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Tackling osteoarthritis during COVID-19 pandemic

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FACR, LPM and FB conceived, wrote, revised and approved the final version of the manuscript.

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3 We read with great interest the study from Gianfrancesco et al.¹ on the characteristics
4 associated with hospitalisation for COVID-19 in people with rheumatic disease based on
5 the data from the COVID-19 Global Rheumatology Alliance physician-reported registry. It
6 provides original and important information concerning the links between chronic
7 inflammatory arthritis and COVID-19. We would like to draw attention to the fact that
8 COVID-19 have also had a significant impact on the most common rheumatic disease,
9 osteoarthritis (OA). Mendy et al.² looked among the 689 COVID19 patients treated in 4
10 hospitals in the Cincinnati area for factors associated with severity and/or with
11 hospitalization. One hundred and five patients had OA. After adjustment, patients with
12 OA were more often hospitalized than patients without osteoarthritis (OR (95% CI) = 1.95
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15 total knee or hip joint replacement for OA and who had to delay it because of the
16 lockdown, there was a significant increase in pain, worsening of physical function and a
17 decrease in physical activity when comparing the clinical condition at the beginning and
18 end of the lockdown³.
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34 **COVID-19 and physical distancing**

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36 The recently characterized Severe Acute Respiratory Syndrome coronavirus
37 (SARS_CoV-2) is the cause of coronavirus disease 2019 (COVID-19), a serious illness
38 responsible for the current pandemic, as declared by the World Health Organization
39 (WHO).^{4,5} The number of deaths associated with COVID-19 has been partially linked to
40 the incapacity of health systems to provide care to infected patients⁶. As of July 15, 2020,
41 the WHO reported 13,119,239 confirmed cases of COVID-19 globally, with a 573,752
42 death toll. There is no curative treatment and a vaccine will most probably not be
43 available, at least to everybody, by the end of this year. Although the Food and Drug
44 Administration in the USA has issued a statement allowing for remdesivir to be used as
45 a treatment for COVID-19,⁷ a defined therapy is yet to be made. Given the huge number
46 of patients affected by COVID-19, health authorities have established rules for “physical
47 distancing” and a “stay at home” strong advice. In some situations, a strict lockdown norm
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3 has been issued in order to limit the number of people exposed in order not to overwhelm
4 the health systems ability to provide assistance for those with more severe disease.⁸

6 **Guidelines on Rheumatic Diseases**

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8 Most immune-mediated rheumatic disease patients are subjected to some sort of
9 immunosuppressive therapy, rendering them more susceptible to infections. Several
10 organizations including the American College of Rheumatology (ACR),⁹ the European
11 League Against Rheumatism (EULAR)¹⁰ and the Brazilian Society of Rheumatology¹¹
12 issued guidances for managing such patients during this pandemic. However,
13 recommendations on dealing with patients affected by highly prevalent musculoskeletal
14 diseases that are not considered to be immune-mediated are lacking. Indeed, neck pain,
15 low back pain, “other musculoskeletal disorders” and falls account for 4 out of the top 10
16 causes of years lost with disability worldwide.¹²

23 **Osteoarthritis management in COVID-19 days**

24
25 Osteoarthritis (OA), the most prevalent chronic arthritis, is a major cause of
26 musculoskeletal pain and years lost with disability. Usually, OA patients are advised to
27 avoid self-medication so that when severe pain ensues, it is not uncommon for them to
28 seek help in emergency care. However, people are currently being strongly encouraged
29 not to seek emergency treatment for fear of getting contaminated with SARS-Cov-2.^{13,14}
30 That is even more true for the elderly, which are exactly those most affected by
31 musculoskeletal “non-immune-mediated” diseases.¹⁴ Some guidance to those patients
32 would be helpful to decrease their demand for emergency care.

33
34 Besides a persistent inflammatory component,¹⁵ OA is also related to mechanical
35 derangement leading to joint failure affecting the cartilage, muscles, tendons, ligaments,
36 menisci and the subchondral bone.¹⁴ Although COVID-19 will virtually infect anybody, old
37 people are more severely affected, particularly those displaying comorbidities including
38 cardiovascular diseases, obesity, diabetes and chronic lung diseases.¹⁶ Obesity is a well-
39 defined risk factor in OA patients, who usually suffer from frailty both secondary to
40 reduced physical inactivity and ageing leading to sarcopenia which impacts respiratory
41 capacity. Cardiovascular risk is also enhanced among OA patients, being significantly
42 associated with the use of non-steroidal anti-inflammatory drugs (NSAIDs).¹⁷

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3 Patient education, information about the disease, stimulation of exercise programs,
4 weight control, nutritional orientation and mind-body exercises compose a core treatment
5 for knee, hip or polyarticular OA, regardless of comorbidities, in the recently updated
6 Osteoarthritis Research Society International (OARSI) guidelines.¹⁸ Actually, similar
7 recommendations have been advocated as a general rule in the management of immune-
8 mediated rheumatic diseases.¹⁹ Restoration of daily life activities may not be fully
9 implemented in the upcoming months, particularly for the elderly, which are the main
10 target to be protected from getting COVID-19. Unfortunately, this group of people, which
11 is heavily affected by OA, is less prone to physical activity.²⁰ Coincidentally, increased
12 age, higher body mass index (BMI), reduced physical activity and cardiovascular
13 diseases, which are more prevalent in the OA patient, have been associated with a worse
14 prognosis among COVID-19 patients. We may then envision that prolonged periods of
15 virtually complete physical inactivity will most likely worsen sarcopenia and frailty as well
16 as cardiovascular risk in OA patients. . .

17
18 A recent article has suggested home-based exercises rheumatic disease patients during
19 this pandemic, as a strategy to reduce their disease burden.²¹ An analysis of a meta-
20 analysis on the effect of exercise in knee OA was so clearly positive that concluded that
21 no further studies are needed to reinforce it.²² Details on the type of exercises that can
22 be performed by elderly people who are isolated because of covid19 have even been
23 published by the Centre for Evidence-Based Medicine at Oxford University based on a
24 systematic literature review (<https://www.cebm.net/covid-19/maximising-mobility-in-the-older-people-when-isolated-with-covid-19/>). Unfortunately, though commendable, such
25 physical practices are probably easier said than done. Actually, being inactive throughout
26 life carries a higher knee OA risk.²³ Adherence to self-exercise programs are very low
27 among those OA patients, questioning the efficacy of such guidances.²⁴ Why would we
28 believe patients will now adhere to home-based “spontaneous” physical activity,
29 especially experimenting a sort of segregation?

30
31 Usually, OA patients rely on pain killers even without a medical prescription.²⁵ That
32 theoretical perfect storm may lead elderly OA patients with movement restrictions to
33 increase NSAIDS use and the risk of a worse prognosis if they get infected by COVID-
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3 19. There are some questionable, though sometimes effective treatment options to
4 mitigate joint pain in OA patients.²⁶
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6 **Strategies for pain relief in OA patients during COVID-19 pandemic**

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8 Current OARSI guidelines¹⁸ have disregarded paracetamol as an effective pain killer in
9 OA. That was due to a very low effect size and safety issues with doses higher than 2 g
10 per day. At least during COVID-19, stimulating on demand usage of paracetamol up to
11 1.5 g daily may provide partial pain relief. That could be to combined to other strategies
12 including topical NSAIDs, which provide a better safety profile, although with
13 undocumented adherence. A recommendation to avoid NSAIDs was disseminated in the
14 media in the early weeks of the epidemy based on some experimental results²⁷. This
15 hypothesis has never been confirmed²⁷. However, a warning to avoid systemic NSAIDs
16 in OA patients with cardiovascular comorbidities exists independently of the epidemy.
17 Such medications can be obtained without a medical prescription, particularly in
18 developing countries. Let us not forget that NSAID use may account for over 40% of the
19 increased cardiovascular risk in OA patients.¹⁷ They should be used on demand, for the
20 shortest period possible, restricting to naproxen given its less deleterious cardiovascular
21 risk profile.²⁸
22

23 Psychological issues most commonly represented by depression carry a worse
24 phenotype prognosis in OA.²⁹ Duloxetine has been recommended in OA patients with
25 depression and widespread pain. The psychological burden to those patients will probably
26 increase in the isolated elderly. Hence, identifying the need for antidepressants might
27 help them cope with the disease. Psychological and/or psychiatric counseling should be
28 stressed as it can be provided using telehealth strategies.³⁰
29

30 Although access to non-urgent hospital facilities is restricted, intra-articular injections of
31 hyaluronic acid could be an interesting alternative, given the relatively long-term pain
32 relief they provide. That could also be said of intra-articular corticosteroids. Despite the
33 fear of the immunosuppressive effect of corticosteroids, usage in a non-infected patient
34 may provide up to 3 weeks pain relief thus reducing the need for systemic NSAIDs without
35 persistent immunosuppression.³¹ Considering the current situation of social isolation, we
36 believe opioids should not be used. Such drugs have been associated with fractures from
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3 falls³² and that risk would probably increase under opioid use given the increased frailty
4 due to persistent inactivity in COVID-19 days.
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6 The elderly OA patient must be seen in complete. Health care professionals (HCP) should
7 try to establish more frequent, even short, online visits as well as encourage social “online
8 gatherings” with family and friends. Adherence to healthy nutrition requirements, probably
9 with further calorie restriction, with attention on protein requirements in those with no
10 physical activity, should be emphasized. Although a high BMI is associated with a worse
11 scenario in knee OA outcome²⁹ weight reduction will be harder in the current pandemic.
12 Publications in social media conveying information that stigmatize weight gain as
13 inevitable may discourage attempts toward weight control.³³ That should not refrain
14 HCP from being proactive in counseling on preventing weight gain as less activity calls
15 for calorie restriction. As said above, psychological distress is expected to impact people.
16 Physical activity can be a favorable double-edged sword helping with both mental and
17 physical harms imposed by the “stay at home” norms.³⁴ Stimulation of the practice of
18 respiratory movements, avoiding being bedridden and long sitting periods is also a
19 prophylactic measure in the event of a respiratory infection. Prophylactic nebulizers with
20 no active drug help prevent mucus clot and strict adherence to cardiovascular and
21 metabolic treatment is a must in order to improve chances if COVID-19 comes. It is
22 noteworthy that some of these recommendations for OA patients can also be applied to
23 patients suffering from other types of RMDs, including immune-mediated ones.
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40 **Concluding remarks**

41 Not uncommonly, the rheumatologist is the physician most tightly linked to the elderly OA
42 patient with musculoskeletal diseases. Being proactive, such specialists might improve
43 our patient’s opportunities to tackle this pandemic. Notwithstanding, spreading similar
44 recommendations for HCP in the primary care setting would increase the number of
45 patients reached. A worsening of symptoms in OA patients after this confinement period
46 might be anticipated. Measures to mitigate this situation should not be overlooked, as
47 they involve both non-pharmacological and pharmacological approaches. In addition to
48 patients affected by immune-mediated rheumatic diseases the burden posed by other
49 musculoskeletal disorders cannot be disregarded.
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Box 1**Points to emphasize to the OA patient during COVID-19 pandemic**

Physical activity is a must need in OA patients, regardless of age;

Rheumatology Organizations should be stimulated to develop home-based supervised exercise programs

Keep physical distancing as long as needed;

Nutritional requirements should be adjusted to the degree of physical activity

NSAIDS should be taken with higher scrutiny

Opioids should be not taken

If indicated, consider Intra-articular steroids and Hyaluronic Acid in the appropriate setting

Psychological care includes medications and psychological/psychiatric counseling

Information should be disseminated to HCP in primary care

Box 2**Research Agenda**

Determine the impact of confinement on OA disability

Determine the loss of physical activity in OA patients during and after the confinement

Determine the impact of confinement on frailty in the OA elderly patient and its influence in mortality at the long term

Determine impact of confinement in OA according to phenotypes

Determine impact of confinement in spine OA pain and function

Determine safety of intra-articular injections in a home-care setting**References**

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12 issued guidances for managing such patients during this pandemic. ~~Some of these~~
13 ~~recommendations can also be applied to patients suffering from other types of RMDs,~~
14 ~~including immune-mediated.~~ However, ~~r,~~ recommendations on dealing with
15 patients affected by highly prevalent musculoskeletal diseases that are not considered to
16 be immune-mediated are lacking. Indeed, neck pain, low back pain, “other
17 musculoskeletal disorders” and falls account for 4 out of the top 10 causes of years lost
18 with disability worldwide.¹²

27 **Osteoarthritis management in COVID-19 days**

29 Osteoarthritis (OA), the most prevalent chronic arthritis, is a major cause of
30 musculoskeletal pain and years lost with disability. Usually, OA patients are advised to
31 avoid self-medication so that when severe pain ensues, it is not uncommon for them to
32 seek help in emergency care. However, people are currently being strongly encouraged
33 not to seek emergency treatment for fear of getting contaminated with SARS-Cov-2.^{13,14}
34 That is even more true for the elderly, which are exactly those most affected by
35 musculoskeletal “non-immune-mediated” diseases.¹⁴ Some guidance to those patients
36 would be helpful to decrease their demand for emergency care.

42 Besides a persistent inflammatory component,¹⁵ OA is also related to mechanical
43 derangement leading to joint failure affecting the cartilage, muscles, tendons, ligaments,
44 menisci and the subchondral bone.¹⁴ Although COVID-19 will virtually infect anybody, old
45 people are more severely affected, particularly those displaying comorbidities including
46 cardiovascular diseases, obesity, diabetes and chronic lung diseases.¹⁶ Obesity is a well-
47 defined risk factor in OA patients, who usually suffer from frailty both secondary to
48 reduced physical inactivity and ageing leading to sarcopenia which impacts respiratory

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3 capacity. Cardiovascular risk is also enhanced among OA patients, being significantly
4 associated with the use of non-steroidal anti-inflammatory drugs (NSAIDs).¹⁷

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6 Patient education, information about the disease, stimulation of exercise programs,
7 weight control, nutritional orientation and mind-body exercises compose a core treatment
8 for knee, hip or polyarticular OA, regardless of comorbidities, in the recently updated
9 Osteoarthritis Research Society International (OARSI) guidelines.¹⁸ Actually, similar
10 recommendations have been advocated as a general rule in the management of immune-
11 mediated rheumatic diseases.¹⁹ Restoration of daily life activities may not be fully
12 implemented in the upcoming months, particularly for the elderly, which are the main
13 target to be protected from getting COVID-19. Unfortunately, this group of people, which
14 is heavily affected by OA, is less prone to physical activity.²⁰ Coincidentally, increased
15 age, higher body mass index (BMI), reduced physical activity and cardiovascular
16 diseases, which are more prevalent in the OA patient, have been associated with a worse
17 prognosis among COVID-19 patients. We may then envision that prolonged periods of
18 virtually complete physical inactivity will most likely worsen sarcopenia and frailty as well
19 as cardiovascular risk in OA patients. .

20
21 A recent article has suggested home-based exercises rheumatic disease patients during
22 this pandemic, as a strategy to reduce their disease burden.²¹ An analysis of a meta-
23 analysis on the effect of exercise in knee OA was so clearly positive that concluded that
24 no further studies are needed to reinforce it.²² Details on the type of exercises that can
25 be performed by elderly people who are isolated because of covid19 have even been
26 published by the Centre for Evidence-Based Medicine at Oxford University based on a
27 systematic literature review (<https://www.cebm.net/covid-19/maximising-mobility-in-the-older-people-when-isolated-with-covid-19/>). Unfortunately, though commendable, such
28 physical practices are probably easier said than done. Actually, being inactive throughout
29 life carries a higher knee OA risk.²³ Adherence to self-exercise programs are very low
30 among those OA patients, questioning the efficacy of such guidances.²⁴ Why would we
31 believe patients will now adhere to home-based “spontaneous” physical activity,
32 especially experimenting a sort of segregation?

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34 Usually, OA patients rely on pain killers even without a medical prescription.²⁵ That
35 theoretical perfect storm may lead elderly OA patients with movement restrictions to

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3 increase NSAIDS use and the risk of a worse prognosis if they get infected by COVID-
4 19. There are some questionable, though sometimes effective treatment options to
5 mitigate joint pain in OA patients.²⁶
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8 **Strategies for pain relief in OA patients during COVID-19 pandemic**

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10 Current OARSI guidelines¹⁸ have disregarded paracetamol as an effective pain killer in
11 OA. That was due to a very low effect size and safety issues with doses higher than 2 g
12 per day. At least during COVID-19, stimulating on demand usage of paracetamol up to
13 1.5 g daily may provide partial pain relief. That could be combined to other strategies
14 including topical NSAIDS, which provide a better safety profile, although with
15 undocumented adherence. A recommendation to avoid NSAIDs was disseminated in the
16 media in the early weeks of the epidemic based on some experimental results²⁷. This
17 hypothesis has never been confirmed²⁷. However, a warning to avoid systemic NSAIDS
18 in OA patients with cardiovascular comorbidities ~~should be reinforced~~exists
19 independently of the epidemic. ~~S~~However, such medications can be obtained without a
20 medical prescription, particularly in developing countries. Let us not forget that NSAID
21 use may account for over 40% of the increased cardiovascular risk in OA patients.¹⁷ They
22 should be used on demand, for the shortest period possible, restricting to naproxen given
23 its less deleterious cardiovascular risk profile.²⁸⁷
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27 Psychological issues most commonly represented by depression carry a worse
28 phenotype prognosis in OA.²⁹⁸ Duloxetine has been recommended in OA patients with
29 depression and widespread pain. The psychological burden to those patients will probably
30 increase in the isolated elderly. Hence, identifying the need for antidepressants might
31 help them cope with the disease. Psychological and/or psychiatric counseling should be
32 stressed as it can be provided using telehealth strategies.³⁰²⁹
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36 Although access to non-urgent hospital facilities is restricted, intra-articular injections of
37 hyaluronic acid could be an interesting alternative, given the relatively long-term pain
38 relief they provide. That could also be said of intra-articular corticosteroids. Despite the
39 fear of the immunosuppressive effect of corticosteroids, usage in a non-infected patient
40 may provide up to 3 weeks pain relief thus reducing the need for systemic NSAIDs without
41 persistent immunosuppression.³¹⁰ Considering the current situation of social isolation, we
42 believe opioids should not be used. Such drugs have been associated with fractures from
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falls³²⁴ and that risk would probably increase under opioid use given the increased frailty due to persistent inactivity in COVID-19 days.

The elderly OA patient must be seen in complete. Health care professionals (HCP) should try to establish more frequent, even short, online visits as well as encourage social “online gatherings” with family and friends. Adherence to healthy nutrition requirements, probably with further calorie restriction, with attention on protein requirements in those with no physical activity, should be emphasized. Although a high BMI is associated with a worse scenario in knee OA outcome²⁹⁸ weight reduction will be harder in the current pandemic. Publications in social media conveying information that stigmatize weight gain as inevitable may discourage attempts toward weight control.³³² That should not refrain HCP from being proactive in counseling on preventing weight gain as less activity calls for calorie restriction. As said above, psychological distress is expected to impact people. Physical activity can be a favorable double-edged sword helping with both mental and physical harms imposed by the “stay at home” norms.³⁴³ Stimulation of the practice of respiratory movements, avoiding being bedridden and long sitting periods is also a prophylactic measure in the event of a respiratory infection. Prophylactic nebulizers with no active drug help prevent mucus clot and strict adherence to cardiovascular and metabolic treatment is a must in order to improve chances if COVID-19 comes. It is noteworthy that some of these recommendations for OA patients can also be applied to patients suffering from other types of RMDs, including immune-mediated ones. Some of these recommendations can also be applied to patients suffering from other types of RMDs, including immune-mediated.

Concluding remarks

Not uncommonly, the rheumatologist is the physician most tightly linked to the elderly OA patient with musculoskeletal diseases. Being proactive, such specialists might improve our patient’s opportunities to tackle this pandemic. Notwithstanding, spreading similar recommendations for HCP in the primary care setting would increase the number of patients reached. A worsening of symptoms in OA patients after this confinement period might be anticipated. Measures to mitigate this situation should not be overlooked, as

they involve both non-pharmacological and pharmacological approaches. In addition to patients affected by immune-mediated rheumatic diseases the burden posed by other musculoskeletal disorders cannot be disregarded.

Box 1

Points to emphasize to the OA patient during COVID-19 pandemic
Physical activity is a must need in OA patients, regardless of age;
Rheumatology Organizations should be stimulated to develop home-based supervised exercise programs
Keep physical distancing as long as needed;
Nutritional requirements should be adjusted to the degree of physical activity
NSAIDS should be taken with higher scrutiny
Opioids should be not taken
If indicated, consider Intra-articular steroids and Hyaluronic Acid in the appropriate setting
Psychological care includes medications and psychological/psychiatric counseling
Information should be disseminated to HCP in primary care

Box 2

Research Agenda
Determine the impact of confinement on OA disability
Determine the loss of physical activity in OA patients during and after the confinement
Determine the impact of confinement on frailty in the OA elderly patient and its influence in mortality at the long term

Determine impact of confinement in OA according to phenotypes

Determine impact of confinement in spine OA pain and function

Determine safety of intra-articular injections in a home-care setting

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Reviewer 1:**Comments to the Author**

Dear authors, thank you very much for addressing the questions and amending the text. I am happy to understand that you added a text that many of the remarks, and advices for OA patients also are of importance for patients with immune mediated RMDs. My suggestion is, however, to put such a remark at the end of paragraph "strategies for pain relief in OA patients during COVID-19 pandemic" Instead of in the paragraph on "guidelines on rheumatic diseases".

There is one additional remark: on page 6 line 10-11 (amended manuscript) NSAIDs are mentioned to lead to a risk of worse prognosis if the elderly get infected by COVID-19. This topic is now debated and controversial. So, please make this controversy more clear and support your statement with a reference (s).

We would like to thank reviewer 1 again for these positive comments.

- 1- We have moved the sentence as proposed.
- 2- With regard to NSAIDs, we did not address the issue of NSAIDs contraindication in the context of sars-cov2 infection but only the contraindication of NSAIDs in general in the cardiovascular setting. Nevertheless, as suggested, we now recall this controversy. We have added the following sentence:
« A recommendation to avoid NSAIDs was disseminated in the media in the early weeks of the epidemic based on some experimental results²⁷. This hypothesis has never been confirmed²⁷. However, a warning to avoid systemic NSAIDs in OA patients with cardiovascular comorbidities exists independently of the epidemic