



# Lower extremity osteoarthritis management needs a paradigm shift

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## ABSTRACT

The current pre-eminent focus in osteoarthritis research and clinical practice is on persons with established radiographic disease. This is the very end-stage of disease genesis and modern therapies are thus largely palliative. A major shift in the focus of osteoarthritis research and clinical practice is critically needed if an impact is to be made for the millions living with the chronic pain and disability of osteoarthritis. The disease management paradigm needs to be revolutionised to focus on persons at high risk of developing or with early disease in which structural changes may be preventable or reversible. Similarly, current palliation should shift towards coordinated conservative management with reorganisation of the delivery of health services.

Osteoarthritis is a heterogeneous disease characterised by failure of the synovial joint organ.<sup>1</sup> The disease occurs when the dynamic equilibrium between the breakdown and repair of joint tissues becomes unbalanced, often in a situation in which the mechanical loads applied exceed those that can be tolerated by the joint tissues.<sup>2</sup> This progressive joint failure may cause pain and disability.

This disease has a formidable individual and societal impact. Recent estimates suggest that symptomatic knee osteoarthritis occurs in 13% of persons aged 60 years and over.<sup>3,4</sup> The risk of mobility disability (defined as needing help walking or climbing stairs) attributable to knee osteoarthritis alone is greater than that due to any other medical condition in people aged 65 years and over.<sup>5,6</sup> By 2020, the number of people with osteoarthritis will have doubled, due in large part to the exploding prevalence of obesity and the greying of the 'baby boomer' generation.<sup>7</sup> Osteoarthritis already accounts for over 95% of total joint replacements. In the estimates for the Global Burden of Disease 2000 study,<sup>8</sup> osteoarthritis is the fourth leading cause of total years lost due to disease at the global level.

## MAJOR RISK FACTORS WITH AN EYE TO PREVENTION

Osteoarthritis is perhaps best understood as resulting from excessive mechanical stress applied in the context of systemic susceptibility. Susceptibility to osteoarthritis may be increased partly by genetic inheritance (a positive family history increases risk), age, ethnicity, nutritional factors and female gender.<sup>9</sup> The susceptibility to osteoarthritis can also be influenced by the mechanical environment. Local mechanical factors such as the adduction moment, malalignment,

the presence of meniscal tears or bone marrow lesions and muscle strength make the knee joint vulnerable to the progression of osteoarthritis.<sup>10</sup>

While the aetiology of osteoarthritis is complex<sup>9</sup> the two major risk factors for osteoarthritis development (obesity and joint injury)<sup>11,12</sup> are modifiable. To date, however, little is being done in a public health setting to address or modify these risk factors. In this context of an increasingly prevalent and disabling disease our management strategies appear somewhat nihilistic; we can do more to prevent the disease but do not, and the treatment of existing disease is largely palliative. While practice patterns may vary, current clinical management for osteoarthritis is often limited to the use of analgesic and/or anti-inflammatory medication and cautious waiting<sup>13</sup> for the eventual referral for total joint replacement. This narrative review reflects on where the current palliative focus of osteoarthritis management is and where we should be redirecting our energy if we are truly to make an impact on this disease before it overwhelms limited healthcare resources (table 1).

Obesity is the single most important risk factor for the development of severe osteoarthritis of the knee and more so than other potentially damaging factors including heredity.<sup>14,15</sup> Because obesity is both a risk factor for osteoarthritis and has been increasing in prevalence over the past four decades,<sup>16,17</sup> it is likely that more individuals will be affected by knee osteoarthritis in the future. Societal trends in obesity are concerning, with some projecting that by 2030 86.3% of adults will be overweight or obese and 51.1% will be obese.<sup>18</sup> Primary prevention of obesity is likely to be challenging and involves complex strategies including tax on processed foods, supporting healthy food alternatives, promoting physical activity, restricting unhealthy food advertising and appropriate labelling of food. While these strategies may be socially challenging, weight reduction at the population level as a public health measure would be very effective in reducing the incidence of knee and hip osteoarthritis. Focusing weight reduction efforts on only women aged 50 years and over could itself prevent anything from 25.1% to 48.3% of knee osteoarthritis in women.<sup>15</sup> Despite trial evidence of efficacy in weight loss, dissemination of this to the wider at-risk community is limited.

Anterior cruciate ligament (ACL) injuries are traumatic knee injuries with an incidence of at least 81 per 100 000 persons annually aged between 10 and 64 years.<sup>19</sup> ACL ruptures are

**Table 1** Osteoarthritis management is currently focused on palliation

|                        | Primary prevention   | Secondary prevention/impacting disease incidence | Tertiary prevention/impacting progression   | Palliation                     |
|------------------------|--|--|---|--------------------------------|
| Phenotype              | Predisposition through obesity or risk of joint injury                                       | FAI, familial risk, previous joint injury        | Malalignment, symptomatic disease   | Joint failure                  |
| Possible interventions | Weight reduction strategies for the obese or neuromuscular training for sports participation | Surgical correction of FAI, disease modification | Alignment correction through mechanical intervention or disease modifying therapy | Analgesia or joint replacement |
| Possible screening     | Overweight and obesity assessment and identification of high-risk sports                     | Joint shape MRI or biochemical markers           | MRI or radiographic assessment  | Self-reported symptoms         |
| Monitoring assessment  | Population level overweight and obesity prevalence or joint injury incidence                 | MRI of shape and joint integrity                 | MRI or radiographic assessment  | Self-reported symptoms         |

More resources and effort should be shifted towards strategies in earlier stages of primary, secondary and tertiary prevention such as the examples outlined below. FAI, femoroacetabular impingement.

associated with marked short-term morbidity and long-term consequences. It typically occurs in the younger population and as such leads to prolonged disability and economic cost,<sup>20</sup> largely due to work loss. Seventy-seven per cent of formerly young and active individuals who sustain ACL injuries end up with moderate to severe disabilities, such as osteoarthritis, instability, meniscal and chondral surface damage.<sup>21</sup> ACL ruptures have been found to be linked to osteoarthritis changes in 50–70% of patients 10–15 years following the injury.<sup>22–24</sup> Knee injury/trauma has been identified as the most important modifiable risk factor for subsequent knee osteoarthritis in men, and is second only to obesity in women.<sup>25</sup> It is estimated that 25% of incident symptomatic knee osteoarthritis could be prevented by preventing knee injuries among men (women, 14%).<sup>15</sup> Numerous trials of neuromuscular conditioning programmes have demonstrated efficacy in reducing the risk of ACL injury by as much as 60%.<sup>12,26</sup> Despite the impact of joint injury and the efficacy of these prevention trials, programme dissemination and implementation has been limited.

### CURRENT MANAGEMENT OF OSTEOARTHRITIS

Despite its frequency and impact from disability, osteoarthritis is a condition that is often poorly managed in clinical practice. Existing therapies for osteoarthritis help to reduce symptoms, but are only moderately effective, leaving our patients with a substantial pain and function burden. For many of our current therapies (including paracetamol, hyaluronic acid, glucosamine, acupuncture and arthroscopic debridement and lavage) placebo effects can be quite substantial, with differences between placebo and active treatment generally indistinguishable.<sup>27,28</sup> This is further compounded by the fact that many of these agents have side-effect profiles that are raising a number of legitimate concerns about their long-term safety.<sup>29</sup>

Recent years have seen a number of evidence-based guidelines developed for osteoarthritis management.<sup>30–35</sup> There is some consistency<sup>36–38</sup> in the numerous guidelines that are available for osteoarthritis management,<sup>30–35</sup> yet despite some dissemination attempts clinical practice does not reflect these recommendations.<sup>13,38–41</sup> In the absence of a cure, current therapeutic modalities are primarily aimed at reducing pain and improving joint function primarily using agents targeted towards symptoms that do not facilitate any improvement in joint structure or long-term disease amelioration.<sup>30–35</sup> With few conservative options offered by their doctors, increasing numbers of patients are turning to untested folk remedies and aggressively marketed dietary supplements with little substantive evidence to support their efficacy.<sup>42</sup> Qualitative information suggests that the needs of patients are not being met with

regard to the quantity and quality of information provided about osteoarthritis and its treatment, the emotional needs of patients and patient–clinician communication.<sup>43,44</sup>

Some areas for divergence from quality care include inadequate uptake of conservative, non-pharmacological treatment options such as weight loss and exercise, inappropriate surgical interventions such as arthroscopic debridement and lavage in the absence of mechanical disturbance in the knee, an increasing volume of arthroplasty surgery that is not sustainable and the inappropriate use of imaging.<sup>41</sup>

The majority of persons with arthritis are either overweight or obese. There is good evidence for the efficacy of weight management,<sup>45</sup> and this is advocated by most osteoarthritis guidelines. However, in practice, weight management is not frequently implemented.<sup>39,46,47</sup> Another pivotal and frequently ignored<sup>39,46,47</sup> aspect of conservative treatment of osteoarthritis is exercise. Guidelines routinely advocate exercise,<sup>30–35</sup> however, clinical practice does not reflect this recommendation.<sup>39,46,47</sup>

Surgery should be resisted when symptoms can be managed by other treatment modalities. Arthroscopic debridement and meniscal resection remains the most frequently performed procedure by orthopaedic surgeons in most developed countries,<sup>48,49</sup> with up to one million knee arthroscopies performed annually in the USA. This surgery has no demonstrable efficacy.<sup>28,50,51</sup>

Imaging can assist in making a diagnosis of osteoarthritis by refuting other diagnoses when the clinical picture from history and physical examination leaves this diagnosis unclear.<sup>52</sup> The diagnosis is, however, a clinical one made by assessing the constellation of presenting clinical features, and radiography should be used only to refute other diagnoses that could plausibly result in the patient's symptoms. Currently, there is an overuse of inappropriate imaging to make a diagnosis that can be made clinically. In light of the current lack of therapy that can modify the disease course and measurement imprecision, there is currently no rationale for obtaining serial radiographs if the clinical state remains unchanged. MRI should only be used in infrequent circumstances to facilitate the diagnosis of other causes of knee pain that can be confused with osteoarthritis (eg, osteochondritis dissecans, avascular necrosis). The presence of a meniscal tear viewed by MRI in a person with knee osteoarthritis is almost uniform and is not necessarily a cause of increased symptoms.<sup>53</sup> The penchant to remove menisci is to be avoided, unless there are symptoms of locking or extension blockade<sup>54</sup> as there are strong data to support the fact that meniscectomy, even partial meniscectomy, increases the risk of progression of osteoarthritis.<sup>55</sup>

This divergence from evidenced-based care is also commonly seen with other diseases, in which it is estimated that half of the treatment rendered by clinicians is inappropriate.<sup>56</sup>

Much of the challenge with current clinical practice targeting inappropriate or potentially harmful therapy and neglecting potentially beneficial conservative treatments such as weight loss and exercise is the opportunity lost for meaningful intervention, impacts on quality of life for patients and pressure on limited healthcare resources. Much of the current focus is on therapeutic interventions that are palliative; they are primarily limited to analgesia and when this fails, surgical intervention. We need to change this paradigm to intervene when structural changes may be reversible (table 1). In the absence of pharmacological agents that can modify disease we need to reappraise our current treatment strategies to focus on modifiable risk factors for disease and symptom genesis and disease progression.

### SHIFT TOWARDS PREVENTION AND PROGRESSION

As outlined already in this review, the majority of disease can be prevented by reducing obesity and joint injury in the community. If disease develops we should shift our focus towards ameliorating symptoms and disease progression, not just palliation.

Recent advances in other prevalent rheumatic diseases has resulted in diseases that were associated with inexorable decline being treated proactively with associated preservation of structure and function. The advance of biological therapy in rheumatoid arthritis has seen dramatic shifts in the preservation of structure and the discussion of a new classification of disease remission. Recent evolution in medical care for osteoporosis has seen a marked reduction in fracture rates with their associated morbidity, with the appropriate institution of antiresorptive therapy. Unfortunately, we do not have this proactive stance available in osteoarthritis, and with current structural definitions and measurement strategies that is unlikely to change. We desperately need to focus on earlier disease in which changes may be reversible if we are not to continue current therapeutic approaches that are largely palliative.

If pharmacological intervention as a single therapy is to be trialed effectively selecting those with earlier disease before the development of marked structural damage and aberrant mechanics is a preferable solution.<sup>57</sup> There is currently no osteoarthritis equivalent to measuring high lipid levels, atherosclerosis, hypertension or high glucose and glucose tolerance, for example, as we have for cardiovascular disease and diabetes, in which one can detect and treat the disease precursors pre-emptively before the associated processes lead to end-organ failure (see table 2).<sup>58</sup> Instead, the 'watchful waiting' of steady decline to end-stage joint disease is a major cause of disablement and loss of quality of life.

Previous human clinical studies with varying levels of efficacy success suggest that a wide array of agents including glucosamine sulphate, chondroitin sulphate, sodium hyaluronan, doxycycline, matrix metalloproteinase inhibitors, bisphosphonates, calcitonin, diacerein and avocado-soybean unsaponifiables can modify disease progression.<sup>59–61</sup> It may be a while before a disease-modifying drug is available as current trial strategies remain neglectful of some simple fundamentals. Cartilage is not a direct source of symptoms and yet this remains the major focus of drug development opportunities. As important as the appropriate focus on tissues likely to be generating symptoms, therapeutic development needs to be cognisant of the aberrant mechanical forces at play in persons with osteoarthritis.<sup>58</sup>

Our current paradigm of studying persons with end-stage irreversible disease needs to change if we are to identify a stage of the disease at which the structural changes may be reversible. The majority of individuals with symptomatic radiographic disease have full thickness cartilage loss over extensive areas in weight-bearing portions of the knee joint.<sup>62</sup> Therefore, most persons presenting with radiographic osteoarthritis already have advanced degrees of damage. Retarding loss in these individuals will thus be more focused upon preserving what they have left. Furthermore, this appears to occur in joints that are malaligned, creating a harsh mechanical environment for putative agents to work in. As Brandt *et al*<sup>63</sup> suggested 'if efforts to develop a disease modifying osteoarthritis drug or biological treatment for osteoarthritis, which are almost always aimed at stimulating the osteoarthritic cartilage with growth factors or inhibiting matrix-degrading enzymes, do not concomitantly correct the mechanical disorder that is the proximate cause of the arthropathy, these treatments are unlikely to produce long-lasting benefit.' Attempts to treat a failing tissue in a grossly malaligned joint is a tall order for any intervention, and thus identification of structural changes that predate this are urgently needed.

Promising therapies are being developed for new osteoarthritis targets for both symptoms and structure, but we need to pay heed to the lessons we have learnt and consider the obstacles to development if they are to be effective.<sup>59</sup>

### HOW SHOULD WE MANAGE OSTEOARTHRITIS NOW WITH THE INTERVENTIONS WE HAVE?

Comprehensive management always includes a combination of treatment options that are directed towards the common goal of improving the patient's pain and tolerance for functional activity. The recommended hierarchy of management should consist of non-pharmacological modalities first, then drugs and then surgery. Too frequently the first step is forgotten or not emphasised sufficiently to the patient's detriment.<sup>13</sup> In addition, combinations of treatments are frequently used in clinical practice and may have additional synergistic benefits.

**Table 2** Osteoarthritis comparisons with other common, chronic diseases with substantive morbidity

| Molecular abnormality              | Silent/subclinical disease                   | Symptomatic disease                 | Organ failure            |
|------------------------------------|--|-------------------------------------|--------------------------|
| Abnormal biochemical markers       | Asymptomatic structural abnormality, eg, MRI | Symptomatic osteoarthritis          | Joint failure            |
| High blood sugar                   | Arteriosclerosis                             | Mild nephropathy, visual impairment | Renal failure, blindness |
| Hyperlipidaemia                    | Atherosclerosis                              | Myocardial infarction               | Heart failure            |
| Elevated anti-CCP and RF           |  | Symmetric polyarthropathy           | Joint deformity          |
| Bone turnover favouring resorption | Osteoporosis on DEXA                         |                                     | Fracture                 |

Our current management paradigm for osteoarthritis targets organ failure (modified from Kraus).<sup>58</sup>  
CCP, cyclic citrullinated peptide; DEXA, dual-energy x-ray absorptiometry; RF, rheumatoid factor.



As a clinician managing osteoarthritis, efforts should be made when possible to influence modifiable risk factors. In the first instance, the clinical encounter should target the identification of individual risk factors (including altered alignment, obesity and muscle weakness) and the therapeutic intervention should be tailored to target the individual. The majority of persons with osteoarthritis are overweight or obese; there is good evidence for the efficacy of weight management for osteoarthritis,<sup>45</sup> and this is advocated by most osteoarthritis guidelines. For each kilogram of weight lost, the knee will experience a fourfold reduction in load during daily activities.<sup>63</sup> Another pivotal and frequently ignored<sup>39 46 47</sup> aspect of conservative treatment of osteoarthritis is exercise. Exercise increases aerobic capacity, muscle strength and endurance, and also facilitates weight loss.<sup>45 64</sup>

Numerous studies have highlighted the importance of mechanical factors on the aetiopathogenesis of this disease.<sup>65–70</sup> Recent studies suggest that mechanical forces play an important role in predisposing to both symptoms and structural change.<sup>65–70</sup> Although it is recognised that joint mechanics is critically important in disease pathogenesis and symptoms, little is done to intervene effectively in these important risk factors. Despite their current underemphasis in clinical trials and practice, therapies targeting the pathomechanics of osteoarthritis are efficacious.<sup>70–74</sup> At present, there are a number of therapeutic options that can modify joint forces, including patella taping, braces, orthotics, shoes and osteotomies for the knee and surgical correction of hip deformity associated with femoroacetabular impingement syndrome.<sup>71–73</sup>

### NEED FOR CHANGE IN HEALTH SYSTEM DELIVERY

Osteoarthritis treatment is multifaceted and involves the contribution of a diverse number of health professionals across different health sectors. It is therefore more appropriate to consider the provision of health care for osteoarthritis within the context of a chronic disease management model than within the current model of episodic healthcare provision. A comprehensive and integrated model of osteoarthritis delivery will facilitate the implementation of best evidence, patient education, patient self-management and collaboration and communication between health providers.<sup>75 76</sup> This chronic disease management model of care focuses in a different way on collaborative multidisciplinary care provided in a setting conducive to the implementation of best practice and continuity of care. This involves patient self-management and coordinated health care from general practitioners, rheumatologists, orthopaedic surgeons and allied health professionals (including physiotherapists, dieticians and psychologists). Such chronic disease management service models are of proved effectiveness for chronic conditions, including chronic heart failure, chronic obstructive pulmonary disease and diabetes.

A comprehensive disease management programme for osteoarthritis will benefit patients through improved quality of life, reduced healthcare utilisation and increased satisfaction with the provision of health care. In patients with established osteoarthritis, it may contribute to reducing or delaying the need for joint replacement. A clinical pathway will also facilitate better healthcare integration between hospital and community care and will improve patient flow through a number of health professional providers. This approach will require concerted collaboration between all interested stakeholders (and their respective professional societies) including patients, physiotherapists, general practitioners, orthopaedic surgeons and rheumatologists.

### CONCLUSION

There are numerous evidence-based guidelines available to practising clinicians that have the potential to improve the quality of health care by promoting interventions of confirmed benefit and discouraging unnecessary, ineffective or harmful interventions. Despite the presence of numerous consistent osteoarthritis management guidelines and some dissemination attempts, clinical practice does not reflect these recommendations. Future efforts to guide the management of osteoarthritis are better directed towards implementing practices known to be effective in a context-dependent manner to optimise healthcare quality. With the convergence of the increase in medical need, progress in information technology, and unsustainable healthcare costs, there is a favourable set of situational conditions for the funding, development, use and publication of this new vision for the linkage of the patient-centred and provider-integrated model for osteoarthritis management.

The current pre-eminent focus in osteoarthritis research and clinical practice is on persons with established radiographic disease. This is the very end-stage of disease genesis and modern therapies are thus largely palliative. Analgesic therapy and end-stage joint replacement are standard medical practice as it relates to osteoarthritis management in 2010. A major shift in the focus of osteoarthritis research and clinical practice is critically needed if an impact is to be made for the millions living with the chronic pain and disability of osteoarthritis. Obesity is the strongest risk factor for disease onset and mechanical factors dominate the risk of disease progression. Greater therapeutic attention to the important role of mechanical factors and obesity in osteoarthritis aetiopathogenesis is required if we are to find ways of reducing the public health impact of this condition. We desperately need to focus on earlier disease in which the structural changes of osteoarthritis may be either preventable or reversible. We need to revolutionise the disease paradigm to focus on persons at high risk of developing disease or with early disease in which structural changes may be preventable or reversible. Similarly, current palliation should shift towards coordinated conservative management with reorganisation of the delivery of health services.

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