


REVIEW ARTICLE OPEN ACCESS

Does COVID-19 Related Lockdown Restrictions Impact People With Musculoskeletal Disorders? A Systematic Review

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ABSTRACT

Background: As a result of coronavirus disease 2019 (COVID-19) related lockdown restrictions, people with musculoskeletal (MSK) disorders could be at increased risk of physical and psychological disabilities. This review aimed to summarise the impact of COVID-19 related lockdown restrictions on people with MSK disorders.

Methods: Six electronic databases were searched for studies in the English language published until June 10, 2024. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses to identify, select, and critically appraise relevant research. Two reviewers independently abstracted data from the included studies. Data were summarised using narrative synthesis, and the Newcastle–Ottawa Scale was used for quality assessment.

Results: The search strategy identified 637 articles, 129 of which were removed as duplicates. Fifteen studies that met the inclusion criteria were analysed. The sample size the studies reviewed ranged from 40 to 1800. Having MSK disorders during COVID-19 related lockdown restrictions led to increased risk of pain, stress, depression, anxiety, MSK related injuries, decreased quality of life and increased use of emergency department.

Conclusions: This is the first study to report that COVID-19 related lockdown restrictions led to increased risk of pain, MSK injuries and healthcare resource utilisation as well as decreased quality of life among patients with MSK disorders. These results may help inform policy and management strategies in future for people with MSK disorders to mitigate the negative impact of pandemic.

1 | Introduction

Coronavirus 2019 (COVID-19) was first reported in December 2019 as an outbreak in China (Zhu et al. 2020) and caused the severe acute respiratory syndrome–Corona Virus 2 (SARS-CoV2) (Giordano et al. 2021). COVID-19 later spread

worldwide, reaching a pandemic in March 2020. The COVID-19 pandemic public health preventive measures as well as lockdowns and stay-at-home orders led to unprecedented toll on healthcare services, as there were significant disruptions and re-prioritisation in healthcare resources and services (Hartnett et al. 2020), business closures, transition to working from home,

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and cessation of organised sports (Xiong et al. 2020), particularly among low-income countries (Nhamo et al. 2021). Changes in care delivery during the COVID-19 pandemic were largely associated with resource limitation or capacity strain (Anesi et al. 2021). As a result, many patients with chronic and long-term conditions such as musculoskeletal (MSK) disorders prior to COVID-19 received little or no services, especially in regions where the pandemic was prevalent (Anesi et al. 2021). While the selective use of digital interventions increased, particularly in developed countries as an aftermath of the pandemic, many patients still had limited access to the required healthcare (Mann et al. 2020).

The disruptions in access to essential care for non-COVID-19 infected patients were associated with significant morbidity and mortality (Robertson et al. 2020). While there are increasing empirical studies on the impact of COVID-19 related public health restriction measures among patients with terminal health conditions such as cancer (Baum et al. 2020; Maringe et al. 2020), there are still limited data on the impact of the pandemic on patients with non-life-threatening chronic conditions. MSK disorders are one of the most prevalent chronic conditions affecting many people globally before the start of COVID-19 pandemic. According to a World Health Organisation report, MSK disorders are the leading contributor to global disability burden, especially with low back pain as the single leading cause of disability based on reports from 160 countries (Liu et al. 2022). Also, based on a recent analysis of Global Burden of Disease (GBD) 2019 data, approximately 1.71 billion worldwide live with MSK disorders (Cieza et al. 2021). In the United States alone, over 61 million MSK injuries were treated in health-care centres, of which the greatest single group involves injuries to tendons or ligaments, namely sprains, strains, and ruptures (Riggin, Morris, and Soslowsky 2015).

Individuals with MSK disorders could have been negatively impacted by COVID-19 restriction measures. According to a report by RAND Europe (2023), rates of self-reported work-related MSK disorders (WRMSDs) declined prior to the COVID-19 pandemic. However, restriction measures which required changes to working practices and environments at individual, organisational and national levels to curb the spread of the infection may have increased exposure to known WRMSD risk factors as well (RAND Europe 2023). As a result of the COVID-19 pandemic, significant delays to patient's care have been observed particularly in orthopaedic surgery (Bram et al. 2020; Gumina et al. 2020). Limited healthcare resources and capacity strain imply that all but the most urgent of non-COVID care would have to be cancelled, including treatments for many MSK disorders. Also, concerns for increased COVID-19 exposure may have led to reluctance for patients to seek medical care during the pandemic (Ciacchini et al. 2020).

Social isolation and social distance recommendations by World Health Organisation were aimed at minimising the spread of SARS-CoV-2 (Ruiz-Roso et al. 2020). Simultaneously, restriction imposed due to the pandemic led to an increase of sedentary behaviour (Alomari, Khabour, and Alzoubi 2020). Overall, the important changes in the lifestyle of people and reduction of 40%–60% of time spent in engaging in physical activity

(Castañeda-Babarro et al. 2020) may also have raised the likelihood of having high risk factors of MSK disorders. In a previous systematic review, Gebrye et al. (2023) observed that COVID-19 related lockdown restrictions led to increased MSK disorders in the general population. However, the review by Gebrye et al. (2023) was on apparently healthy general population and not individuals with pre-existing MSK disorders prior to the pandemic. A number of studies exist on the impact of COVID-19 related lockdown restrictions in people with MSK disorders. However, to date, there are no studies that have summarised the literature on the impact of COVID-19 related lockdown restrictions in people with MSK disorders. Therefore, this study synthesised evidence on the impact of COVID-19 related lockdown restrictions on people who already had MSK disorders prior to the pandemic.

2 | Methods

We searched for published articles using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Liberati et al. 2009) in this systematic review. A protocol for this systematic review was prospectively registered on PROSPERO and can be found at https://www.crd.york.ac.uk/PROSPERO/display_CRD:42024555069.

2.1 | Data Sources and Search Strategy

Searches were performed to retrieve studies that were published in peer-reviewed journals until June 10, 2024. The following databases were used: MEDLINE, CINAHL, PsycINFO, Web of Science, and Scopus, and Allied and Complementary Medicine Database (AMED) and Google Scholar. The searches were combinations of COVID-19 or coronavirus or 2019-ncov or sars-cov-2 or cov-19, MSK disorders, musculoskeletal problems, impact on pain severity, quality of life, productivity, economic, and healthcare resource utilisation. Then, these searches were combined with the conjunctions of 'AND' & 'OR'. The search was delimited to articles published in the English language. References of the included studies were performed for any studies we missed during the electronic search.

2.2 | Inclusion and Exclusion Criteria

The inclusion criteria were as follows: studies on people with MSK disorders (>18 years of age, no restriction of sex, and race) including injuries or disorders of the joints, tendons, muscles, nerves, spinal disc, and cartilage; the condition being considered was MSK disorders, and the intervention was COVID-19 related lockdown restrictions. We included cross-sectional survey studies, cohort studies, case controlled, prospective studies and retrospective studies. The exclusion criteria were as follows: studies that had reviews, editorials, conference papers, case reports or series studies, and animal experiments.

2.3 | Study Selection and Assessment of Methodological Quality

Following removal of duplicates, two reviewers (T.G. and C.M.) independently screened titles, abstracts, and full-text articles to decide whether an article was relevant to the review. Any difference was resolved by discussion and consensus with the third reviewer (F.F.). The quality assessment of the risk of bias of the included studies was evaluated using the Newcastle–Ottawa quality assessment scale (Stang 2010). This instrument includes three domains: selection, comparability and outcomes. The selection domain is composed of four items, comparability of one item, and outcomes of three items. The article could receive one star in each item, receiving a maximum of four stars in selection, one or two in comparability, and three in outcomes. Studies were scored using a scale with a possible maximum of nine points where a score ≥ 7 indicated low, a score between 5 and 6 indicated moderate and a score ≤ 5 stars indicated high risk of bias with an overall quality score of 9 stars.

2.4 | Data Extraction

Excel data sheets were used to extract the data from the included studies. The following data were extracted from each eligible article: author, country, study design, sample size, outcome, outcome measure and results or key findings. Data extraction and determination of information eligibility were conducted by two reviewers (T.G. and C.M.) independently following the criteria above, while discrepancies were resolved by consensus or with a third reviewer (F.F.), as appropriate.

2.5 | Data Synthesis

Findings from the studies were summarised by one reviewer (T. G.), while the research team (F.F., C.M., C.F. and J.L.) provided

modifications and discussion as necessary in order to generate evidence on the impact of COVID-19 related lockdown restrictions on MSK disorders.

3 | Results

The searches generated 637 (284 records in MEDLINE, EMBASE, AMED, CINAHL, and PsycINFO, 156 records in Web of Science, 197 records in Scopus) studies. A total of 129 articles were duplicated. After reviewing their titles and abstracts, 438 studies were excluded. A total of 70 potentially relevant records were retrieved for detailed full-text evaluation. Finally, 15 articles met the selection criteria and were deemed to contain data relevant to the systematic review. A further updated search yielded two new additional articles. A flowchart detailing the results of the literature selection process is shown in Figure 1.

3.1 | Study Quality Assessment

All 15 studies were assessed using the Newcastle–Ottawa Scale and can be found in Table 1. After assessing the study quality by the Newcastle–Ottawa scale, six studies received a quality score of 8, six studies received a quality score of 7 and the remaining three studies (Chatkoff et al. 2022; Johnson et al. 2021; MacDonald et al. 2020) received a quality score of 6.

3.2 | Study Population and Sample Size

The 15 included studies originated from seven countries and contained 11,316 MSK disorder patients (Table 2). The included studies were conducted in France (Crenn et al. 2020), India (Dahuja et al. 2021; Rathi et al. 2021), Italy (Longo et al. 2022; Marotta et al. 2021; Pasta et al. 2022; Tarantino et al. 2021), Turkey (Yalçinkaya, Kirmizi, and Şengül 2022), Spain (Garrido-

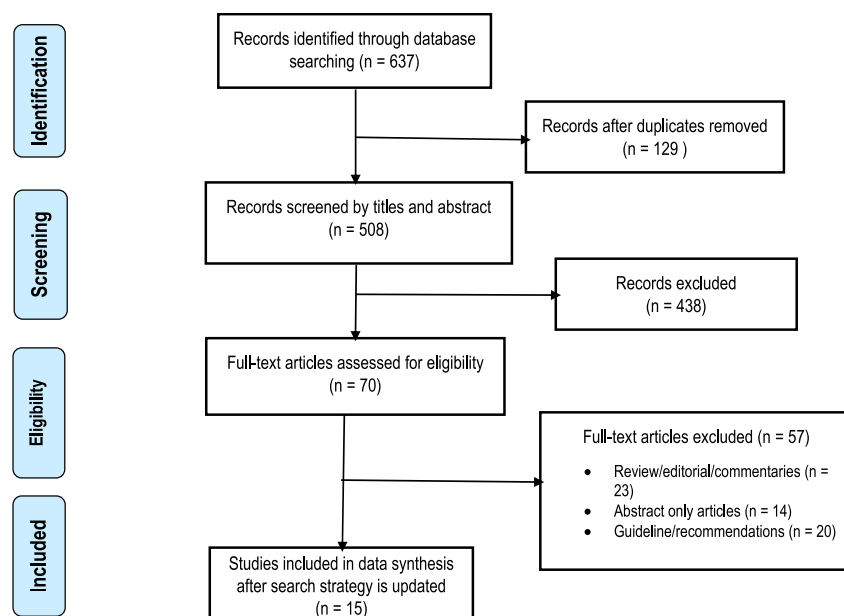


FIGURE 1 | Flow diagram of publications included and excluded in the review.

TABLE 1 | Quality assessment of the included studies.

Reference, year	Quality assessment criteria			
	Selection	Comparability	Exposure (outcome)	Overall quality
Chatkoff et al. (2022)	****	*	*	6
Crenn et al. (2020)	****	*	**	7
Dahuja et al. (2021)	****	**	**	8
Garrido-Cumbrera et al. (2021)	****	**	**	8
Johnson et al. (2021)	****	*	*	6
Longo et al. (2022)	****	**	**	8
Macfarlane et al. (2021)	****	*	**	7
MacDonald et al. (2020)	****	*	*	6
Marotta et al. (2021)	****	*	**	7
Pasta et al. (2022)	****	*	**	7
Rathi et al. (2021)	****	*	**	7
Santos-Ruiz et al. (2021)	****	*	**	7
Smith et al. (2021)	****	**	**	8
Tarantino et al. (2021)	****	*	***	8
Yalçinkaya, Kirmizi, and Şengül (2022)	****	**	**	8

Note: See Table A1 for quality assessment criteria.

Cumbrera et al. 2021; Santos-Ruiz et al. 2021), UK (MacDonald et al. 2020; Macfarlane et al. 2021; Tarantino et al. 2021) and United States of America (Chatkoff et al. 2022; Johnson et al. 2021). The sample size of the populations studied ranged from 40 to 1800 participants.

All included studies were cross-sectional in nature and did not follow participants over time. Six studies used survey method (Chatkoff et al. 2022; Garrido-Cumbrera et al. 2021; Longo et al. 2022; Macfarlane et al. 2021; Santos-Ruiz et al. 2021; Tarantino et al. 2021), while five studies used a retrospective design (Crenn et al. 2020; Dahuja et al. 2021; Johnson et al. 2021; Marotta et al. 2021; Pasta et al. 2022). The remaining studies were based on case controlled (Tarantino et al. 2021) and prospective design (MacDonald et al. 2020).

3.3 | Overall Study Results

In comparison with previous (pre-pandemic) assessment, there was a small decrease in quality of life (QoL) measured by EQ-5D [-0.020 (95% CI $-0.030, -0.009$)] in people with MSK disorders during COVID-19 related lockdown restrictions (Macfarlane et al. 2021). During the lockdown restrictions, pain experienced by people with MSK disorders worsened (Chatkoff et al. 2022; MacDonald et al. 2020; Longo et al. 2022; Smith et al. 2021; Tarantino et al. 2021; Yalçinkaya, Kirmizi, and Şengül 2022). On the other hand, a significant decline (Johnson et al. 2021; Marotta et al. 2021) and increment (Crenn et al. 2020; Dahuja et al. 2021) of MSK injuries were observed for patients with sport injury and in those treated at the emergency department, respectively. Individuals with MSK disorder have experienced disruption in access to healthcare services (Garrido-Cumbrera et al. 2021; Pasta et al. 2022). Compared to men, women had worsening of chronic pain experience (Chatkoff et al. 2022).

4 | Discussion

To our knowledge, this is the first systematic review of the impact of COVID-19 related lockdown restrictions on people with MSK disorders. Exclusively, studies that assessed the impact of COVID-19 related lockdown restrictions on individuals with MSK disorders were reviewed. The quality of the included studies was assessed as low risk of bias. The results of the systematic review indicate that people with MSK disorders had increased risk of pain intensity, reduced QoL, and increased prevalence of MSK injuries as a result of COVID-19 related lockdown restrictions. In addition, the results suggest that there was a considerable increase in emergency department visits by patients with MSK disorders. In contrast, the incidence of muscle injuries did not significantly change after the first COVID-19 lockdown in Italian professional soccer players (Marotta et al. 2021).

A decrease in quality of life was observed during the period of public health restrictions in the UK due to COVID-19 compared to before the pandemic on patients with MSK disorders (Macfarlane et al. 2021). The contributing factors to the poor quality of life in people with MSK disorders may be related to higher levels of anxiety around the pandemic and concerns about health. Similar findings were reported for gout-specific health-related quality of life during COVID-19 related lockdown restrictions in a cross-sectional internet survey (Singh et al. 2022). These results may provide some lessons that in the absence of healthcare services, addressing anxiety is crucial for future similar situations.

With regard to the association between MSK injuries and sports, it was observed that there was a significant decline in MSK injuries during COVID-19 related lockdown restrictions (Johnson et al. 2021; Marotta et al. 2021). The majority of injuries were

TABLE 2 | Characteristics of studies included in the systematic review.

Author/ country	Study design	Sample size, age (mean/range)	Study endpoint	Outcome measure	Results	Comment
Chatkoff et al. (2022)/USA	Survey	487 self-reported patients with MSK, neuropathic, or postsurgical pain	Pain severity/functional impact	A 53-item survey	Average pain severity with 62.4% of patients reporting a little more or notably more pain and 5.3% reporting a little less or notably less change in average pain since the pandemic onset	A pandemic-related general worsening of the chronic pain experience with a more deleterious impact to women, relative to men
Macfarlane et al. (2021)/UK	Survey	1054 (596 axial spondyloarthritis; 162 psoriatic arthritis; 296 regional pain)	Quality of life (EQ-5D- 5L), sleep problems, quantitative measurement of fibromyalgia symptoms	Nordic MSK Questionnaire	A significant ($p = -0.009$) small decrease in quality of life measured by EQ-5D [-0.020 (95% CI -0.030)]	Only a small average decrease in quality of life by people with MSK disorders
Santos-Ruiz et al. (2021)/ Spain	Cross-sectional study (questionnaire)	428 women with SLE, with a mean age of 41.83 (SD = 11.29)	Stress levels, depression, anxiety, phobic anxiety, interpersonal sensitivity, and psychotacticism	#Perceived Stress Scale, the Stress #Vulnerability Inventory and #Psychopathological symptoms of the SCL-90- R Symptom Inventory	Statistically significant differences in vulnerability to stress, depression, anxiety, phobic anxiety, interpersonal sensitivity, and psychotacticism	The lock down and threat of the COVID-19 outbreak had important repercussions on the psychological state of patients with SLE
Yalçınkaya, Kirmizi, and Şengül (2022)/ Turkey	Case-control study	#156 spinal pain (Spinal pain group ($n = 70$, mean (SD) = 29.17 (9.26)) #Asymptomatic group ($n = 86$), #Mean (SD) = 31.57 (10.86))	Physical activity, health anxiety, and spinal pain history in people experiencing	#Nordic MSK Questionnaire (NMQ), #International Physical Activity Questionnaire- Short Form, #The Short Health Anxiety Inventory	The percentage of people who experienced spinal pain was higher	People experiencing spinal pain during the COVID-19 lockdown were physically less active and more concerned about their health
Longo et al. (2022)/Italy	Survey (questionnaire)	110 participants with lumbar and/or cervical spine pain	Spine pain	The Neck Disability Index Questionnaire (NDIQ) or the Roland and Morris Disability Questionnaire (RMDQ)	#The age group most affected by spinal pain is between 41 and 60 years #Pain increased due to the lockdown period	The majority of participants perceived their spine pain was having arisen or increased during the lockdown period

(Continues)

TABLE 2 | (Continued)

Author/ country	Study design	Sample size, age (mean/range)	Study endpoint	Outcome measure	Results	Comment
Marotta et al. (2021)/Italy	Retrospective study	234 injuries	The epidemiology of muscle injuries	Severity of injuries were assessed according to Union of European Football Associations (UEFA)	Pre-lockdown: 16.9 [13.0–20.7], Post-lockdown: 15.5 [9.9–21.1]	The incidence of muscle injuries has not significantly changed after the first COVID- 19 lockdown in Italian professional soccer players
Smith et al. (2021)/UK	Mixed-methods (online longitudinal survey and embedded qualitative study)	703 people with rheumatic and MSK diseases	#Disability and symptom status including: Pain, fatigue, sleep and anxiety. #Short assessment of social isolation	#Clinical Health Assessment Questionnaire12 to assess disability and symptom status including: Pain, fatigue, sleep and anxiety #The Lubben Social Network Scale 613 #University of California, Los Angeles three-item loneliness scale #Six-item Brief Resilience Scale #Revised Life Orientation Test	#52% reported increase #6% reported a decrease #The greatest change in daily life was experienced by those in employment	People with rheumatic and musculoskeletal diseases reported a deterioration in symptoms when COVID-19 pandemic social restriction
Tarantino et al. (2021)/Italy	Survey	#40 (M = 28, F = 12) patients with MSK disorders #Age range was 42– 82 years	Patients with MSK disorders receiving infiltrative treatment	Structuralised questionnaire	#83.3% noticed increased pain and stiffness in the joint. #Patient's QoL was reduced by 61.66 ± 15.72%	A significantly worsen the physical condition of subjects with MSK disorders
Crenn et al. (2020)/ France	Retrospective study	Prelockdown (n = 1661) Lockdown (early lockdown n = 646, late lockdown n = 942) MSK injuries	#MSK injuries treated at the emergency department as well as the surgical indications	MSK injury: Defined by the ICD-10 classification and cross-checked with injury admissions patterns	#There was a 52.1% decrease in MSK injuries among patients presenting to the emergency department #Increase in the incidence of surgical high severity trauma (Injury Severity Score > 16)	The proportion of MSK injuries have increased

(Continues)

TABLE 2 | (Continued)

Author/ country	Study design	Sample size, age (mean/range)	Study endpoint	Outcome measure	Results	Comment
Dahuja et al. (2021)/ India	Retrospective cross-sectional study	291 patients presenting with MSK injuries to the Trauma Unit	#The pattern of injury over a period of 2 months	Data was extracted for patient's age and sex, mode of injury, and site of injury from the case records	#MSK injuries increased by 23.4% in 2020 #Lower limbs and upper limbs (contributing up to 85%)	The proportion of MSK injuries have increased
Garrido- Cumbrera et al. (2021)/ Spain	A cross-sectional study using an online survey	#1800 patients with rheumatic and MSK diseases (RMDs) #Mean age was 53, and 80% female	Healthcare access, daily activities, disease activity and function, well-being health status, anxiety/ depression and access to information were evaluated	#The WHO Five Well- Being Index (WHO-5): #Hospital Anxiety and Depression Scale #Visual Analogue Scale (VAS) for disease activity and Patient Acceptable Symptom Scale	#Self-reported disease activity was high (5.3 ± 2.7) and 75.6% reported elevated pain #Half the patients (49.0%) reported poor well-being (WHO-5) and 46.6% that their health had changed for the worse during lockdown	Patients with RMDs have experienced disruption in access to healthcare services, poor lifestyle habits and negative effects on their overall health, well-being and mental health
Johnson et al. (2021)/USA	Retrospective cohort study	#1455 patients with injuries #12.1 ± 4.5 years	Paediatric MSK injuries associated with sports	Based on review of emergency department and outpatient clinic records for first-time presentations	#The most common presenting injury was ankle sprains (47.8%), and the least common was tibial spine fractures (1.4%) #A decrease in the proportion of injuries attributed to sports (48.8% vs. 33.3%; $p < 0.001$) and those occurring at school (11.9% vs. 4.0%; $p = 0.001$) was observed	A significant decline in paediatric MSK injuries associated with sports during the COVID-19 pandemic was observed

(Continues)

TABLE 2 | (Continued)

Author/ country	Study design	Sample size, age (mean/range)	Study endpoint	Outcome measure	Results	Comment
MacDonald et al. (2020)/UK	Prospective study	1315 patients received operative treatment from March 23, 2020 to May 28, 2020 compared with 1791 in 2019 and 1719 in 2018 (MSK trauma requiring operative treatment)	#Rates, types, mechanisms, and mortality of MSK trauma	Injuries sustained were categorised according to six anatomical regions	#All injury types decreased #Hip fractures increased (36.3% in 2020 vs. 30.2% in 2019, and 30.7% in 2018) #Cycling injuries increased	Marked reduction in MSK trauma patients undergoing surgery in Scotland
Rathi et al. (2021)/ India	Cross-sectional study (questionnaire)	#1040 (90% females) SLE patients #Mean age was 27.5 ± 19.1 years	#Incidence of COVID- 19, access to health care professionals and availability of medicines, adherence, fear of COVID-19	Patient global assessment	Financial difficulty, problems in getting their prescribed medicines, none of the patients developed COVID-19 infection, and spent more money on health during the pandemic	COVID-19 pandemic has made a huge impact on our SLE patients
Pasta et al. (2022)/Italy	Retrospective and prospective study	542 patients with MSK disorders	Non-traumatic or low- severity MSK disorders access to care	Modalities of access between the 2019 and 2020 cohorts	A total of 87.30% of patients presenting to the emergency department with a MSK disorders followed their general practitioner's advice/referral in 2019, and 73.87% did so in 2020	An inappropriate use of the emergency department related to patients with MSK disorders

Abbreviations: EQ-5D-5L = five level version of the EuroQol 5 dimensions (EQ-5D-5L); MSK = musculoskeletal; QoL = Quality of life; SCL-90-R = The Symptom Checklist-90-Revised; SLE = Systemic Lupus Erythematosus; UK = United Kingdom; USA = United States of America; WHO = World Health Organisation.

most likely attributable to increased involvement in competitive sports (Apostolovic et al. 2011; Atkin et al. 2000). Reduction of injuries during COVID-19 related lockdown restrictions resulted in decreased organised sports. The most important finding of the current study was that the type of sports that continued to cause injuries to children during the pandemic were basketball and soccer. Continued education on how best to protect players by medical providers and parents remains important (Childrens Hospital of Richmond at VCU 2020).

This systematic review has some strengths and limitations. This review employed strict criteria in the final selection of the searched literature and implemented procedures to ensure high-quality implementation of the methodology. The reviewers followed a protocol to perform the data extraction, data analysis, and quality assessment of the methods of the included systematic reviews. The search was limited to journal articles published in English. Therefore, it is possible that relevant literature published in other languages may have been excluded. It was not possible to undertake a meta-analysis for the included studies due to the adoption of different outcomes and did not present mean or standard deviation (SD) for the outcomes (Higgins et al. 2011). Despite these limitations, the present systematic review provides a valuable summary of the impact of COVID-19 related lockdown restrictions in people with MSK disorders.

5 | Conclusions

COVID-19 related lockdown restrictions led to increased risk of pain, MSK injuries and healthcare resource utilisation as well as decreased quality of life among patients with MSK disorders. This is an interesting finding given the negative impact of the pandemic. These results may inform policy and management strategies in future for people with MSK disorders to mitigate the negative impact of pandemic.

Author Contributions

T.G., C.M. and F.F. contributed to the study design, data collection, interpretation of results, and drafting the manuscript. All authors conceived, designed, analysed the data, and interpreted the results of the work. All authors approved the final version of this manuscript.

Ethics Statement

The authors have nothing to report.

Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data generated or analysed during this study are included in this published article. Please contact Professor Francis Fatoye if you have any queries regarding this study.

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Appendix A

TABLE A1 | Quality assessment checklist for nonrandomized studies.

Domain	Checklist criteria	Additional information
Selection	1. Is the case definition adequate? a. yes, with independent validation* b. yes, for example, record linkage or based on self-reports c. no description	Assumption: Given the nature of the review, studies received a star if they discuss representation (and reasons for their study being representative) or if they are multicentre/regional/national Assumption: It was assumed that if the study was in a hospital setting in which cases were hospital patients, hospital controls were accepted Assumption: History of disease/infection was used in this criteria even in studies looking at mortality or other burden outcomes 2 * maximum allotted for this criteria Assumption: For studies in which hospital associated cases and LoS were being analysed, two stars were only given if time dependency was controlled for Assumption: Studies which utilised lab techniques were used to ascertain exposure received one star
	2. Representativeness of the cases a. consecutive or obviously representative series of cases* b. potential for selection biases or not stated	
	3. Selection of controls a. community controls* b. hospital controls c. no description	
	4. Definition of controls a. no history of disease (endpoint)* b. no description of source	
Comparability	1. Comparability of cases and controls on the basis of the design or analysis a. study controls for age/sex/comorbidities* b. study controls for any additional factor*	
Exposure	1. Ascertainment of exposure a. secure record (e.g., surgical records)* b. structured interview where blind to case/control status* c. interview not blinded to case/control status d. written self-report or medical record only e. no description	
	2. Same method of ascertainment for cases and controls a. yes* b. no	
	3. Non-response rate a. same rate for both groups* b. non respondents described c. rate different and no designation	Assumption: No description of data cleaning or linkage and loss to missing data for retrospective studies was penalised by not awarding a star