

# Feasible non-surgical options for management of knee osteoarthritis during the COVID-19 pandemic and beyond

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## Introduction

Osteoarthritis (OA) is a common degenerative joint disease involving progressive deterioration of joint cartilage and underlying bone. It most commonly affects the distal interphalangeal, hip, and knee joints through degeneration resulting in progressive loss of function, increasing stiffness, and worsening pain.<sup>1</sup> Knee OA is a common debilitating disease among older adults. In 2018, 1.27 million (17.9%) Hong Kong residents were aged  $\geq 65$  years; this number is projected to double to 2.44 million by 2038.<sup>2</sup> The increasing ageing population and worsening obesity epidemic are expected to greatly increase the number of individuals with knee OA. Although early-stage OA can be asymptomatic, subsequent joint pain often causes healthcare-seeking behaviour.

Patients with knee OA experience rapidly worsening pain and decreasing joint functionality during prolonged inactivity. The social distancing measures enforced during the coronavirus disease 2019 (COVID-19) pandemic in Hong Kong have hindered patient adherence to international OA guidelines.<sup>3</sup> Due to the possibility of future pandemics and outbreaks, it is crucial that we provide patients with practical non-surgical approaches to pain management and minimising the risk of progression. Considering language barriers, treatment availability, and variations in COVID-19 regulations, locality-specific recommendations are essential. Primary healthcare practitioners and Hong Kong residents can utilise the therapeutic tools described in this article to promote self-management of knee OA in Hong Kong throughout the COVID-19 pandemic and beyond.

## Overview of knee osteoarthritis treatment during coronavirus disease 2019

A recent analysis of COVID-19 effects on arthroplasty

services in Hong Kong showed large (>50%) decreases in elective arthroplasties and surgical volume from January to June 2020.<sup>4</sup> Although the rate of revision operations remained similar during this period, the number of primary arthroplasty operations decreased by 91%, emphasising the importance of effective non-surgical treatment options for knee OA.<sup>4</sup> The multifactorial aetiology and slow progression of knee OA enable implementation of diverse therapeutic regimens. Non-surgical treatments can be broadly divided into non-pharmacological (preferred) and pharmacological options (Fig).

## Non-pharmacological treatments

Non-pharmacological options are the first-line treatment for OA. Despite their high efficacy and favourable side-effect profiles, such treatments are often overlooked in favour of pharmacological or surgical approaches.<sup>5</sup> Non-pharmacological options involve patient education, weight reduction and exercise, physical and occupational therapy, and orthotic assistance. Their principle outcomes include slower disease progression, pain relief, and improved functionality.

## Education

A better understanding of knee OA and its progression can motivate patients to assume an active role in their treatment plan, thereby improving compliance and promoting health-seeking behaviours. Knowledgeable patients can recognise relevant symptoms, reducing anxiety and enabling clear reporting. Patient education also limits misinformation and misconceptions. In a qualitative study of patients with hip and knee OA during the COVID-19 pandemic, most individuals failed to utilise first-line interventions for OA (ie, therapeutic exercises) despite pandemic-related restrictions; they believed that complementary

OA treatments (ie, physiotherapy) offered better therapeutic effects than exercise.<sup>6</sup> The Elderly Health Service, a subsidiary of the Department of Health of Hong Kong, has published official OA fact sheets, instructional exercise videos, and treatment guidelines in Cantonese, English and Mandarin, facilitating use by the Hong Kong population, where Cantonese is the first language.<sup>7</sup> There are also other web-based education programmes worldwide (online supplementary Table 1).

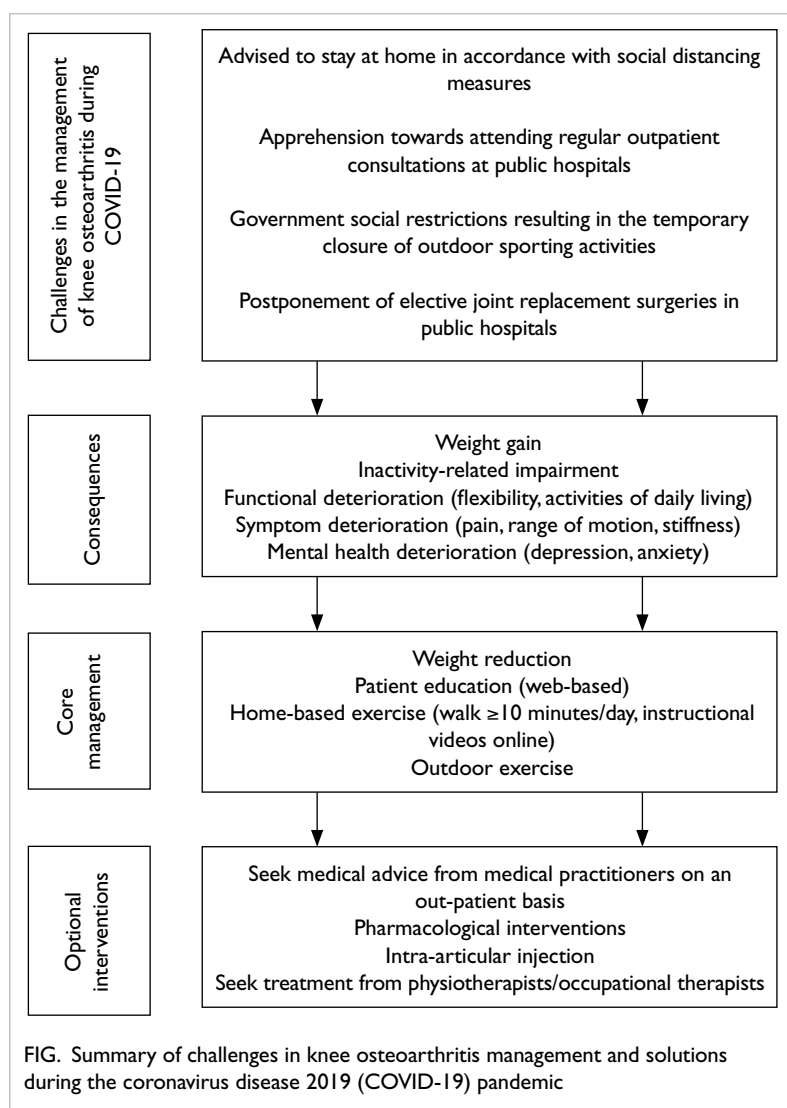
### Weight reduction

Knee OA is strongly associated with obesity. The 2014/15 Hong Kong Population Health Survey revealed that approximately 50% of adults in the general population were obese or overweight.<sup>8</sup> A meta-analysis<sup>9</sup> found that obesity and overweight increased the risk of knee OA by 35% for every 5 kg/m<sup>2</sup> increase in body mass index. Weight reduction can decrease the mechanical and inflammatory stressors involved in knee OA.

Treatment methods include lifestyle modification, calorie restriction, regular physical activity, pharmacological means, and surgical approaches. Pandemic-related social restrictions have hampered outdoor physical activity. Additionally, stress-related calorie intake may increase during lockdown. Access to outpatient dietetic services has been limited during the pandemic, hindering patient accountability for eating habits. In Hong Kong, telemedicine consultations with dietitians were more effective than face-to-face dietetic services for promoting intermediate- and long-term weight reduction in overweight individuals.<sup>10</sup> There is evidence showing the benefits of weight reduction on pain and physical disability.<sup>11</sup>

### Exercise

Exercise can help reduce body weight and strengthen surrounding muscles. Although exercises involving excessive joint loads should be avoided, low-impact aerobic exercises can reduce pain, improve limb mobility, and restore joint function.<sup>12</sup> International OA guidelines recommend multimodal exercise programmes that incorporate targeted resistance and flexibility training.<sup>3</sup> Resistance programmes can include resistance training machines (isokinetic) and body weight (isotonic) exercises to strengthen quadriceps muscles, improving joint stability and reducing pain severity. Recent COVID-19 restrictions in Hong Kong have resulted in temporary closures of fitness centres and mandatory mask usage during physical activity. These new restrictions have precluded the exercise intensity needed to improve knee OA outcomes. Nevertheless, a randomised controlled trial showed that simple home-based exercises led to 30% reduction in the WOMAC (Western Ontario and McMaster



Universities Osteoarthritis Index) compared with educational control and diet groups.<sup>13</sup> A prospective cohort study assessing the effects of the COVID-19 lockdown on hip and knee OA revealed significant pain exacerbation (according to visual analogue scale score) and reduced joint functionality (according to WOMAC score for pain, stiffness, and physical function) among individuals with decreased physical activity.<sup>14</sup> To prevent inactivity-related impairment, adults with knee OA are advised to walk at least 10 minutes per day<sup>15</sup>; this goal is feasible for individuals confined to their homes during the fifth wave of the COVID-19 pandemic in Hong Kong.

### Physiotherapy

Physiotherapy is important for patients with knee OA. Full-range active and passive joint movements can prevent contractures that limit joint function and precede disability. Resistance training restores periarticular muscle strength, thus improving physical function, reducing joint pain, and slowing

cartilage degeneration. The clinical effects on knee OA include improvements in walking speed, walking distance, timed up and go test outcomes, and stair climbing. A community-based aquatic exercise programme for patients with knee OA recently demonstrated effectiveness and feasibility in Hong Kong. Improvements in joint functionality and quadricep strength were observed after 10 weeks of physiotherapist-led aquatic exercises.<sup>16</sup> Although pandemic-related rehabilitation service disruption interrupted treatment for some patients, tele-rehabilitation usage in Hong Kong significantly increased during the pandemic.<sup>17</sup> Among 9101 patients utilising tele-rehabilitation, rates of satisfaction and adherence to prescribed rehabilitation activities were high; moreover, 1112 therapists (50.6% of the workforce) prescribed tele-rehabilitation during the pandemic.<sup>17</sup>

### Orthotics

Considering their affordability, negligible adverse effects, and relative ease of application, braces are ideal for Hong Kong patients with knee OA in the COVID-19 era. The use of a soft knee brace improves knee instability and functionality. A cohort study of bracing and orthotics efficacy showed improvements in pain and joint functionality among patients with knee OA in Hong Kong after 24 weeks.<sup>18</sup> Although shoe insoles had a compliance rate exceeding 90%, bracing had a compliance rate of 54.5%; skin discomfort in the hot and humid climate contributed to poor adherence.<sup>18</sup>

### Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation has become a convenient option for in-home pain relief among patients with knee OA. Retail chains throughout Hong Kong offer affordable stimulation devices, reducing barriers to treatment. A recent randomised controlled trial demonstrated considerable improvements in the visual analogue scale score for pain and distance walked in the 6-minute walk test, following a trial of transcutaneous electrical nerve stimulation in patients with minimal knee pain.<sup>19</sup>

### Pharmacological treatments

Pharmacological agents may be indicated for patients with recalcitrant symptomatic knee OA. No available pharmacological therapies for knee OA are disease-modifying; they should only be used during symptom worsening. A step-up approach should be utilised regarding pharmacological treatments, with careful and deliberate assessment of the clinical context before administration. According to international guidelines, paracetamol is not considered first-line treatment for knee OA because of its clinically

insignificant effects on pain management.<sup>3</sup> However, Hong Kong guidelines recommend paracetamol as first-line treatment.<sup>20</sup>

### Non-steroidal anti-inflammatory drugs

Topical and oral formulations of non-steroidal anti-inflammatory drugs (NSAIDs) can be administered to patients with knee OA. Under Hong Kong and international guidelines, topical NSAIDs are strongly recommended for the first-line management of knee OA because of their pain management efficacy and satisfactory safety.<sup>20</sup> Patients with inadequate symptom relief from topical NSAIDs may transition to oral NSAIDs with satisfactory gastrointestinal, cardiovascular, and renal profiles. The minimum necessary dose of oral NSAIDs for pain control should be used because of possible side-effects. Patients with gastrointestinal complications should receive a proton pump inhibitor along with NSAIDs.<sup>21</sup>

### Glucosamine and chondroitin sulphate

Glucosamine and chondroitin sulphate are considered safe and useful conservative treatments in oral supplement form. Both compounds have anti-inflammatory and immunomodulatory activities that can decrease cartilage degeneration and increase hyaluronic acid (HA) synthesis.<sup>22</sup> Despite strong international recommendations against glucosamine usage, Hong Kong guidelines support its application in mild to moderate knee OA.<sup>20</sup> Although active prescribing of glucosamine and chondroitin sulphate is discouraged, clinicians should not prohibit its use among patients who experience clear benefits.

### Opioids

Opioid administration for pain relief should be reserved for patients with severe recalcitrant pain. Similar to NSAIDs, the minimum necessary dosage of opioids should be used while monitoring for common side-effects. Opioid use is discouraged because of negative impacts on patients and society. The high incidences of short-term side-effects and long-term consequences highlight the importance of limiting opioid use.<sup>23</sup> There is a negligible pain reduction benefit during long-term use of opioid medications for knee OA. The risks of opioid use consistently outweigh the benefits of such treatment. Clinicians should utilise alternative non-surgical treatments in a stepwise manner.<sup>23</sup>

### Topical capsaicin

Topical capsaicin is an alternative treatment option for patients with mild recalcitrant knee OA. Capsaicin alleviates pain by depleting substance P and inhibiting the TRPV1 receptor on nociceptive sensory neurons. Prolonged capsaicin application

can desensitise nociceptive fibres and inhibit pain transmission. Low-concentration capsaicin formulations have consistently demonstrated safety and efficacy. Nevertheless, topical NSAIDs remain preferable as first-line treatment for knee OA because of their favourable side-effect profile and greater evidence of efficacy. A trial regimen of capsaicin should be offered to patients with a poor response (or contraindications) to topical NSAIDs.<sup>24</sup>

## Injection

### Intra-articular corticosteroids

Intra-articular corticosteroids are useful for patients with symptoms recalcitrant to NSAIDs. Although they are highly effective in reducing short-term pain, they have poor long-term efficacy.<sup>3</sup> Corticosteroids exhibit both anti-inflammatory and immunosuppressive effects: after treatment, patients typically experience improved joint mobility and rapid reductions of erythema, swelling, heat, and tenderness in affected joints.<sup>3</sup> Frequent intra-articular corticosteroid use should be avoided because of the increased infection risk and potential damage to joints and cartilage.

### Intra-articular hyaluronic acid

Hyaluronic acid, a naturally occurring glycosaminoglycan, increases the viscosity and elasticity of synovial fluid, thereby facilitating joint lubrication and reducing cartilage stress. Additionally, HA has anti-inflammatory and chondroprotective properties. Elevated levels of inflammatory cytokines and proteolytic enzymes in OA interfere with these properties and contribute to knee joint deterioration.<sup>25</sup> Intra-articular injection of HA may restore viscoelasticity to synovial fluid. A Cochrane review comparing intra-articular HA with corticosteroids revealed no significant differences 4 weeks after administration; however, intra-articular HA was more effective 5 to 13 weeks after injection.<sup>26</sup> Other studies have shown that HA treatment for moderate OA decreased the mean number of opioid prescriptions (both existing and new), improved the maintenance of medial and lateral joint space areas, and delayed the need for total knee replacement surgery.<sup>27</sup> Although various intra-articular HA preparations exist (online supplementary Table 2), their clinical effects remain controversial because of conflicting data. The American College of Rheumatology and American Academy of Orthopaedic Surgeons do not recommend using HA as an analgesic for OA. Although there is evidence of HA safety and efficacy in knee OA, this expensive treatment may be unsuitable for some patients.<sup>26</sup> In Hong Kong, HA is recommended because it significantly reduces pain and has an excellent safety profile. A study of hylan G-F 20 injection safety

and efficacy among patients with knee OA in Hong Kong showed significant improvements in pain and function over 6 months after a single 6-mL intra-articular injection; that study also demonstrated the feasibility of locality-wide HA use in outpatient settings.<sup>28</sup>

### Platelet-rich plasma

Platelet-rich plasma (PRP) is a minimally invasive, inexpensive method to obtain biologically active molecules for the treatment of knee OA.<sup>29</sup> Whereas HA requires exogenous fermentation, PRP is obtained by centrifugation of autologous blood. There are four common PRP preparations (Table). Extracted plasma can exhibit considerably higher concentrations of platelets compared with normal blood. The extracted platelets degranulate upon reinjection, releasing growth factors and bioactive molecules that promote healing at injured sites. Improvements in chondrocyte apoptosis, cartilage proteoglycan concentrations, and OA progression have been observed after intra-articular injection of PRP. Furthermore, pain relief, knee function, and quality of life are improved, compared with HA level.<sup>30</sup> The Osteoarthritis Research Society International discourages PRP usage considering the low quality of evidence and lack of standardisation among formulations. However, applications of PRP persist in private clinics in Hong Kong; thus, patients and clinicians should be knowledgeable regarding the available formulations.

### Mesenchymal stem cells

Mesenchymal stem cells (MSCs) are multipotent progenitors that can be obtained from numerous tissues. Although they do not have unlimited differentiation potential, MSCs are preferred among stem cell treatments for OA because of their widespread availability.<sup>31</sup> The pluripotency of MSCs enables differentiation into osteoblasts, chondrocytes, and adipocytes, facilitating the recovery of knee joints with OA. Additionally, MSCs secrete cytokines and growth factors with anti-inflammatory and immunomodulatory properties that can enhance cartilage regeneration, reduce inflammation, and improve angiogenesis. Primary isolated stromal cells constitute the best option for knee OA treatment. Bone marrow-derived stromal cells (from the posterior superior iliac spine) and adipose tissue-derived stromal cells (from the infrapatellar fat pad and subcutaneous sites) are most commonly utilised in clinical settings.<sup>32</sup> Despite the promising potential of MSCs, existing evidence has been obtained from small uncontrolled studies with diverse cell preparation methods and short follow-up. The optimal tissue source and cell dose also remain unclear, hindering conclusions about the clinical effects of MSCs. Randomised controlled

TABLE. Comparison of common platelet-rich plasma preparations\*

	Autologous Conditioned Plasma double-syringe system <sup>†</sup>	GPS III <sup>‡</sup>	RegenKit A-PRP <sup>§</sup>	SmartPrep 3 System <sup>  </sup>
Manufacturer	Arthrex, Naples [FL], US	Zimmer Biomet, Warsaw [IN], US	RegenLab, Le Mont-sur-Lausanne, Switzerland	Harvest Technologies, Belton [TX], US
Volume of blood, mL	9	27 or 54	10	20, 30, 60, or 120
Centrifuge time, min	5	15	5	14
Centrifugal force, g	350	1900	1500	1000
Final PRP volume, mL	3 to 5	3 or 6	5 to 6	3, 4, 10, or 20
Recovery of available platelets, %	N/A	90	80	67
Platelet concentration	2-3x	9.3x	1.6x	4.4-7.6x
Factor (native)				
Activator	None	Calcium chloride/thrombin	Thixotropic gel/citrate	Thrombin
Treatment regimen	3-5 mL, single-dose	3 or 6 mL, single-dose	5-6 mL, single-dose	3/4/10/20 mL, single-dose

Abbreviations: N/A = not available; PRP = platelet-rich plasma

\* All information were obtained from each product manufacturer

<sup>†</sup> Arthrex. Arthrex ACP double-syringe system. Available from: <https://www.arthrex.com/orthobiologics/autologous-conditioned-plasma>. Accessed 16 Mar 2022

<sup>‡</sup> Zimmer Biomet. GPS III platelet concentration system. Available from: <https://www.zimmerbiomet.com/en/products-and-solutions/products/restorative-therapies/gps-iii-platelet-concentration-system.html>. Accessed 16 Mar 2022

<sup>§</sup> RegenLab. RegenKit A-PRP. Available from: <https://www.regenlab.com/products/regenkit-a-prp-2/>. Accessed 16 Mar 2022

<sup>||</sup> Harvest Technologies. SmartPrep 3 System. Available from: <https://www.globusmedical.com/products/harvest/>. Accessed 31 Jan 2024

trials with larger patient cohorts are needed to confirm the safety and efficacy of MSCs in knee OA.

## Exacerbation of knee pain during coronavirus disease 2019

Numerous underlying aetiologies may explain the pronounced exacerbation of OA-related knee pain throughout the COVID-19 pandemic. Prolonged inactivity and inadequate non-surgical management have been associated with worsening knee pain and joint functionality during the pandemic.<sup>14</sup> There have also been reports of COVID-19-related arthritis; although its clinical presentation was similar to knee OA, affected patients had reactive or inflammatory arthritis that could require disease-modifying antirheumatic drugs.<sup>33</sup> Accordingly, primary healthcare practitioners should make referrals to appropriate specialists when doubt arises.

## Conclusion

Social distancing measures during the COVID-19 pandemic have hindered care for patients with knee OA. Prolonged inactivity has been associated with worsening symptoms, disease progression, and poor functional outcomes. The non-surgical modalities highlighted in this article are specifically tailored to the Hong Kong population; they are feasible under stringent social distancing. Primary healthcare practitioners should utilise and promote these tools to enhance self-management and prepare patients

for future outbreaks and pandemics.

### Author contributions

Concept or design: PK Chan, C Wen, LCM Lau, TKC Leung, MH Luk, VWK Chan, A Cheung, MH Cheung, H Fu, KY Chiu. Acquisition of data: JR Khoo.

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All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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All authors have disclosed no conflicts of interest.

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### Supplementary material

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