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Increased Prolonged Sitting in Patients with Rheumatoid Arthritis during the COVID-19 Pandemic: A Within-Subjects, Accelerometer-Based Study

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Abstract: Background: Social distancing measures designed to contain the COVID-19 pandemic can restrict physical activity, a particular concern for high-risk patient groups. We assessed rheumatoid arthritis patients' physical activity and sedentary behavior level, pain, fatigue, and health-related quality of life prior to and during the social distancing measures implemented in Sao Paulo, Brazil. Methods: Post-menopausal females diagnosed with rheumatoid arthritis were assessed before (from March 2018 to March 2020) and during (from 24 May to 7 July 2020) social distancing measures to contain COVID-19 pandemic, using a within-subjects, repeated-measure design. Physical activity and sedentary behavior were assessed using accelerometry (ActivPAL micro). Pain, fatigue, and health-related quality of life were assessed by questionnaires. Results: Mean age was 60.9 years and BMI was 29.5 Kg/m^2. Disease activity ranged from remission to moderate activity. During social distancing, there were reductions in light-intensity activity (13.0% [−0.2 h/day, 95% CI: −0.4 to −0.04; $p = 0.016$]) and moderate-to-vigorous physical activity (38.8% [−4.5 min/day, 95% CI: −8.1 to −0.9; $p = 0.015$]), but not in standing time and sedentary time. However, time spent in prolonged bouts of sitting ≥30 min increased by 34% (1.0 h/day, 95% CI: 0.3 to 1.7; $p = 0.006$) and ≥60 min increased by 85% (1.0 h/day, 95% CI: 0.5 to 1.6). There were no changes in pain, fatigue, and health-related quality of life (all $p > 0.050$). Conclusions: Imposed social distancing measures to contain the COVID-19 outbreak were associated with decreased physical activity and increased prolonged sedentary behavior, but did not change clinical symptoms sitting among patients with rheumatoid arthritis.

Keywords: sedentary behavior; physical activity level; inflammatory arthritis; pain; fatigue; health-related quality of life

1. Introduction

A preliminary, multinational survey reporting step counts provided by smartphones showed that social distancing measures to contain the spread of SARS-CoV-2 have induced physical inactivity (i.e., not meeting the physical activity guidelines) [1]. The onset of the

coronavirus disease 2019 (COVID-19) pandemic has placed further spotlight on participation in sedentary behavior (i.e., time spent in a sitting or reclining posture with a low energy expenditure [≤1.5 METs]), with reported increases in daily sitting time from pre-pandemic levels ranging from 30 min up to 3 h in different populations [2,3].

Extensive epidemiological evidence has indicated that physical inactivity is a major risk factor for early mortality and chronic diseases, including obesity, type 2 diabetes, cardiovascular diseases, metabolic syndrome, certain type of cancers, and others [4]. Even though time spent in moderate-to-vigorous intensity physical activity has the strongest detrimental associations with health outcomes [5–7], similar (albeit, detrimental) relationships have been broadly observed for excessive time in sedentary behaviors [7–16]. Importantly, both total sitting time and prolonged, uninterrupted sitting time are associated with increased risk of all-cause mortality even after consideration of the influence of participation in moderate-to-vigorous intensity physical activity [7,8,17]. Moreover, the deleterious associations of sedentary behavior with cardiometabolic risk and all-cause mortality are most pronounced in those who are physically inactive [6,11,18–20].

Rheumatoid arthritis is a rheumatic autoimmune disease characterized by chronic inflammation, pain, and physical disability [21]. Clinical disease symptoms can include joint pain, swelling, stiffness, and deformity, fatigue, muscle weakness, and reduced physical functioning [22,23]. Patients with rheumatoid arthritis have a higher risk of morbidity and mortality from cardiovascular diseases [24]. This increased risk can be at least partially explained by the complex interplay between chronic inflammation, adverse effects of drugs, associated comorbidities (e.g., dyslipidemias, insulin resistance, hypertension), and lifestyle [25,26]. Despite physical activity being advocated as an integral part of disease standard care [27], physical inactivity and sedentary behavior are highly prevalent among patients with rheumatoid arthritis [28].

Physical inactivity and sedentary behavior are modifiable risk factors considered to be potential targets to prevent morbimortality in autoimmune rheumatic diseases [28,29]. Among patients with rheumatoid arthritis, sedentary behavior is associated with higher disease scores, increased pain, fatigue [30] and number of comorbidities, reduced aerobic capacity [31] and physical function [30], and poor self-efficacy [32]. Furthermore, physically inactive patients with rheumatoid arthritis exhibit higher cardiovascular risk factors (e.g., higher systolic blood pressure and homeostasis model assessment (HOMA) index, abnormal lipid profile) when compared to their physically active counterparts.

Patients with rheumatoid arthritis have been shown to be more susceptible to COVID-19 infection [33] and, therefore, may be subjected to more restrictive measures of social distancing, potentially with significant impacts on their activity options, and, hence, on their burden of cardiovascular disease risk, the main cause of mortality in this population [26].

In this prospective study using a within-subjects design, we assessed physical activity and sedentary behavior levels using accelerometers in patients with rheumatoid arthritis prior to and during the imposed measures of social distancing to combat COVID-19 in Sao Paulo, Brazil. Additionally, we have assessed whether potential changes in physical activity and sedentary behavior levels would be associated with changes in pain, fatigue, and health-related quality of life.

2. Materials and Methods

2.1. Participants

Sixty-four patients diagnosed with rheumatoid arthritis were recruited from the Outpatient Rheumatoid Arthritis Clinic of the Clinical Hospital (School of Medicine, University of Sao Paulo) between March 2018 and March 2020 to participate in a randomized controlled trial (clinicaltrials.gov: NCT03186924). Thirty-five out of 64 patients with rheumatoid arthritis accepted to participate in this ancillary study.

Post-menopausal female patients diagnosed with rheumatoid arthritis, according to American College of Rheumatology European League against rheumatism collaborative initiative revised criteria [34], were recruited directly from the Rheumatoid Arthritis Outpa-

tient Clinic of the Rheumatology Division. The exclusion criteria included: (1) participation in structured exercise training programs within the last 12 months; (2) unstable drug therapy in the last 3 months prior to and during the study; (3) Health Assessment Questionnaire score >2.0 (i.e., severe to very severe physical impairment).

This trial was approved by the local ethical committee (Commission for Analysis of Research Projects, CAPPesq; protocol code: 58340316.0.0000.0068; approval number: 1.735.096). Patients signed an informed consent form before participation in the study.

2.2. Experimental Design

All patients with rheumatoid arthritis had been through a clinical and physical activity assessment before the official set of social distancing measures to contain the COVID-19 outbreak, adopted on the 24 of March 2020. This facilitated the unique opportunity to track physical activity levels during the pandemic in a within-subjects, repeated measure design. We then obtained a new approval from the ethics committee for collecting data during the social distancing. Three members of our staff (DR, SMS, KM) delivered the accelerometers (ActivPAL micro™, PAL Technology, Glasgow, UK) and questionnaires to the patients at home from the 24 May to 7 July. The time elapsed for data collection between baseline and during social distancing was 12.5 months (9.9, 15.2). Patients were asked if they had adhered to the social distancing measures. All but two responded affirmatively. Data were assessed with and without the two non-compliers, and results remained the same. Thus, we reported the full data in this manuscript.

2.3. Physical Activity Level

Physical activity level was measured using activPAL micro™ (PAL Technology, Glasgow, UK) activity-based accelerometers before and during social distancing. Patients wore the accelerometer for 7 consecutive days (24 h/day), which was fitted using tape (3M, Tegaderm®, adhesive tape) on the right medial front thigh, orientated with the x-axis pointing downward, y-axis horizontally to the left and z-axis horizontally forward. Data were exported and analyzed using ActivPAL3™ software, version 8.10.9.46 (PAL Technology, UK). Data was checked by an experienced researcher and also crosschecked with a sleep diary. All data were standardized to a 16-h day in order to avoid bias from differences in patients' wear time, by the formula: (data × 16)/wear time. Data were reported as follows: time spent sitting and lying (h/day), in prolonged sitting (h/day), standing (h/day), stepping (h/day), time spent in light-intensity physical activity (step cadency <100 steps/min [35]), time spent in moderate-to-vigorous intensity physical activity (step cadence of ≥100 steps/min [35]), and number of sit to stand (i.e., breaks) in time spent in sedentary behavior.

2.4. Clinical Assessment

Clinical characteristics were assessed at baseline, before the set of social distancing, Disease activity was assessed by the Disease Activity Score in 28 joints (DAS28 PCR) [36] and Clinical Disease Activity Index (CDAI) [37], in which higher scores represent more severe disease activity. The Health Assessment Questionnaire (HAQ) [38], which evaluates physical functioning in eight domains of daily life, was also used; higher scores represent greater physical disability. Disease duration, presence of comorbidities (e.g., hypertension, dyslipidemia, type 2 diabetes, depression, and other rheumatic diseases), current dose of prednisone, current use of biological agents (e.g., anti-TNF, anti-IL6, anti-IL1, B-cell depleting agents, and T-cell activation inhibitors), non-biological disease-modifying anti-rheumatic drugs (e.g., methotrexate and leflunomide), and other medications (i.e., anti-inflammatory drugs, pain killers, antihypertensive drugs, antihyperlipidemic drugs, antidiabetic drugs, and anti-depressants) were obtained by reviewing medical records and interviewing patients with rheumatoid arthritis. Blood samples (~10 mL) were collected after a 12-h overnight fast for measuring the following parameters: C-reactive protein and erythrocyte sedimentation rate. Samples were collected in vacutainer tubes

and subsequently analyzed at the Clinical Hospital Central Laboratory (School of Medicine, University of Sao Paulo). C-reactive protein was determined by immunoturbidimetry. Erythrocyte sedimentation rate was assessed using an automated analyzer.

Pain, fatigue, and health-related quality of life were assessed before and during social distancing. Pain was assessed by the Visual Analogic Scale [39], in which patients graded their pain using a 10-point scale; zero means no pain and 10 means severe or unbearable pain. Fatigue was assessed by the Fatigue Severity Scale [40], in which scores range from 9 to 63; lower scores indicate lower fatigue. Physical and mental health-related quality of life were assessed by the 36-Item Short Form Survey (SF-36) questionnaire [41], in which scales (physical health: physical function, role-physical, bodily pain, and general health; mental health: vitality, social function, and role-emotional) range from 0 to 100; higher scores indicate better quality of life.

2.5. Statistical Analysis

Dependent variables were tested using repeated measures mixed models, with time (Before social distancing versus During social distancing) as fixed factor and participants as random factor, with a compound symmetry covariance matrix. Delta changes in all dependent variables were calculated with the following formula: delta change = data during social distancing—data before social distancing. Associations between changes in physical activity and sedentary behavior level and changes in pain, fatigue, and health-related quality of life were tested using Pearson correlation tests.

Statistical analysis was performed in SAS 9.3 (SAS Institute Inc., Cary, NC, USA). Data are presented as mean, estimated mean difference from the repeated measures mixed models, and 95% confidence intervals (95% CI). The significance level was set at $p \leq 0.05$.

3. Results

Patients' clinical characteristics are presented in Table 1. In summary, mean age was 60.9 years (95% CI: 58.0 to 63.7) and BMI was 29.5 Kg/m^2 (95% CI: 27.2 to 31.9). Disease activity ranged from remission to moderate activity, as assessed by DAS28 PCR and CDAI. Disability assessed by HAQ ranged from mild to severe. Mean disease duration was 18.5 years (95% CI: 14.7, 22.3). Mean C-reactive protein was 10.8 mg/dL (95% CI: 5.5 to 16.2) and erythrocyte sedimentation rate was 28.4 mm/H (95% CI: 15.7 to 41.1). Most of the patients were using disease-modifying anti-rheumatic drugs and prednisone (85.7% and 74.3%, respectively). Hypertension, dyslipidemia and type 2 diabetes were the most frequent comorbidities (51.4%, 48.6% and 34.3%, respectively). Before social distancing, mean pain was 5.0 (95% CI: 4.1 to 6.0), fatigue was 39.3 (95% CI: 33.8 to 44.8), and physical and mental health-related quality of life were 39.8 (95% CI: 33.1 to 46.5) and 62.0 (95%CI: 52.3 to 71.7), respectively.

Table 1. Patients' characteristics prior to the COVID-19 pandemic.

Variable	*n* = 35
Age, years	60.9 (58.0 to 63.7)
BMI, kg/m^2	29.5 (27.2 to 31.9)
Disease Activity Score (DAS28 PCR)	3.4 (2.9 to 3.8)
Clinical Disease Activity Index (CDAI)	10.1 (6.7 to 13.4)
Health Assessment Questionnaire (HAQ)	1.2 (0.9 to 1.4)
C-reactive protein, mg/L	10.8 (5.5 to 16.2)
Erythrocyte sedimentation rate, mm/H	28.4 (15.7 to 41.1)
Disease duration, years	18.5 (14.7 to 22.3)
Comorbidities, *n* (%)	
Hypertension	18 (51.4%)
Dyslipidemias	17 (48.6%)
Type 2 diabetes	12 (34.3%)
Fibromyalgia	11 (31.4%)
Other rheumatic diseases	18 (51.4%)

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Table 1. *Cont.*

Variable	$n = 35$
Depression	7 (20.0%)
Medication, *n* (%)	
DMARDs	30 (85.7%)
Leflunomide	19 (54.3%)
Methotrexate	16 (45.7%)
Prednisone	26 (74.3%)
Biological agents	12 (34.3%)
Anti-inflammatory drugs	11 (31.4%)
Pain killers	20 (57.1%)
Antihypertensive drugs	18 (51.4%)
Antihyperlipidemic drugs	17 (48.6%)
Antidiabetic drugs	12 (34.3%)
Anti-depressants	14 (40.0%)

Data presented as mean (95% CI) or *n* (%). Other rheumatic diseases include osteoarthritis, osteoporosis and/or Sjogren's syndrome. Abbreviations: DMARDs, disease-modifying antirheumatic drugs; TNF, tumor necrosis factor.

During social distancing, there were reductions in total stepping time (15.7% [-0.3 h/day, 95% CI: -0.4 to -0.1; $p = 0.004$]), in light-intensity physical activity (13.0% [-0.2 h/day, 95% CI: -0.4 to -0.04; $p = 0.016$]) and in moderate-to-vigorous physical activity (38.8% [-4.5 min/day, 95% CI: -8.1 to -0.9; $p = 0.015$]), but no changes in total standing time (-0.1 h/day, 95% CI: -0.7 to 0.5; $p = 0.767$) or total sedentary time (0.3 h/day, 95% CI: -0.4 to 1.0; $p = 0.335$) in patients with rheumatoid arthritis. However, time spent in prolonged bouts of sitting $\geq$ 30 min increased by 34% (1.0 h/day, 95% CI: 0.3 to 1.7; $p = 0.006$; Figure 1A) and sitting bouts $\geq$60 min increased by 85% (1.0 h/day, 95% CI: 0.5 to 1.6; $p < 0.001$; Figure 1B). Sit-stand transitions were reduced by 10% (-5.1/day, 95% CI: -10.3 to 0.0; $p = 0.051$). Figures 1C and 1D illustrate the accelerometer data from a patient who experienced decreased activity and increased prolonged sitting after social distancing.
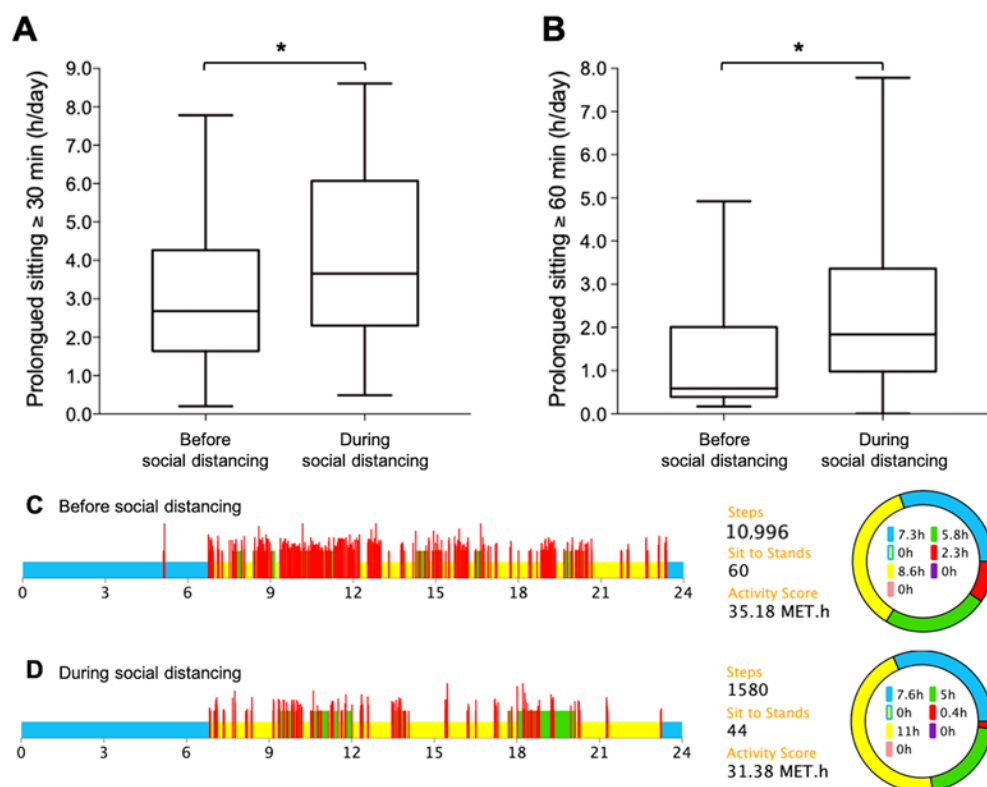

Figure 1. Prolonged sitting and physical activity in rheumatoid arthritis. Panels (**A**) and (**B**) depict total time spent in prolonged sitting $\geq$ 30 min and $\geq$60 min (*n* = 35). In the bottom, illustrative data

showing the fall in activity and the rise in prolonged sitting in a rheumatoid arthritis patient assessed before (Panel **C**) and during the social distancing (Panel **D**). Legend: blue, sleeping time; yellow, sedentary time; green, standing time; red, stepping time (irrespective of intensity); * $p < 0.05$.

During social distancing, there were no changes in pain (0.31 [95% CI: −1.04 to 1.67; $p = 0.652$), fatigue (−2.3 [95% CI: −10.0 to 5.4]; $p = 0.550$), and physical and mental health-related quality of life (1.2 [95% CI: −8.2 to 10.7]; $p = 0.796$ and −9.3 [95% CI: −23.0 to 4.5], $p = 0.183$, respectively) in patients with rheumatoid arthritis.

Changes in physical activity and sedentary behavior levels were not associated with changes in pain, fatigue, and physical and mental health-related quality of life during social distancing (all $p > 0.050$).

4. Discussion

To our knowledge, this is the first study to track physical activity and sedentary behavior patterns before and during the COVID-19 pandemic using validated accelerometry and a within-subjects design. Our main findings suggest that social distancing (including stay-at-home order) can lead to reduced ambulatory activities and increased physical inactivity as well as increased prolonged sitting among patients with rheumatoid arthritis. In contrast, social distancing was not associated with worsened pain, fatigue, and physical and mental health-related quality of life. Physical inactivity along with too much sitting emerge as a risk factor that could be detrimental to cardiometabolic health in such a high-risk group of patients during and possibly after the COVID-19 pandemic.

As those confined at home are less prone to perform physical activity, it has been speculated that inactivity and sedentary behavior could peak during the COVID-19 pandemic [29]. In fact, a rapid review has shown a substantial decrease in physical activity with a concomitant increase in sedentary behavior across all age groups during COVID-19 lockdown [42]. As for the Brazilian population, a national retrospective survey comprising 39,693 adults and older adults has shown a significant increase on self-reported physical inactivity and screen-based sedentary behaviors during the COVID-19 pandemic [43,44], which corroborates the objectively measured data presented herein. Such an increase in inactivity and sedentary behavior is of particular concern for those who are usually hypoactive and show higher risk of cardiovascular diseases, this being the case of patients with rheumatoid arthritis (see the patients' comorbidities in Table 1) [26,28].

Observational and experimental evidence demonstrates that inactivity can predispose to pathological states and poor outcomes [45]. Sedentary behavior can add to the adverse impacts of physical inactivity in impairing cardiovascular health [46]. Consequently, individuals who are both physically inactive and highly sedentary are at the highest risk for poor outcomes [6,20], which might be the case for patients with autoimmune rheumatic diseases, as they commonly spent most of their daily hours engaged in sedentary behavior and did not achieve minimum levels of moderate-to-vigorous physical activity [28]. Namely in rheumatoid arthritis, the estimates of physical inactivity and sedentary behavior are comparable to those of other chronic diseases (e.g., type 2 diabetes and cardiovascular diseases), groups in which both physical inactivity and sedentary behaviors are associated with poor disease prognosis and mortality [9–11,13,47], as well as poor health-related outcomes (i.e., higher disease activity score, disease symptoms and number of comorbidities, and lower physical capacity and functioning) [28]. In rheumatoid arthritis, regular participation in exercise improves disease symptoms, inflammatory markers, cardiometabolic risk factors, and physical capacity [48,49]. However, regular participation in moderate-to-vigorous physical activity may not be feasible for some patients, especially those with poor mobility or during disease flares.

Interestingly, we observed that even in the absence of changes in total sedentary time, prolonged sitting time rose considerably. Prolonged, uninterrupted bouts of sedentary behavior are associated with all-cause mortality [8], whereas well-controlled studies show that very-light to light-intensity active interruptions in prolonged sedentary time (e.g., 2 min of walking for every 30 min of sitting) can elicit immediate improvements in cardiometabolic

risk factors [50]. Recent evidence has shown that light-intensity physical activity is associated with lower disability, disease activity and cardiovascular risk in rheumatoid arthritis, in contrast to excessive sitting [28,51]. Additionally, a crossover randomized trial demonstrated that performing 3-min bouts of light-intensity walking every 30 min of sitting (total: 42 min) resulted in improved glycemic (i.e., glucose, insulin, and c-peptide) and inflammatory (i.e., IL-1β, IL-1ra, IL-10, and TNF-α) markers when compared to 8 h of prolonged, uninterrupted sitting in postmenopausal females with rheumatoid arthritis [52]. This raises the need for widespread recommendation of breaking-up prolonged sitting whenever possible (e.g., 3 min breaks of light-intensity walking every 30 min of sitting) to avoid poor health outcomes during the pandemic, which tend to be more restrictive for high-risk groups for COVID-19, such as those with autoimmune rheumatic diseases [33], a condition associated with lower vaccine responses, which may enforce more vulnerable patients to maintain some degree of physical distance and home isolation for as long as the pandemic endures.

Our findings suggested social distancing did not affect pain, fatigue, and physical and mental health-related quality of life. Qualitative evidence in patients with rheumatoid arthritis demonstrate that patients reported no changes in physical health outcomes. Conversely, they noted social distancing resulted in worsened mental health-related symptoms [53]. Additionally, changes in these variables did not associate with changes in physical activity and sedentary behavior. Because this study was performed 2 to 4 months after the set of social distancing measures, we cannot rule out that such a short period of exposure did not allow detecting impairments in these outcomes. Alternatively, it is possible that patients with rheumatoid arthritis may be more resilient than general population to the detrimental impacts of the pandemic on overall health.

The main strengths of this study are its within-subjects design and the use of posture-based accelerometers, which enables an objective and a comprehensive assessment of sedentary behavior patterns. The limitations include the relatively low sample size; lack of measurement of mood and use of medication and supplements during social distancing, which may also alter habitual physical activity; and the inability to stablish a cause-and-effect relationship between changes in behavior with social distancing measures, although elements of temporality and plausibility do support our assumptions.

5. Conclusions

Imposed social distancing measures to contain the COVID-19 outbreak were associated with decreased physical activity and increased prolonged sitting time, but no changes in clinical symptoms (pain, fatigue, and health-related quality of life) among patients with rheumatoid arthritis. Since this has the potential to increase the burden of cardiovascular diseases in such high-risk group of patients, attention to maintaining their activity levels is an urgent consideration during the pandemic, and possibly thereafter since inactivity and sedentariness may carry over as consequences of the outbreak.

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References

1. Tison, G.H.; Avram, R.; Kuhar, P.; Abreau, S.; Marcus, G.M.; Pletcher, M.J.; Olgin, J.E. Worldwide Effect of COVID-19 on Physical Activity: A Descriptive Study. *Ann. Intern. Med.* **2020**, *173*, 767–770. [CrossRef]
2. Hall, G.; Laddu, D.R.; Phillips, S.A.; Lavie, C.J.; Arena, R. A tale of two pandemics: How will COVID-19 and global trends in physical inactivity and sedentary behavior affect one another? *Prog. Cardiovasc. Dis.* **2021**, *64*, 108–110. [CrossRef]
3. Ammar, A.; Brach, M.; Trabelsi, K.; Chtourou, H.; Boukhris, O.; Masmoudi, L.; Bouaziz, B.; Bentlage, E.; How, D.; Ahmed, M.; et al. Effects of COVID-19 Home Confinement on Eating Behaviour and Physical Activity: Results of the ECLB-COVID19 International Online Survey. *Nutrients* **2020**, *12*, 1583. [CrossRef]
4. Lee, I.M.; Shiroma, E.J.; Lobelo, F.; Puska, P.; Blair, S.N.; Katzmarzyk, P.T.; Lancet Physical Activity Series Working, G. Effect of physical inactivity on major non-communicable diseases worldwide: An analysis of burden of disease and life expectancy. *Lancet* **2012**, *380*, 219–229. [CrossRef]
5. Chastin, S.; McGregor, D.; Palarea-Albaladejo, J.; Diaz, K.M.; Hagstromer, M.; Hallal, P.C.; van Hees, V.T.; Hooker, S.; Howard, V.J.; Lee, I.M.; et al. Joint association between accelerometry-measured daily combination of time spent in physical activity, sedentary behaviour and sleep and all-cause mortality: A pooled analysis of six prospective cohorts using compositional analysis. *Br. J. Sports Med.* **2021**, *55*, 1277–1285. [CrossRef]
6. Ekelund, U.; Tarp, J.; Fagerland, M.W.; Johannessen, J.S.; Hansen, B.H.; Jefferis, B.J.; Whincup, P.H.; Diaz, K.M.; Hooker, S.; Howard, V.J.; et al. Joint associations of accelero-meter measured physical activity and sedentary time with all-cause mortality: A harmonised meta-analysis in more than 44 000 middle-aged and older individuals. *Br. J. Sports Med.* **2020**, *54*, 1499–1506. [CrossRef]
7. Ekelund, U.; Tarp, J.; Steene-Johannessen, J.; Hansen, B.H.; Jefferis, B.; Fagerland, M.W.; Whincup, P.; Diaz, K.M.; Hooker, S.P.; Chernofsky, A.; et al. Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: Systematic review and harmonised meta-analysis. *BMJ* **2019**, *366*, l4570. [CrossRef]
8. Diaz, K.M.; Howard, V.J.; Hutto, B.; Colabianchi, N.; Vena, J.E.; Safford, M.M.; Blair, S.N.; Hooker, S.P. Patterns of Sedentary Behavior and Mortality in U.S. Middle-Aged and Older Adults: A National Cohort Study. *Ann. Intern. Med.* **2017**, *167*, 465–475. [CrossRef]
9. Nicholas, J.A.; Lo Siou, G.; Lynch, B.M.; Robson, P.J.; Friedenreich, C.M.; Csizmadi, I. Leisure-Time Physical Activity Does not Attenuate the Association Between Occupational Sedentary Behavior and Obesity: Results From Alberta's Tomorrow Project. *J. Phys. Act. Health* **2015**, *12*, 1589–1600. [CrossRef]
10. van der Berg, J.D.; Stehouwer, C.D.; Bosma, H.; van der Velde, J.H.; Willems, P.J.; Savelberg, H.H.; Schram, M.T.; Sep, S.J.; van der Kallen, C.J.; Henry, R.M.; et al. Associations of total amount and patterns of sedentary behaviour with type 2 diabetes and the metabolic syndrome: The Maastricht Study. *Diabetologia* **2016**, *59*, 709–718. [CrossRef]
11. Wilmot, E.G.; Edwardson, C.L.; Achana, F.A.; Davies, M.J.; Gorely, T.; Gray, L.J.; Khunti, K.; Yates, T.; Biddle, S.J. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: Systematic review and meta-analysis. *Diabetologia* **2012**, *55*, 2895–2905. [CrossRef] [PubMed]
12. Patterson, R.; McNamara, E.; Tainio, M.; de Sa, T.H.; Smith, A.D.; Sharp, S.J.; Edwards, P.; Woodcock, J.; Brage, S.; Wijndaele, K. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: A systematic review and dose response meta-analysis. *Eur. J. Epidemiol.* **2018**, *33*, 811–829. [CrossRef] [PubMed]
13. Engelen, L.; Gale, J.; Chau, J.Y.; Hardy, L.L.; Mackey, M.; Johnson, N.; Shirley, D.; Bauman, A. Who is at risk of chronic disease? Associations between risk profiles of physical activity, sitting and cardio-metabolic disease in Australian adults. *Aust. N. Z. J. Public Health* **2017**, *41*, 178–183. [CrossRef] [PubMed]
14. Lynch, B.M. Sedentary behavior and cancer: A systematic review of the literature and proposed biological mechanisms. *Cancer Epidemiol. Biomark. Prev.* **2010**, *19*, 2691–2709. [CrossRef] [PubMed]
15. Matthews, C.E.; George, S.M.; Moore, S.C.; Bowles, H.R.; Blair, A.; Park, Y.; Troiano, R.P.; Hollenbeck, A.; Schatzkin, A. Amount of time spent in sedentary behaviors and cause-specific mortality in US adults. *Am. J. Clin. Nutr.* **2012**, *95*, 437–445. [CrossRef] [PubMed]
16. Falck, R.S.; Davis, J.C.; Liu-Ambrose, T. What is the association between sedentary behaviour and cognitive function? A systematic review. *Br. J. Sports Med.* **2016**, *51*, 800–811. [CrossRef]

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17. Dempsey, P.C.; Strain, T.; Winkler, E.A.H.; Westgate, K.; Rennie, K.L.; Wareham, N.J.; Brage, S.; Wijndaele, K. Association of Accelerometer-Measured Sedentary Accumulation Patterns With Incident Cardiovascular Disease, Cancer, and All-Cause Mortality. *J. Am. Heart Assoc.* **2022**, *11*, e023845. [CrossRef]

18. Biswas, A.; Oh, P.I.; Faulkner, G.E.; Bajaj, R.R.; Silver, M.A.; Mitchell, M.S.; Alter, D.A. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: A systematic review and meta-analysis. *Ann. Intern. Med.* **2015**, *162*, 123–132. [CrossRef]

19. Katzmarzyk, P.T.; Powell, K.E.; Jakicic, J.M.; Troiano, R.P.; Piercy, K.; Tennant, B.; Physical Activity Guidelines Advisory, C. Sedentary Behavior and Health: Update from the 2018 Physical Activity Guidelines Advisory Committee. *Med. Sci. Sports Exerc.* **2019**, *51*, 1227–1241. [CrossRef]

20. Ekelund, U.; Steene-Johannessen, J.; Brown, W.J.; Fagerland, M.W.; Owen, N.; Powell, K.E.; Bauman, A.; Lee, I.M.; Lancet Physical Activity Series 2 Executive, C.; Lancet Sedentary Behaviour Working, G. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *Lancet* **2016**, *388*, 1302–1310. [CrossRef]

21. Scott, D.L.; Wolfe, F.; Huizinga, T.W. Rheumatoid arthritis. *Lancet* **2010**, *376*, 1094–1108. [CrossRef]

22. Lee, D.M.; Weinblatt, M.E. Rheumatoid arthritis. *Lancet* **2001**, *358*, 903–911. [CrossRef]

23. Pincus, T. Long-term outcomes in rheumatoid arthritis. *Br. J. Rheumatol.* **1995**, *34* (Suppl. S2), 59–73. [CrossRef] [PubMed]

24. Gabriel, S.E. Cardiovascular morbidity and mortality in rheumatoid arthritis. *Am. J. Med.* **2008**, *121*, 9–14. [CrossRef] [PubMed]

25. Sarzi-Puttini, P.; Atzeni, F.; Gerli, R.; Bartoloni, E.; Doria, A.; Barskova, T.; Matucci-Cerinic, M.; Sitia, S.; Tomasoni, L.; Turiel, M. Cardiac involvement in systemic rheumatic diseases: An update. *Autoimmun. Rev.* **2010**, *9*, 849–852. [CrossRef] [PubMed]

26. Hollan, I.; Meroni, P.L.; Ahearn, J.M.; Cohen Tervaert, J.W.; Curran, S.; Goodyear, C.S.; Hestad, K.A.; Kahaleh, B.; Riggio, M.; Shields, K.; et al. Cardiovascular disease in autoimmune rheumatic diseases. *Autoimmun. Rev.* **2013**, *12*, 1004–1015. [CrossRef] [PubMed]

27. Rausch Osthoff, A.K.; Niedermann, K.; Braun, J.; Adams, J.; Brodin, N.; Dagfinrud, H.; Duruoz, T.; Esbensen, B.A.; Gunther, K.P.; Hurkmans, E.; et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. *Ann. Rheum. Dis.* **2018**, *77*, 1251–1260. [CrossRef] [PubMed]

28. Pinto, A.J.; Roschel, H.; de Sa Pinto, A.L.; Lima, F.R.; Pereira, R.M.R.; Silva, C.A.; Bonfa, E.; Gualano, B. Physical inactivity and sedentary behavior: Overlooked risk factors in autoimmune rheumatic diseases? *Autoimmun. Rev.* **2017**, *16*, 667–674. [CrossRef] [PubMed]

29. Pinto, A.J.; Dunstan, D.W.; Owen, N.; Bonfa, E.; Gualano, B. Combating physical inactivity during the COVID-19 pandemic. *Nat. Rev. Rheumatol.* **2020**, *16*, 347–348. [CrossRef]

30. Henchoz, Y.; Bastardot, F.; Guessous, I.; Theler, J.M.; Dudler, J.; Vollenweider, P.; So, A. Physical activity and energy expenditure in rheumatoid arthritis patients and matched controls. *Rheumatology* **2012**, *51*, 1500–1507. [CrossRef]

31. Yu, C.A.; Rouse, P.C.; Veldhuijzen Van Zanten, J.J.; Ntoumanis, N.; Kitas, G.D.; Duda, J.L.; Metsios, G.S. Subjective and objective levels of physical activity and their association with cardiorespiratory fitness in rheumatoid arthritis patients. *Arthritis Res. Ther.* **2015**, *17*, 59. [CrossRef] [PubMed]

32. Huffman, K.M.; Pieper, C.F.; Hall, K.S.; St Clair, E.W.; Kraus, W.E. Self-efficacy for exercise, more than disease-related factors, is associated with objectively assessed exercise time and sedentary behaviour in rheumatoid arthritis. *Scand. J. Rheumatol.* **2015**, *44*, 106–110. [CrossRef] [PubMed]

33. Zhong, J.; Shen, G.; Yang, H.; Huang, A.; Chen, X.; Dong, L.; Wu, B.; Zhang, A.; Su, L.; Hou, X.; et al. COVID-19 in patients with rheumatic disease in Hubei province, China: A multicentre retrospective observational study. *Lancet Rheumatol.* **2020**, *2*, e557–e564. [CrossRef]

34. Aletaha, D.; Neogi, T.; Silman, A.J.; Funovits, J.; Felson, D.T.; Bingham, C.O., 3rd; Birnbaum, N.S.; Burmester, G.R.; Bykerk, V.P.; Cohen, M.D.; et al. 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum.* **2010**, *62*, 2569–2581. [CrossRef] [PubMed]

35. Tudor-Locke, C.; Sisson, S.B.; Collova, T.; Lee, S.M.; Swan, P.D. Pedometer-determined step count guidelines for classifying walking intensity in a young ostensibly healthy population. *Can. J. Appl. Physiol.* **2005**, *30*, 666–676. [CrossRef] [PubMed]

36. Prevoo, M.L.; van't Hof, M.A.; Kuper, H.H.; van Leeuwen, M.A.; van de Putte, L.B.; van Riel, P.L. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum.* **1995**, *38*, 44–48. [CrossRef]

37. Aletaha, D.; Smolen, J. The Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI): A review of their usefulness and validity in rheumatoid arthritis. *Clin. Exp. Rheumatol.* **2005**, *23*, S100–S108.

38. Ferraz, M.B.; Oliveira, L.M.; Araujo, P.M.; Atra, E.; Tugwell, P. Crosscultural reliability of the physical ability dimension of the health assessment questionnaire. *J. Rheumatol.* **1990**, *17*, 813–817.

39. Price, D.D.; Bush, F.M.; Long, S.; Harkins, S.W. A comparison of pain measurement characteristics of mechanical visual analogue and simple numerical rating scales. *Pain* **1994**, *56*, 217–226. [CrossRef]

40. Pouchot, J.; Kherani, R.B.; Brant, R.; Lacaille, D.; Lehman, A.J.; Ensworth, S.; Kopec, J.; Esdaile, J.M.; Liang, M.H. Determination of the minimal clinically important difference for seven fatigue measures in rheumatoid arthritis. *J. Clin. Epidemiol.* **2008**, *61*, 705–713. [CrossRef]

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41. Ciconelli, R.M.; Ferraz, M.B.; Santos, W.; Meinão, I.; Quaresma, M.R. Brazilian-Portuguese version of the SF-36. A reliable and valid quality of life outcome measure. *Rev. Bras. Rheumatol.* **1999**, *39*, 8.

42. Freiberg, A.; Schubert, M.; Romero Starke, K.; Hegewald, J.; Seidler, A. A Rapid Review on the Influence of COVID-19 Lockdown and Quarantine Measures on Modifiable Cardiovascular Risk Factors in the General Population. *Int. J. Environ. Res. Public Health* **2021**, *18*, 8567. [CrossRef]

43. Silva, D.R.; Werneck, A.O.; Malta, D.C.; Souza-Junior, P.R.B.; Azevedo, L.O.; Barros, M.B.A.; Szwarcwald, C.L. Incidence of physical inactivity and excessive screen time during the first wave of the COVID-19 pandemic in Brazil: What are the most affected population groups? *Ann. Epidemiol.* **2021**, *62*, 30–35. [CrossRef]

44. Silva, D.; Werneck, A.O.; Malta, D.C.; Souza Junior, P.R.B.; Azevedo, L.O.; Barros, M.B.A.; Szwarcwald, C.L. Changes in the prevalence of physical inactivity and sedentary behavior during COVID-19 pandemic: A survey with 39,693 Brazilian adults. *Cad. Saude Publica* **2021**, *37*, e00221920. [CrossRef]

45. Booth, F.W.; Roberts, C.K.; Thyfault, J.P.; Ruegsegger, G.N.; Toedebusch, R.G. Role of Inactivity in Chronic Diseases: Evolutionary Insight and Pathophysiological Mechanisms. *Physiol. Rev.* **2017**, *97*, 1351–1402. [CrossRef]

46. Bellettiere, J.; Winkler, E.A.H.; Chastin, S.F.M.; Kerr, J.; Owen, N.; Dunstan, D.W.; Healy, G.N. Associations of sitting accumulation patterns with cardio-metabolic risk biomarkers in Australian adults. *PLoS ONE* **2017**, *12*, e0180119. [CrossRef]

47. van Dijk, S.B.; Takken, T.; Prinsen, E.C.; Wittink, H. Different anthropometric adiposity measures and their association with cardiovascular disease risk factors: A meta-analysis. *Neth Heart J* **2012**, *20*, 208–218. [CrossRef]

48. Pedersen, B.K.; Saltin, B. Exercise as medicine—Evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand. J. Med. Sci. Sports* **2015**, *25* (Suppl. S3), 1–72. [CrossRef] [PubMed]

49. Benatti, F.B.; Pedersen, B.K. Exercise as an anti-inflammatory therapy for rheumatic diseases-myokine regulation. *Nat. Rev. Rheumatol.* **2015**, *11*, 86–97. [CrossRef] [PubMed]

50. Saunders, T.J.; Atkinson, H.F.; Burr, J.; MacEwen, B.; Skeaff, C.M.; Peddie, M.C. The Acute Metabolic and Vascular Impact of Interrupting Prolonged Sitting: A Systematic Review and Meta-Analysis. *Sports Med.* **2018**, *48*, 2347–2366. [CrossRef] [PubMed]

51. Fenton, S.A.M.; Veldhuijzen van Zanten, J.; Kitas, G.D.; Duda, J.L.; Rouse, P.C.; Yu, C.A.; Metsios, G.S. Sedentary behaviour is associated with increased long-term cardiovascular risk in patients with rheumatoid arthritis independently of moderate-to-vigorous physical activity. *BMC Musculoskelet. Disord.* **2017**, *18*, 131. [CrossRef] [PubMed]

52. Pinto, A.J.; Meireles, K.; Pecanha, T.; Mazzolani, B.C.; Smaira, F.I.; Rezende, D.; Benatti, F.B.; Ribeiro, A.C.M.; Pinto, A.L.S.; Lima, F.R.; et al. Acute cardiometabolic effects of brief active breaks in sitting for patients with rheumatoid arthritis. *Am. J. Physiol. Endocrinol. Metab.* **2021**, *321*, E782–E794. [CrossRef] [PubMed]

53. Ryan, S.; Campbell, P.; Paskins, Z.; Hider, S.; Manning, F.; Rule, K.; Brooks, M.; Hassell, A. Exploring the physical, psychological and social well-being of people with rheumatoid arthritis during the coronavirus pandemic: A single-centre, longitudinal, qualitative interview study in the UK. *BMJ Open* **2022**, *12*, e056555. [CrossRef] [PubMed]