and health behaviors, and that anxiety is highly prevalent among adults in general, and among adults with a variety of medical disorders [2] and chronic physical conditions, in particular [3], it seems plausible to continue to examine if anxiety is a potentially important, albeit underestimated osteoarthritis disease disabler or a determinant that warrants more careful and consistent attention. In particular, if the observation by Gay *et al.* [4] that the osteoarthritis population is less active, and more sedentary, with higher numbers of comorbidities and more barriers to physical activity practices than the overall population is potentially related in some way to the presence of unidentified and treated anxiety, addressing this correlate may arguably foster more opportunities to reduce disease outcomes due to inactivity, feeling overwhelmed, catastrophizing, and excess comorbidity than standard approaches.

Aims

This work aimed to update our knowledge base of this topic as this pertains to the wellbeing of the older adult diagnosed with osteoarthritis. The key question driving this updated work was whether a reasonable body of updated literature continues to support the idea of implementing some routine examination that would identify the presence of excess or unwanted anxiety levels among osteoarthritis cohorts, regardless of setting. Another was whether osteoarthritis pain and disability are likely to be affected by the presence or absence of anxiety in a significant way and to what degree. Another was whether it would be possible to limit, prevent, or minimize anxiety where it exists among osteoarthritis cases, regardless of disease status.

Methods

To obtain representative salient publications that might provide relevant peer reviewed data, the PsycINFO, PUBMED, Scopus, Science Direct, and Web of Science consolidated data bases over the last five years [January 2014-August 2018] were explored using the search terms *anxiety* and *osteoarthritis*. The items retrieved were carefully examined and selected for discussion only if they addressed one or more of the study

questions. Selected data extracted from this data base were then scrutinized and summarized largely in narrative or tabular formats if they appeared to assist in answering the review questions. That is, recent studies that focused on exploring the extent to which anxiety appears to prevail among adults with osteoarthritis were specifically sought, along with studies that showed either an important clinical association with the disease or did not demonstrate this. Interventions recommended for ameliorating excess anxiety in the face of chronic osteoarthritis, and gaps in the literature were also specifically sought and reviewed.

This mini review did not differentiate articles examining trait anxiety from state anxiety, or focus on any specific form of osteoarthritis, and given the limited data base, all forms of research design were deemed acceptable. Excluded were foreign articles, incomplete reports, reports older than 6 years, and those that examined mixed cohorts of arthritis. The term anxiety, a psychological disturbance representing a form of emotional distress, was employed in a generic sense throughout to represent all three variants of clinical anxiety, generalized anxiety disorder, state anxiety and trait anxiety, rather than their unique and differential effects in the context of the disease. Readers seeking a prior update on this topic are referred to reference [5].

Results

General Observations

Despite the possible utility of studying anxiety in the context of osteoarthritis, this mini review found very few studies specifically focused on anxiety as a clinically important osteoarthritis disease correlate, especially when compared to other topics [See Box 1]. Moreover, as shown in Box 2, almost no data on this topic prevail for joints other than the knee and hip, which have for example 244 and 94/500 articles specifically listed from 1980-on PUBMED, with 22 or less for all other joints that can be affected, in this context. Similarly, targeted intervention studies were not readily available, and even if proposed, have not been conducted, or remain pilot or incomplete studies. However, of the articles published over the last five years, a small number, do appear to stress some important and valuable clinical and research related points that warrant consideration in our view, even if this is only due to selection bias, where negative studies are often not widely published. The Hospital Anxiety and Depressions [HAD] and Spielberger Anxiety Scales were most commonly used, even though these do not prove anxiety is clinically present. Other self-report instruments used were the Beck Anxiety Scale, the Mental Health Inventory, or anxiety assessed using a single question.

Osteoarthritis: 24475*Osteoarthritis + Treatment 15726; Anxiety + Treatment 32258**Osteoarthritis + Pain 8365; Anxiety + Pain 8577**Osteoarthritis + Physical Symptoms 5376; Anxiety + Physical Symptoms 8544**Osteoarthritis + Replacement Surgery 5132**Osteoarthritis + Exercise 2198**Osteoarthritis + Inflammation 2082**Osteoarthritis + Obesity 882; Anxiety + Obesity 1336**Osteoarthritis + Muscle 1513**Osteoarthritis + Depression: 474, Depression + Anxiety 6350***Osteoarthritis + Anxiety 243**

Box 1: Number of Item Listings on PubMed January 2014– August 2018 Using Different Key Words, showing Minimal Overlap between Mainstream Anxiety Literature and Osteoarthritis

Knee osteoarthritis-249
 Hip osteoarthritis-34
 Spinal osteoarthritis-24
 Hand osteoarthritis-22
 Neck osteoarthritis-11
 Temporomandibular osteoarthritis-11
 Foot osteoarthritis-6
 Wrist osteoarthritis-2
 Thumb-3

Box 2: PUBMED Search Results 1980–2018 Depicting Joints Studied in Context of Anxiety and Osteoarthritis

Research Observations

As outlined in relatively recent studies, for example, that by Tan *et al.* [6] and consistent with earlier studies, for example, that by Murphy *et al.* [7], the presence of a state of anxiety appears quite common in the context of osteoarthritis, regardless of how this is assessed. Additionally, where anxiety exists, the condition often co-exists with depression [5], along with other long-term health conditions. In addition to that, those suffering from anxiety alone, or anxiety and depression are also more likely than not to suffer from chronic pain or excess chronic pain, among other factors [see Figure 1]. As well, even though Kang *et al.* [8] negated a role

for anxiety in terms of trapeziometacarpal arthritis, and anxiety was not mentioned as a pain correlate by Heidari *et al.* [9], the presence of anxiety, alone or in combination with other health conditions, is consistently found to reduce health-related quality of life and to manifest in poorer clinical outcomes for all comorbid conditions, including osteoarthritis. Anxiety is also a significant clinical feature of knee osteoarthritis [10], especially among women [11], as well as a consistent predictor of total joint arthroplasty outcomes [12], including an increased risk of post-operative complications [13], and levels of experienced pain [14], and possibly centralized osteoarthritis pain [15]. Findings by Nazarinasab *et al.* [16] who studied 94 patients with osteoarthritis, 30 male patients (31.9%) and 64 female (68.1%), showed that 58.5% of these patients had a mental health disorder including anxiety. In addition, the prevalence of mental health problems in their osteoarthritis groups was significantly higher in the age range of 18 to 20 years old ($p = 0.002$) than in older cases, and in the first months of diagnosis. Patients taking corticosteroids also appeared at high risk for mental health disorders including anxiety ($p = 0.00$).

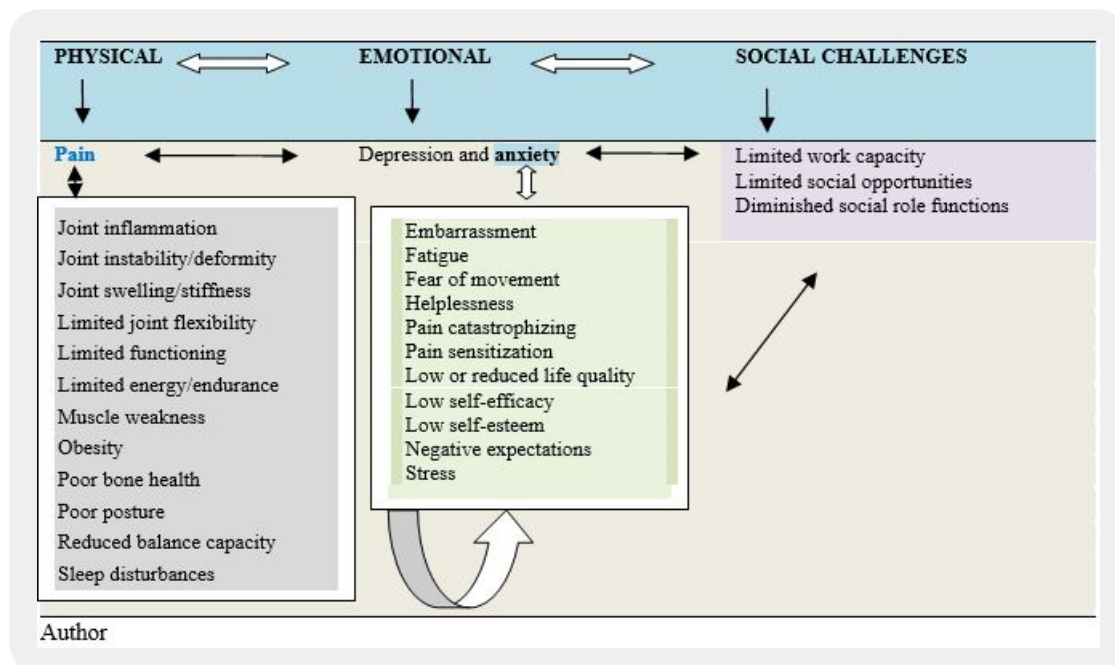


Figure 1: Hypothetical Depiction of Multiple Somatic and Cognitive Disease Challenges Commonly Faced by People with Osteoarthritis that are Amenable to Modification or Amelioration and Which Can Interact with or Induce Anxiety

In a related study, Nur *et al.* [17] similarly confirmed anxiety to be among the factors contributing to knee pain and function in women with knee osteoarthritis. Barnett *et al.* [18] likewise found adults with joint pain reporting clinical anxiety, were quite numerous, in general, and were those more likely to exhibit severe, rather than mild pain. It was further observed that the number of pain sites was also positively associated with the presence of clinical anxiety, and that those adults with symptoms of clinical anxiety appeared less likely to undertake general fitness exercises. They were also more likely to use walking aids and assistive devices, plus opioids than non-anxious adults with joint pain. While not universally present among

osteoarthritis cases, Jones *et al.* [19] found 44 percent of knee replacement surgery cases were clearly anxious as deduced by a 14 item self-reported survey. While this high number of cases may have been due in part to the method of calculating anxiety as normal or abnormal in that study, Wong *et al.* [20] as well as Castano *et al.* [21], Stubbs *et al.* [5] and Guglielmo *et al.* [22] reported the presence of anxiety to be of the order of 20 percent or higher in various osteoarthritis or arthritis samples where this has been examined. Moreover, anxiety levels were elevated in community dwelling knee osteoarthritis cases compared to the general population [23], and where present, these anxious osteoarthritis patients had higher pain levels at rest and on activity than non-anxious patients. Bierke *et al.* [24] found rates of trait anxiety alone to be approximately 14 percent among cases with disabling osteoarthritis awaiting treatment, suggesting a number of osteoarthritis patients may not only suffer from state anxiety, which is understandable, but from a generalized anxiety disorder or a form of chronic anxiety. Importantly, those identified as having a habitual pattern of anxiety behavior had higher mean dissatisfaction scores at 6 and 12 months after surgery than those with no anxiety. Khan *et al.* [11] similarly found high levels of anxiety among osteoarthritis cases compared to non-osteoarthritis cases, especially among women.

According to Harmelink *et al.* [25] and others such as Liddle *et al.* [26], even if anxiety rates are deemed acceptable or clinically unimportant, acknowledging the presence of any form of anxiety is arguably very crucial in osteoarthritis remediation efforts in light of the fact that unrelieved anxiety can be expected to impact the pain experience quite negatively and significantly [27,28]. As well, unrelieved anxiety can potentially exacerbate harmful chronic oxidative stress levels and inflammatory responses [29], while markedly reducing daily activity participation rates [30], and functional ability [23]. Research in the surgical realm further shows the presence of anxiety can delay healing, while reducing satisfaction with the surgical results [31], and impeding attainment of anticipated functional benefits [19,32-36]. Anxious patients may also be more reluctant to participate in optimal forms of exercises or processes at restoring fitness, and especially after total joint replacement surgery may experience a lower subjective assessment of the possibility of any return to work during the lengthy post-operative rehabilitation period and readiness to undergo treatment [37]. Although Janikowska-Holowenko *et al.* [37] found the subjective assessment of pain after post-surgical rehabilitation was not significantly associated with anxiety as a trait, and no connection was found between anxiety and subjective assessments of physical activity, the assessment of pain was correlated with the level of anxiety after secondary rehabilitation. Hernandez *et al.* [38] who conducted a systematic review of 37 studies concluded that pre-surgical anxiety does indeed influence post-operative pain in a consistent manner. It also impacts life quality negatively and significantly [39,40], as well as sleep [41], the onset or perpetuation of neuropathic pain [27], pain intensity and pain distress [42], and non-surgical multidisciplinary treatment outcomes [43].

Indeed, data show that even where anxiety rates can be considered to be quite low, the presence of anxiety still has substantive negative implications for the osteoarthritis patient [44,45]. Conversely, Helminen *et al.* [46] who employed the Beck Anxiety Inventory to examine the severity of anxiety found adults with knee osteoarthritis with lower anxiety symptoms had better pain outcomes and function over a one-year follow-up of joint replacement surgery as did Hassett *et al.* [47].

Unfortunately, despite these potentially relevant findings that concur quite strongly with others that precede them, recent community-based efforts to address and treat anxiety among osteoarthritis cases were deemed largely unsuccessful in this regard [48], did not substantially reduce patients' pain and disability [49], and in the realm of cost-effectiveness, were not effective [50]. However, as pointed out by Hiraakawa *et al* [51], and other researchers highlighted in Table 1, at a minimum, efforts to uncover and reduce persistent and oftentimes pervasive negative thoughts regarding future pain among osteoarthritis cases scheduled for total joint replacement surgery remain warranted in efforts to limit delays in returning to work, the onset of low self-efficacy beliefs, and lower than desirable overall life quality [52]. Unfortunately, the interventions that might help to minimize, avert, or prevent anxiety among cases with osteoarthritis are not well studied-thus claims that intervention does not benefit subjects cannot be made with any robust certainty at the present time. The optimal time course for those behavioral and other interventions recommended for minimizing anxiety related problems outlined in Table 2-is also unknown.

Table 1: Summary of Key findings of Selected Representative Prospective Studies Examining Anxiety in the Context of Osteoarthritis

Research Group	Subjects Studied	Measure	Key Findings
Ali <i>et al.</i> [53]	Mixed surgical samples	HAD	Anxious patients had worse 13 yr outcomes
Dhurve <i>et al.</i> [54]	Primary knee replacement cases	DASS	Anxious patients are less satisfied post-surgery
Duivoorden <i>et al.</i> [55]	Knee + Hip patients	HAD	Anxious patients had worse surgical outcomes
French <i>et al.</i> [56]	Hip OA cases	HAD	Positive mental health predicted short term outcomes
Hanlandsmyth <i>et al.</i> [42]	Total knee arthroplasty cases	STAI	Anxiety was related to pain intensity and distress
Hanush <i>et al.</i> 1. [57]	Knee OA cases	HAD	Anxiety affects surgical outcomes
Helminen <i>et al.</i> [46]	Knee OA cases	BAI	Anxiety predicted pain and function at one year
Jones <i>et al.</i> [19]	Knee arthroplasty cases	HADS	Knee surgery cases are not impacted by pre-surgical anxiety
Liddle <i>et al.</i> [26]	Mixed surgical samples	Unclear	Anxiety affected 8 year outcomes
McHugh <i>et al.</i> [58]	Hip OA cases	HAD	Anxiety impacted post-surgical outcomes adversely
O'Leary <i>et al.</i> [43]	Mixed sample	DASS-21	Higher anxiety levels predicted worse outcomes
Pinto <i>et al.</i> [36]	Hip + Knee OA surgery cases	HADS	Anxiety predicted health outcomes of surgery
Utrillas-Compaired <i>et al.</i> [39]	Mixed sample	HAD	Anxiety worsens one year surgical outcomes

BAI-Beck Anxiety Inventory; DASS-Depression, anxiety and stress scale; STAI-State trait anxiety inventory; HADS-Hospital Anxiety and depression Scale; OA=osteoarthritis

Table 2: *Commonly Advocated Strategies for Countering Anxiety and Improving Osteoarthritis Outcomes*

Acceptance therapy
Address dissatisfaction [54]
Cognitive behavioral therapy
Counselling
Early detection and frequent monitoring
Education [51]
Exercise [16,59]
Group therapy
Holistic individualized treatment [60]
Medication monitoring and usage
Music
Neuroscience education [61]
QiJong [62]
Pain relief and control [40,63]
Pastoral care and religious support [64]
Physical therapy
Psychotherapy
Relaxation and deep breathing
Skills training
Social support
Spa therapy [65]
Stress control
Weight control

Discussion

Osteoarthritis, a highly prevalent health condition remains a serious impediment to many older individuals who seek to remain independent and mobile. This mini narrative review, which examined recent evidence concerning the possible role of anxiety, a highly prominent psychological condition in its own right among older adults was undertaken in an effort to evaluate the status quo concerning the topic of anxiety in potentially playing a significant role in mediating, moderating, or exacerbating osteoarthritis disability. As an osteoarthritis correlate that been examined quite recently, this mini review was specifically focused on data that has emerged in the past five years or so in the key data bases believed to house state of the art and gold standard articles on this topic.

Results showed that while still limited, and much less studied than either topic alone and others, these data were generally consistent with similar previous literature that concluded this realm of endeavor holds promise and needs more careful exploration.

However, even though the current evidence base tended to support the value of previous recommendations to screen the osteoarthritis patient for anxiety, and to treat this as indicated more routinely, this view is by no means conclusive, or universal. Limiting the progress made in this field are clearly the lack of well-designed longitudinal studies that focus on osteoarthritis samples other than surgical candidates, or in the context of joints other than the knee or hip [See Box 2 and Table 1]. At the same time, those that have examined anxiety in the context of osteoarthritis do not follow any consistent research design, and often employ mixed samples, and diverse data collection procedures, precluding any meaningful synthesis. The additional failure to examine whether anxiety if present, is a longstanding intrapersonal trait or whether it is a reactive state as a result of the disease or both, further clearly impedes the emergence of any unified understanding of the implications of anxiety in its diverse forms among various stages and degrees of disabling osteoarthritis. As well, the mechanisms whereby anxiety can impact osteoarthritis disability and what its unique determinants are in this respect are also very poorly defined, despite the potential importance of this information.

These research related limitations, and others, which have now persisted for at least three decades according to conclusions reached by several researchers are undoubtedly extremely disappointing given the failure of most current approaches to ameliorate osteoarthritis disability safely and effectively, and the fact anxiety is a modifiable disease correlate. They are especially disadvantageous for improving the outlook for adults with osteoarthritis in our view for at least two reasons. First, because anxiety may not always be favourably impacted by standard pharmacologic and surgical approaches used to treat osteoarthritis, and indeed may be associated with the excess intake of a variety of over-the-counter, or prescribed potentially addictive or harmful medications. Second, and most importantly, this omission arguably increases the extent of the prevailing disability experienced by a sizeable number of osteoarthritis sufferers, while diminishing or retarding the achievement of anticipated goals of remediation [66-72].

They also imply that distressed osteoarthritis cases who remain untreated may have worse functional scores than those with no anxiety [52,73,74], as well as higher perceived levels of current and forthcoming pain [69,75-79], plus lower local pain pressure thresholds [76].

Additional data show that untreated or unrecognized anxiety routinely leads to delayed healing, and attainment of optimal post-surgical outcomes [23,37,51,68]. Osteoarthritis patients who suffer from excess untreated anxiety may also be at a heightened need for arthroplasty revision surgery [26]. They can also be expected to experience a lower than necessary life quality [37,60], and diminished responsiveness to standard interventions, along with the heightened risk of acquiring subsequent chronic health conditions [15], states of physical inactivity and sedentary behaviours [78].

Other data reveal osteoarthritis patients suffering from concomitant anxiety may be vulnerable to excess opioid usage [18], fear-avoidance versus active resolution strategies, sedentary behaviors that could contribute to weakness and joint instability [80], and failure to attain exercise benefits- the most frequently prescribed osteoarthritis self-management remedy [81]. The enormous associated social and fiscal costs associated with a failure to address anxiety in a timely way are surely incalculable as well.

In addition, potential causes and predictors of anxiety such as other medical illnesses, pain, factors in the environment, including the subjects' physical, psychological and dietary environment, obesity, having limited health insurance and having low perceived health and high levels of disability [73] are rarely examined in a systematic way despite their bearing on the resultant disease prognosis and treatment recommendations as was discussed 10 years ago by Smith and Zautra [77]. There is also almost no evidence to guide the clinician as far as best intervention practices for ameliorating anxiety go and whether a possible reduction in the extent of osteoarthritis disability will accrue through a timely anxiety diagnosis and its subsequent treatment.

Unfortunately, even where anxiety is examined clinically, results may be confounded if they include simultaneous measures made to rheumatoid arthritis patients [39], patients with hip fractures, osteoporosis, or back pain, and correlates of depression [26,57], and mixed forms of osteoarthritis, known to have differential outcomes [12]. As well, there are very few hypothesis testing research designs that provide salient follow up data [75], and among those that do, most are unable to clearly establish if anxiety is a key outcome determinant and to what degree given the questionable reliability of the presently documented anxiety, function, or pain measures [19]. Subject to error, under reporting, over reporting, inadequate reporting, lack of methodologic collection rigor, and misclassification because anxiety is usually assessed through self-reported data survey estimates, the present anxiety estimates and their relationships with other self-reports are insufficient for purposes of producing compelling evidence and advancing more universal consensus concerning the clinical significance of anxiety as a possible highly relevant osteoarthritis outcome determinant.

In short, although a case for examining anxiety in the context of routine osteoarthritis care has prevailed for some time [68-69, 82] and this call for a more consistent focus on this correlate in the realm of treatment is continuing [eg 43,68], the weaknesses of most prevailing and past studies, including their limited numbers, along with the relative absence of longitudinal studies that examine anxiety presence and any possible long-term functional as well as structural disease relationships among clearly defined osteoarthritis cohorts, greatly limits acceptance of the rationale for recommending this line of action as a standard clinical approach, regardless of disability status. It also limits understanding of the cause-effect relationship between osteoarthritis pain and anxiety-and its resultant omission in the therapeutic treatment realm may simply increase-rather than decrease- in the face of prevailing undetected anxiety levels. As well, what the most profound determinants of anxiety are relative to osteoarthritis, such as whether these stem from body image concerns, functional concerns, fear, perceived diminished control, financial factors, and limited ability among other factors remains unknown.

The present observations are disappointing, because in terms of the conceptual model presented in Figure 1, and the possible cost savings and heightened well-being alone that could be realized by comprehending this potentially relevant set of clinical factors, one can anticipate that excess suffering will prevail among millions of older adults with osteoarthritis whose anxiety states remain undiagnosed and untreated. Sufficient evidence of a possible consistent link to the osteoarthritic patients' overall pain experience, plus their life quality and ability to carry out self-care actions, including exercising motivation [63] alone are valuable factors to consider in efforts to reduce the immense burden of this disease. Less anxious patients may also sleep more soundly, and experience less depression, risk of acquiring comorbid medical conditions, and drug dependence [83]. The osteoarthritis patient who is able to remain calm or is calmed appropriately despite their disabling health condition may also be more willing to undergo reconstructive surgery earlier-rather than later-when they stand a better chance of success, and returning to work, rather than only agreeing to undergo surgery when the condition is very severe, and their heightened anxiety state limits their overall chances of a successful physical and social as well as emotional outcomes [24].

Conclusion

Although recent and past research provides a tentative rationale and degree of support for routinely examining and treating the correlate of anxiety in the context of osteoarthritis care, it is concluded that more robust research efforts are needed to solidify this idea.

To this end given the potential importance of unravelling the role of anxiety in the osteoarthritis disease process, as conceptually illustrated in Figures 1 and 2, it is concluded extensive interdisciplinary research efforts, rather than stand-alone efforts are desirable.

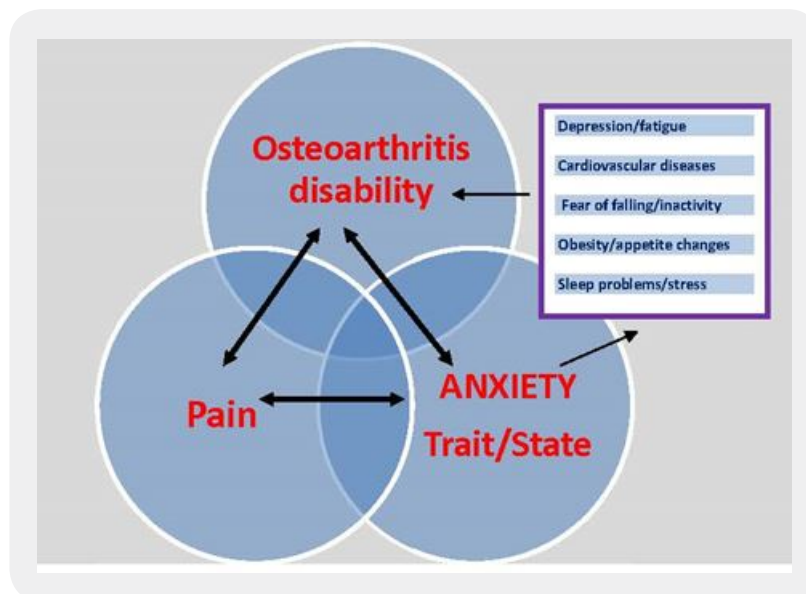


Figure 2: Conceptual Representation of Salient Anxiety, Pain, and Osteoarthritis Disability Relationships

It is also concluded that to further advance the knowledge base examining anxiety in the context of various osteoarthritis, validated anxiety assessment instruments coupled with quantitative sensory testing [68] is imperative. Sorely needed as well are carefully controlled studies that evaluate the relative efficacy of various forms of treating anxiety, where it exists among diverse osteoarthritis cases. In addition, examining the voices of sufferers through qualitative approaches and if any attendant excess anxiety accompanying this painful disease can be reduced or prevented by employing an empathetic and holistic approach on the part of the provider [60,84] appears warranted.

In the interim, as per Figures 1 and 2, plus Table 1, it can be tentatively concluded that this topic warrants more attention to assess the value of routine screening [7], and -where apparent- what its treatment implications are [24,25,74]. In addition, whether following up on routine screenings of the osteoarthritis patient deemed at risk for state or trait anxiety or both, is efficacious or not in attenuating the burden of the disease should be examined [12,30,67,75,78].

Alternately, it is concluded that failing to carry out concerted future research efforts in this realm will preclude a considerable number of older adults with this disease from attaining a high life quality and maximum available treatment benefits. On the other hand, efforts to broaden and solidify the knowledge base regarding anxiety across the time course of the disease, and to resolve negative study findings [85-87], and to do this sooner rather than later may yield significant long-term social and fiscal benefits, even though short term costs of doing this may be substantive [88,89].

In particular, specific attention to examining anxiety and its causes as a potentially highly relevant therapeutic target in the context of various forms of osteoarthritis, which has not been well examined, along with careful consideration to minimize confounding factors in related studies should be forthcoming [76].

Bibliography

1. Williams, A., Kamper, S. J., Wiggers, J. H., O'Brien, K. M., Lee, H., *et al.* (2018). Musculoskeletal conditions may increase the risk of chronic disease: A systematic review and meta-analysis of cohort studies. *BMC Med.*, 16(1), 167.
2. Fava, G. A., Porcelli, P., Rafanelli, C., Mangelli, L. & Grandi, S., (2010). The spectrum of anxiety disorders in the medically ill. *J Clin Psychiatr.*, 71(7), 910-914.
3. Sareen, J., Jacobi, F., Cox, B. J., Belik, S. L., Clara, I., *et al.* (2006). Disability and poor quality of life associated with comorbid anxiety disorders and physical conditions. *Arch Int Med.*, 166(19), 2109-2116.
4. Gay, C., Guiguet-Auclair, C., Mourgues, C., Gerbaud, L. & Coudeyre, E. (2018). Physical activity level and association with behavioral factors in knee osteoarthritis. *Ann Phys Rehabil Med.*, 62(1), 14-0.

5. Stubbs, B., Aluko, Y., Myint, P. K. & Smith, T. O. (2016). Prevalence of depressive symptoms and anxiety in osteoarthritis: a systematic review and meta-analysis. *Age Ageing*, *45*(2), 228-235.
6. Tan, V., Jinks, C., Chew-Graham, C., Healey, E. L. & Mallen, C. (2015). The triple whammy anxiety depression and osteoarthritis in long-term conditions. *BMC Fam Pract.*, *16*, 163.
7. Murphy, L. B., Sacks, J. J., Brady, T. J., Hootman, J. M. & Chapman, D. P. (2012). Anxiety and depression among US adults with arthritis: prevalence and correlates. *Arthritis Care Res (Hoboken)*, *64*(7), 968-976.
8. Kang, L., Nguyen, J., Hashmi, S. Z., Lee, S. K., Weiland, A. J., *et al.* (2017). What demographic and clinical characteristics correlate with expectations with trapeziometacarpal arthritis? *Clin Orthop Relat Res.*, *475*(11), 2704-2711.
9. Heidari, B., Hajian-Tilaki, K. & Babaei, M. (2016). Determinants of pain in patients with symptomatic knee osteoarthritis. *Caspian J Intern Med.*, *7*(3), 153-161.
10. Carmona-Terés, V., Moix-Queraltó, J., Pujol-Ribera, E., Lumillo-Gutiérrez, I., Mas, X., *et al.* (2017). Understanding knee osteoarthritis from the patients' perspective: A qualitative study. *BMC Musculoskelet Disord.*, *18*(1), 225.
11. Khan, S., Hanifa, B., Begum, R. & Kalsoom, U. (2017). Anxiety, depression and psychological distress in patients with osteo-arthritis. *JPMI: J Postgrad Medical Ins.*, *31*(4), 410-413.
12. Lindner, M., Nosseir, O., Keller-Pliessnig, A., Teigelack, P., Teufel, M., *et al.* (2018). Psychosocial predictors for outcome after total joint arthroplasty: A prospective comparison of hip and knee arthroplasty. *BMC Musculoskelet Disord.*, *19*(1), 159.
13. Schwartz, F. H. & Lange, J. (2017). Factors that affect outcome following total joint arthroplasty: a review of the recent literature. *Curr Rev Musculoskelet Med.*, *10*(3), 346-355.
14. Hanssen, M. M., Peters, M. L., Boselie, J. J. & Meulders, A. (2017). Can positive affect attenuate (persistent) pain? State of the art and clinical implications. *Curr Rheumatol Rep.*, *19*(12), 80.
15. Akin-Akinyosoye, K., Frowd, N., Marshall, L., Stocks, J., Fernandes, G. S., *et al.* (2018). Traits associated with central pain augmentation in the Knee Pain In the Community (KPIC) cohort. *Pain*, *159*(6), 1035-1044.
16. Nazarinasab, M., Motamedfar, A. & Moqadam, A. E. (2017). Investigating mental health in patients with osteoarthritis and its relationship with some clinical and demographic factors. *Reumatologia*, *55*(4), 183-188.
17. Nur, H., Sertkaya, B. S. & Tuncer, T. (2018). Determinants of physical functioning in women with knee osteoarthritis. *Aging Clin Exp Res.*, *30*(4), 299-306.

18. Barnett, L. A., Pritchard, M. G., Edwards, J. J., Afolabi, E. K., Jordan, K. P. *et al.* (2018). Relationship of anxiety with joint pain and its management: A population survey. *Musculoskeletal Care.*, 16(3), 353-362.
19. Jones, A. R., Al-Naseer, S., Bodger, O., James, E. T. R. & Davies, A. P. (2018). Does pre-operative anxiety and/or depression affect patient outcome after primary knee replacement arthroplasty? *Knee.*, 25(6), 1238-1246.
20. Wong, L. Y., Yiu, R. L., Chiu, C. K., Lee, W. K., Lee, Y. L., *et al.* (2015) Prevalence of psychiatric morbidity in Chinese subjects with knee osteoarthritis in a Hong Kong orthopaedic clinic. *East Asian Arch Psychiatr.*, 25(4), 150-158.
21. Castaño Carou, A., Pita Fernández, S., Pértega Díaz, S., de Toro Santos, F. J., Grupo de estudio EVALÚA (2015). Clinical profile, level of affection and therapeutic management of patients with osteoarthritis in primary care: The Spanish multicenter study EVALÚA. *Reumatol Clin.*, 11(6), 353-360.
22. Guglielmo, D., Hootman, J. M., Boring, M. A., Murphy, L. B., Theis, K. A., *et al.* (2018). Symptoms of anxiety and depression among adults with arthritis - United States, 2015-2017. *MMWR Morb Mortal Wkly Rep.*, 67(39), 1081-1087.
23. Sinikallio, S. H., Helminen, E. E., Valjakka, A. L., Väisänen-Rouvali, R. H. & Arokoski J. P. (2014). Multiple psychological factors are associated with poorer functioning in a sample of community-dwelling knee osteoarthritis patients. *J Clin Rheumatol.*, 20(5), 261-217.
24. Bierke, S. & Petersen, W. (2017). Influence of anxiety and pain catastrophizing on the course of pain within the first year after uncomplicated total knee replacement: a prospective study. *Arch Orthop Trauma Surg.*, 137(12), 1735-1742.
25. Harmelink, K. E. M., Zeegers, A. V. C.M., Hullegie, W., Hoogeboom, T. J., Nijhuis-van der Sanden, M. W. G., *et al.* (2017). Are there prognostic factors for one-year outcome after total knee arthroplasty? A systematic review. *J Arthroplasty.*, 32(12), 3840-3853.
26. Liddle, A. D., Judge, A., Pandit, H. & Murray, D. W. (2014). Determinants of revision and functional outcome following unicompartmental knee replacement. *Osteoarthritis Cartilage.*, 22(9), 1241-1250.
27. Aşkın, A., Özkan, A., Tosun, A., Demirdal, Ü.S. & İsnaç, F. (2017). Quality of life and functional capacity are adversely affected in osteoarthritis patients with neuropathic pain. *Kaohsiung J Med Sci.*, 33(3), 152-158.
28. Petrovic, N. M., Milovanovic, D. R., Ignjatovic Ristic, D., Riznic, N., Ristic, B. *et al.* (2014). Factors associated with severe postoperative pain in patients with total hip arthroplasty. *Acta Orthop Traumatol Turc.*, 48(6), 615-622.

29. Vida, C., González, E. M. & De la Fuente, M. (2014). Increase of oxidation and inflammation in nervous and immune systems with aging and anxiety. *Curr Pharm Des.*, 20(29), 4656-4678.
30. Stamm, T. A., Pieber, K., Crevenna, R. & Dorner, T. E. (2016). Impairment in the activities of daily living in older adults with and without osteoporosis, osteoarthritis and chronic back pain: a secondary analysis of population-based health survey data. *BMC Musculoskelet Disord.*, 17, 139.
31. Jacobs, C. A., Christensen, C. P. & Karthikeyan, T. (2015). Chronic non-orthopedic conditions more common in patients with less severe degenerative changes that have elected to undergo total knee arthroplasty. *J Arthroplasty.*, 30(7), 1146-1149.
32. Battali, S. L, Glette. M, Alschuler. K. N. & Jensen, M. P. (2018). Anxiety, depression, and function in individuals with chronic physical conditions: A longitudinal analysis. *Rehabil Psychol.*, 63(4), 532-541.
33. Hirschmann, M. T., Testa, E., Amsler, F. & Friederich. N. F. (2013). The unhappy total knee arthroplasty (TKA) patient: Higher WOMAC and lower KSS in depressed patients prior and after TKA. *Knee Surg Sports Traumatol Arthroscopy.*, 21(10), 2405-2411.
34. de Koning, E. J., Timmermans, E. J., van Schoor, N. M., Stubbs, B., van den Kommer, T. N., *et al.*, EPOSA Group (2018). Within-person pain variability and mental health in older adults with osteoarthritis: an analysis across 6 European cohorts. *J Pain.*, 19(6), 690-698.
35. Gil, J. A., Goodman, A. D. & Mulcahey, M. K. (2018). Psychological factors affecting outcomes after elective shoulder surgery. *J Am Acad Orthop Surg.*, 26(5), e98-e104.
36. Pinto, P. R., McIntyre, T., Ferrero, R., Almeida, A. & Araújo-Soares V. (2013). Risk factors for moderate and severe persistent pain in patients undergoing total knee and hip arthroplasty: a prospective predictive study. *PLoS One.*, 8(9), e73917.
37. Janikowska-Hołoweńko. D., Zaborowska-Sapeta, K. & Bidzan, I. (2014). The level of anxiety and the subjective assessment of the quality of life in patients post hip replacement after primary and secondary rehabilitation. *Acta Neuropsychologica.*, 12(2), 143-154.
38. Hernández, C., Díaz-Heredia, J., Berraquero, M. L., Crespo, P., Loza, E., *et al.* (2015) Pre-operative predictive factors of post-operative pain in patients with hip or knee arthroplasty: a systematic review. *Reumatol Clinics.*, 11(6), 361-380.
39. Utrillas-Compared, A., De la Torre-Escuredo, B. J., Tebar-Martínez, A. J. & Asúnsolo-Del Barco, Á. (2014). Does preoperative psychologic distress influence pain, function, and quality of life after TKA? *Clin Orthop Relat Res.*, 472(8), 2457-2465.

40. Ferreira, A. H., Godoy, P. B., Oliveira, N. R., Diniz, R. A., Diniz, R. E., *et al.* (2015). Investigation of depression, anxiety and quality of life in patients with knee osteoarthritis: a comparative study. *Rev Bras Reumatol.*, 55(5), 434-438.
41. Chen, C. J., McHugh, G., Campbell, M. & Luker, K. (2014). Subjective and objective sleep quality in individuals with osteoarthritis in Taiwan. *Musculoskeletal Care.*
42. Hadlandsmyth, K., Sabic, E., Zimmerman, M. B., Sluka, K. A., Herr, K. A., *et al.* (2017). Relationships among pain intensity, pain-related distress, and psychological distress in pre-surgical total knee arthroplasty patients: A secondary analysis. *Psychol Health Med.*, 22(5), 552-563.
43. O'Leary, S., Cottrell, M., Raymer, M., Smith, D. & Khan, A. (2018). General health factors maybe a barrier to effective non-surgical multidisciplinary rehabilitation of common orthopaedic conditions in tertiary care settings. *BMC Musculoskelet Disord.*, 19(1), 348.
44. Hayashi, K., Kako, M., Suzuki, K., Hattori, K., Fukuyasu, S., *et al.* (2015). Gait speeds associated with anxiety responses to pain in osteoarthritis patients. *Pain Med.*, 17(3), 606-613.
45. Hsieh, R. L., Lee, W. C., Lo, M. T. & Liao, W. C. (2013). Postural stability in patients with knee osteoarthritis: comparison with controls and evaluation of relationships between postural stability scores and International Classification of Functioning, Disability and Health components. *Arch Phys Med Rehabil.*, 94(2), 340-346.
46. Helminen, E. E., Sinikallio, S. H., Valjakka, A. L., Väisänen-Rouvali, R. H. & Arokoski, J. P. (2016). Determinants of pain and functioning in knee osteoarthritis: A one-year prospective study. *Clin Rehabil.*, 30(9), 890-900.
47. Hassett, A. L., Marshall, E., Bailey, A. M., Moser, S., Clauw, D. J., *et al.* (2018). Changes in anxiety and depression are mediated by changes in pain severity in patients undergoing lower-extremity total joint arthroplasty. *Reg Anesth Pain Med.*, 43(1), 14-18.
48. Mallen, C. D., Nicholl, B. I., Lewis, M., Bartlam, B., Green, D., *et al.* (2017). The effects of implementing a point-of-care electronic template to prompt routine anxiety and depression screening in patients consulting for osteoarthritis (the Primary Care Osteoarthritis Trial): A cluster randomised trial in primary care. *PLoS Medicine.*, 14(4), 1-23.
49. Hay, E., Dziedzic, K., Foster, N., Peat, G., van der Windt, D., *et al.* (2018). Optimal primary care management of clinical osteoarthritis and joint pain in older people: a mixed-methods programme of systematic reviews, observational and qualitative studies, and randomized controlled trials. *Southampton (UK): NIHR Journals Library.*

50. Kigozi, J., Jowett, S., Nicholl, B. I., Lewis, M., Bartlam, B., *et al.* (2018). Cost-utility analysis of routine anxiety and depression screening in patients consulting for osteoarthritis: Results from the POST Trial. *Arthritis Care Res.*, *70*(12), 1787-1794.
51. Hirakawa, Y., Hara, M., Fujiwara, A., Hanada, H. & Morioka, S. (2014). The relationship among psychological factors, neglect-like symptoms and postoperative pain after total knee arthroplasty. *Pain Res Manag.*, *19*(5), 251-256.
52. Ozcetin, A., Ataoglu, S., Kocer, E., Yazici, S., *et al.* (2007). Effects of depression and anxiety on quality of life of patients with rheumatoid arthritis, knee osteoarthritis and fibromyalgia syndrome. *West Indian Med J.*, *56*(2), 122-129.
53. Ali, A., Lindstrand, A., Sundberg, M. & Flivik, G. (2017). Preoperative anxiety and depression correlate with dissatisfaction after total knee arthroplasty: A prospective longitudinal cohort study of 186 patients, with 4-year follow-up. *J Arthroplasty.*, *32*(3), 767-770.
54. Dhurve, K., Scholes, C., El-Tawil, S., Shaikh, A., Weng, L. K., *et al.* (2017). Multifactorial analysis of dissatisfaction after primary total knee replacement. *Knee.*, *24*(4), 856-862.
55. Duivenvoorden, T., Vissers, M. M., Verhaar, J. A., Busschbach, J. J., Gosens, T., *et al.* (2013). Anxiety and depressive symptoms before and after total hip and knee arthroplasty: a prospective multicentre study. *Osteoarthritis Cartilage.*, *21*(12), 1834-1840.
56. French, H. P., Galvin, R., Cusack, T. & McCarthy, G. M. (2014). Predictors of short-term outcome to exercise and manual therapy for people with hip osteoarthritis. *Phys Ther.*, *94*(1), 31-39.
57. Hanusch, B. C., O'Connor, D. B., Ions, P., Scott, A. & Gregg, P. J. (2014). Effects of psychological distress and perceptions of illness on recovery from total knee replacement. *Bone Joint J.*, *96-B*(2), 210-216.
58. McHugh, G. A., Campbell, M. & Luker, K. A. (2013). Predictors of outcomes of recovery following total hip replacement surgery: A prospective study. *Bone Joint Res.*, *2*(11), 248-254.
59. Kelley, G. A., Kelley, K. S. & Callahan, L. F. (2018). Community-deliverable exercise and anxiety in adults with arthritis and other rheumatic diseases: A systematic review with meta-analysis of randomised controlled trials. *BMJ Open.*, *8*(2), e019138.
60. Sharma, A., Kudesia, P., Shi, Q. & Gandhi, R. (2016). Anxiety and depression in patients with osteoarthritis: Impact and management challenges. *Open Access Rheumatol.*, *8*, 103-113.
61. Lluch, E., Dueñas, L., Falla, D., Baert, I., Meeus, M., *et al.* (2018). Preoperative pain neuroscience education combined with knee joint mobilization for knee osteoarthritis: a randomized controlled trial. *Clin J Pain.*, *34*(1), 44-52.

62. Wang, C. W., Chan, C. H., Ho, R. T., Chan, J. S., Ng, S. M., *et al.* (2014). Managing stress and anxiety through Qigong exercise in healthy adults: A systematic review and meta-analysis of randomized controlled trials. *BMC Complement Altern Med.*, 14, 8.
63. Youngcharoen, P., Hershberger, P. E. & Aree-Ue, S. (2017). Pain in elderly patients with knee osteoarthritis: an integrative review of psychosocial factors. *Int J Orthop Trauma Nurs.*, 25, 19-28.
64. Đurović, A., Sovilj, S., Đokić, I., Brdareski, Z., Vukomanović, A., *et al.* (2017). Pastoral care and religious support as a part of treatment of religious patient with the severe form of osteoarthritis. *Vojnosanit Pregl.*, 74(1), 69-77.
65. Özkuk, K., Uysal, B., Ateş, Z., Ökmen, B. M., Sezer, R., *et al.* (2018). The effects of inpatient versus outpatient spa therapy on pain, anxiety, and quality of life in elderly patients with generalized osteoarthritis: A pilot study. *Int J Biometeorol.*, 62(10), 1823-1832.
66. Creamer, P. & Hochberg, M. C. (1998). The relationship between psychosocial variables and pain reporting in osteoarthritis of the knee. *Arthritis Care Res.*, 11(1), 60-65.
67. Memel, D. S., Kirwan, J. R., Sharp, D. J. & Hehir, M. (2000). General practitioners miss disability and anxiety as well as depression in their patients with osteoarthritis. *Brit J Gen Pract.*, 50(457), 645-648.
68. Rice, D. A., Kluger, M. T., McNair, P. J., Lewis, G. N., Somogyi, A. A., *et al.* (2018). Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors. *Br J Anaesth.*, 121(4), 804-812.
69. Alattas, S. A., Smith, T., Bhatti, M., Wilson-Nunn, D. & Donell, S. (2017). Greater pre-operative anxiety, pain and poorer function predict a worse outcome of a total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc.*, 25(11), 3403-3410.
70. Summers, M. N., Haley, W. E., Reveille, J. D. & Alarcón, G. S. (1988). Radiographic assessment and psychologic variables as predictors of pain and functional impairment in osteoarthritis of the knee or hip. *Arthritis Rheum.*, 31(2), 204-209.
71. Badura-Brzoza, K., Zajac, P., Kasperska-Zajac, A., Brzoza, Z., Matysiakiewicz, J., *et al.* (2008). Anxiety and depression and their influence on the quality of life after total hip replacement: Preliminary report. *Int J Psychiatr Clin Practice.*, 12(4), 280-284.
72. Marks, R. (2009). Comorbid depression and anxiety impact hip osteoarthritis disability. *Disabil Health J.*, 2(1), 27-35.
73. Zambon, S., Siviero, P., Denking, M., Limongi, F., Victoria Castell, M., *et al.*, Eposa Research Group (2016). Role of osteoarthritis, comorbidity, and pain in determining functional limitations in older populations: European Project on Osteoarthritis. *Arthritis Care Res (Hoboken).*, 68(6), 801-810.

74. De Caro, M. F., Vicenti, G., Abate, A., Picca, G., Leoncini, V., *et al.* (2015). Optimal improvement in function after total hip and knee replacement: how deep do you know your patient's mind? *J Biol Regul Homeost Agents.*, 29(4 Suppl), 95-102.
75. Khatib, Y., Jenkin, D., Naylor, J. M., Harris, I. A. (2016). Psychological traits in patients waiting for total knee arthroplasty. a cross-sectional study. *J Arthroplasty.*, 31(8), 1661-1666.
76. King, C. D., Jastrowski Mano, K. E., Barnett, K. A., Pfeiffer, M., Ting, T. V., *et al.* (2017). Pressure pain threshold and anxiety in adolescent females with and without juvenile fibromyalgia: A pilot study. *Clin J Pain.*, 33(7), 620-626.
77. Smith, B. W. & Zautra, A. J. (2008). The effects of anxiety and depression on weekly pain in women with arthritis. *Pain.*, 138(2), 354-361.
78. Bonnin, M. P., Basigliani, L. & Archbold, H. A. (2011). What are the factors of residual pain after uncomplicated TKA? *Knee Surg Sports Traumatol Arthrosc.*, 19(9), 1411-1417.
79. Wood, T. J., Thornley, P., Petrucci, D., Kabali, C., Winemaker, M., *et al.* (2016). Preoperative predictors of pain catastrophizing, anxiety, and depression in patients undergoing total joint arthroplasty. *J Arthroplasty.*, 31(12), 2750-2756.
80. Dekker, J., van Dijk, G. M. & Veenhof, C. (2009). Risk factors for functional decline in osteoarthritis of the hip or knee. *Curr Opin Rheumatol.*, 21(5), 520-524.
81. Hurley, M., Dickson, K., Hallett, R., Grant, R., Hauari, H., *et al.* (2018). Exercise interventions and patient beliefs for people with hip, knee or hip and knee osteoarthritis: a mixed methods review. *Cochrane Database Syst Rev.*, 4, CD010842.
82. Zhang, L., Fu, T., Zhang, Q., Yin, R., Zhu, L., *et al.* (2018). Effects of psychological interventions for patients with osteoarthritis: A systematic review and meta-analysis. *Psychol Health Med.*, 23(1), 1-17.
83. Tetsunaga, T., Tetsunaga, T., Nishida, K., Kanzaki, H., Misawa, H., *et al.* (2018). Drug dependence in patients with chronic pain: A retrospective study. *Medicine (Baltimore).*, 97(40), e12748.
84. Lincoln, N., Moreton, B., Turner, K. & Walsh, D. (2017). The measurement of psychological constructs in people with osteoarthritis of the knee: A psychometric evaluation. *Disabil Rehabil.*, 39(4), 372-384.
85. Jiménez Ortiz, M., Espinosa Ruiz, A., Martínez Delgado, C., Barrena Sánchez, P. & Salido Valle, J. A. (2018). Do preoperative anxiety and depression influence the outcome of knee arthroplasty? *Reumatol Clin.*, pii: S1699-258X(18)30126-8.

-
86. Wylde, V., Trela-Larsen, L., Whitehouse, M. R. & Blom, A. W. (2017). Preoperative psychosocial risk factors for poor outcomes at 1 and 5 years after total knee replacement. *Acta Orthop.*, 88(5), 530-536.
87. Duarte, N., Rodrigues, A. M., Branco, J. D. C., Canhão, H., Hughes, S. L., *et al.* (2017). Health lifestyles factors associated with osteoarthritis among older adults in Portugal. *Front Med (Lausanne)*., 4, 192.
88. Bélair, M. A., Kohen, D. E., Kingsbury, M. & Colman, I. (2018). Relationship between leisure time physical activity, sedentary behaviour and symptoms of depression and anxiety: evidence from a population-based sample of Canadian adolescents. *BMJ Open.*, 8(10), e021119.
89. Rillo, O., Riera, H., Acosta, C., Liendo, V., Bolaños, J., *et al.* (2018). Self-reported symptoms of depression, anxiety and stress among patients with Rheumatoid Arthritis in a Malaysian rheumatology centre - prevalence and correlates. *Med J Malaysia.*, 73(4), 226-232.