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Association between physical activity and musculoskeletal pain: an analysis of international data from the ASAP survey

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Association between physical activity and musculoskeletal pain: an

analysis of international data from the ASAP survey

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ABSTRACT

Objective: To investigate the association of physical activity (PA) with musculoskeletal pain (MSK-pain).

Design: Cross-sectional study

Setting: 14 countries (Argentina, Australia, Austria, Brazil, Chile, France, Germany, Italy, the Netherlands, Singapore, South Africa, Spain, Switzerland, and the United States of America)

Participants: Individuals aged 18 or older living in participating countries. Recruitment was performed online using promotion by health-related organizations, mailing lists, and social media advertising.

Primary and secondary outcome measures: PA volumes were assessed with an adapted version of the Nordic physical activity questionnaire-short questionnaire. Prevalence of MSK-pain was captured by means of a 20-item checklist of body locations. Based on the WHO recommendation on PA, participants were classified as non-compliers (0-150 min/week), compliers (150-300 min/week), double compliers (300-450 min/week), triple compliers (450-600 min/week), quadruple compliers (600-750 min/week), quintuple compliers (750-900 min/week), and top compliers (more than 900 min/week). Multivariate logistic regression was used to obtain adjusted odds ratios of the association between PA and MSK-pain for each body location, correcting for age, sex, employment status, and depression risk.

Results: Compared to non-compliers, individuals with simple compliance had smaller odds of MSK-pain in one location (thoracic pain, OR 0.77). Double compliance was associated with reduced pain occurrence in six locations (elbow, OR 0.70; forearm, OR 0.63; wrist, OR 0.74; hand, OR 0.57; fingers, OR 0.72; abdomen, OR 0.61). Triple to top compliance was also linked with lower odds of MSK-pain (five locations in triple compliance, three in quadruple compliance, two in quintuple compliance, three in top compliance), but, at the same time, presented increased odds of MSK-pain in some of the other locations.

Conclusion: A dose of 300-450 min WHO-equivalent PA/week may be optimal to reduce MSKpain. Excessive doses of PA may have harmful effects for certain body locations.

Strengths and Limitations of this study

- This is the first large-scale analysis of associations between MSK pain and PA considering multiple anatomical locations
- Large sample size enabled to investigate the associations between different degrees of compliance to physical activity recommended by WHO and MSK-pain
- Administration of the survey in 14 countries allowed participation of diverse populations
- Self-reported data may be subject to recall bias
- Cross-sectional observational design prohibits causal inference

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INTRODUCTION

Musculoskeletal pain (MSK-pain) is a common condition that can have negative physical, psychological, and social impacts.¹ A summary of previous epidemiological studies conducted with diverse techniques and populations revealed that the prevalence of MSK-pain was approximately 30%.² One study reported 15% of 20–72-year-olds were pain-free whereas 15% had MSK-pain every day during the previous year and 58% reported MSK-pain within the past week.³ Musculoskeletal impairments may contribute to functional limitations particularly in developed countries. ² A separate investigation reported that musculoskeletal conditions accounted for 40% of all chronic conditions and contributed to over half of causes for long-term disability.⁴ It has been reported that disability-adjusted life-years (DALYs), which reflects the years of life lost due to premature mortality and years of life lived with disability, increased by 62% between 1990 and 2016 around the world with 20% surge during the ten-year interval from 2006 to 2016.⁵ Given the aging of global population, the burden of MSK disorders is expected to further increase in the future.⁶

Achieving sufficient physical activity (PA) is associated with a variety of positive health outcomes such as substantial risk reduction in all-cause mortality⁷ as well as multiple chronic diseases including type 2 diabetes and metabolic syndrome,⁸ cancer,⁸ and cardiovascular disease.⁹ In the light of these positive impacts, World Health Organization (WHO) recommends 150-300 min of moderate-intensity PA, or 75-150 min of vigorous-intensity PA, or aerobic PA with some combination of moderate and vigorous intensities.¹⁰ PA is also considered one of the most important strategies to prevent and manage MSK pain.¹¹ However, most studies focused on the association of PA with non-communicable disease, and there is a literature gap regarding MSK-pain. Furthermore, it is still less clear whether these amounts are sufficient to elicit benefits

in terms of addressing MSK-pain. The few available studies examining the relation of regular PA and MSK-pain tended to focus on influence of PA for specific location or diagnoses such as low back pain, neck pain, or osteoarthritis and found inconsistent results.¹² Other studies have evaluated the associations between PA and pain in occupational settings such as among physical therapists or teaching staff.^{13 14} Particularly, the interplay between the volume of PA and MSK-pain within the general population has been less explored.

The purpose of this study was to investigate the association of total PA with MSK-pain by anatomical location (upper vs lower extremity). We hypothesize that greater time spent in PA would reduce overall MSK-pain, but excess time performing PA might contribute to higher pain resulting from associated overuse injuries

METHODS

Study Design

This article presents an analysis of pre-pandemic baseline data on PA and MSK-pain assessed during the ASAP (Activity and Health during the SARS-CoV-2 Pandemic) survey. It was performed between April 3 and May 9, 2020, including participants from 14 countries (Argentina, Australia, Austria, Brazil, Chile, France, Germany, Italy, the Netherlands, Singapore, South Africa, Spain, Switzerland, and the United States of America (USA)).¹⁵⁻¹⁸ Ethical approval was obtained from the ethics committees of the study center and collaborating institutions. All participants provided digital informed consent.

Participants

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Eligibility for participation in the ASAP survey was limited to individuals aged 18 or older living in participating countries. Recruitment was performed online using promotion by health-related organizations, mailing lists, and social media advertising (e.g. Facebook, Instagram, Twitter).

Questionnaire

To capture PA, the ASAP survey incorporated an adapted version of the Nordic Physical Activity Questionnaire-short (NPAQ-short). In detail, with its four questions, the instrument retrospectively assessed the amounts of moderate and combined moderate and vigorous activities (min/week) during leisure and occupational time. The NPAQ-short has been shown to be reliable (test-retest reliability: rho = 0.80 to 0.82) and valid for observing compliance with the WHO recommendations on PA.¹⁹

Prevalence of MSK-pain was captured by means of binary responses (yes/no) to an adapted 20-item checklist from a consensus statement on epidemiological injury reporting.²⁰ Body locations were categorized as follows: neck/cervical spine, shoulder, upper arm, elbow, forearm, wrist, hand, fingers, thoracic spine, ribs, lower back, abdomen, pelvis/gluteal, hip, groin, thigh, knee, lower leg, ankle/Achilles tendon, foot/toe.

Data Processing and Statistical Analysis

Self-reported PA was categorized as multiples of compliance with WHO guidelines which recommend 150-300 minutes/week of moderate activity, 75-150 minutes/week of vigorous activity, or any adequate combination of both.¹⁰ We used the formula (moderate-tovigorous PA – vigorous PA) + vigorous PA *2 to classify participants as non-compliers (0-150

min/week), compliers (150-300 min/week), double compliers (300-450 min/week), triple compliers (450-600 min/week), quadruple compliers (600-750 min/week), quintuple compliers (750-900 min/week), and top compliers (more than 900 min/week).

For each body region, univariate logistic regression was conducted to calculate the unadjusted odds ratio (OR) of the association between pain (dependent variable) and PA. In a similar way, univariate logistic regression was then used to identify associations of pain (dependent variable) and potential confounding variables (sex, age, employment status, depression risk). Finally, multivariate logistic regression was performed including these confounding variables (if relevant) to obtain the adjusted ORs and 95% confidence interval (CI) of the association between the volume of PA and pain. All data analyses were conducted using SPSS 22 (SPSS INC., Armonk, NY, USA), and the significance level was set to $\alpha = 0.05$.

Patient and Public Involvement

Members of the target population without medical background were involved in the designing phase of the ASAP questionnaire. They completed the preliminary version of the survey and helped refine and clarify wording of the survey, an involvement which was intended to increase face validity.

RESULTS

Valid datasets were identified for 13,741 participants (38 ± 15 years, 59% females). 2604 individuals did not meet the WHO recommendation of PA while n=2735 belonged to 150-300 min group, n=1957 to 300-450 min group, n=1749 to 450-600 min group, n=1066 to 600-750

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min group, n=849 to 750-900 min group, and n=2781 to 900+ min group. Comprehensive results are summarized in the Table 1 and 2.

Compared to inactive individuals, simple compliance was associated with reduced MSKpain in one body location (thoracic pain, OR 0.77, Table 1). Double compliance increased the number of locations with less pain to six (elbow, OR 0.70; forearm, OR 0.63; wrist, OR 0.74; hand, OR 0.57; fingers, OR 0.72; abdomen, OR 0.61). Although higher amounts of PA were linked to lower pain levels to a variable degree (five body locations in triple compliance, three in quadruple compliance, two in quintuple compliance, three in top compliance), they also showed increased pain in other locations. Specifically, triple compliance was associated with higher pain in thigh (OR 1.41), knee (OR 1.25), and ankle/Achilles tendon (OR 1.47). Quadruple compliance increased pain locations to four, quintuple compliance to six, and top compliance to seven.

Triple compliance was associated with lower odds to have a total of 5 or more (OR 0.75) or 10 or more (OR 0.36) pain locations, and quadruple compliance was associated with lower odds to have 5 or more pain locations (OR 0.73). However, quintuple and top compliances were associated with higher odds of having a minimum one pain location (OR 1.28 and 1.30, respectively).

DISCUSSION

The purpose of the present study was to understand the relation between PA and MSKpain. Previous research focused on the impact of PA on specific locations of MSK-pain (e.g., low back and neck²¹) or certain occupational settings.^{13 14} Our large-scale multinational study is novel in that it identified the associations between different degrees of compliance to PA recommended by WHO and multiple body locations in the general population.

Simple guideline compliance (150-300 min per week) was weakly associated with MSK pain, showing lower odds of developing pain only in thoracic spine but higher odds in foot/toes. In contrast, double compliance (300-450 min per week) substantially increased the number of beneficial associations to six and thus seems to represent the optimal dose when PA is undertaken to prevent MSK. Finally, higher levels of PA (triple to top compliance) were associated with less odds of developing pain in multiple upper body locations but paradoxically contributed to higher odds of lower extremity pain. Notably, participating in 300-600 min of PA per week was associated with lower odds of developing pain in upper extremities, neck, and thoracic and lumbar spine. In contrast, participating in greater than 450 min of PA per week was associated with higher odds of developing pain in the lower extremity.

Time spent in PA and pain in neck, back, and upper extremity

A previous systematic review showed that there was limited evidence for no association between PA and neck pain.²¹ However, our study found that participating in PA between 450-900+ min was associated with lower odds of developing pain in neck/cervical spine. Several epidemiological studies have demonstrated that certain postures sustained for prolonged duration combined with sedentary lifestyle were associated with neck pain.²²⁻²⁴ Therefore, increased PA levels may be helpful to consider in those at risk for neck pain.

Association between PA and thoracic spine has been less explored,²⁵ but a recent observational study found that PA less than 150 min per week was associated with reduced thoracic mobility.²⁶ Our findings build on previous research in that PA less than 150 min per week is also associated with higher odds of developing pain in the thoracic spine. Page 11 of 22

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While it is generally accepted that PA and exercise are beneficial in the management of acute and chronic low back pain, a previous systematic review could not identify either positive or negative relationship.²⁷ One study suggested that the relationship between the level of activity and back pain might be explained by a U-shaped curve that suggests both low and excessive PA may increase the risk of low back pain.²⁸ Our findings partly support this concept as PA of 450-750 min was associated with lower odds of low back pain while lower or higher PA than that range did not have significant association.

Beneficial effects of PA in the range of 300-600 min were also noted in several locations in the upper extremity such as elbow, forearm, wrist, hand, and fingers. PA exceeding 750 min was associated with higher odds of shoulder pain. The underlying mechanisms of how PA modulates pain are not completely understood, but several pathways have been proposed. Animal study findings suggest regular PA may act on the central nervous system (CNS) and alter rate of pain hypersensitivity, dysregulation of pain modulation, and development of chronic pain.²⁹⁻³¹ In humans, it has been proposed that PA may intervene excitability and inhibition in the CNS,³²⁻³⁴ and anti-inflammatory and antioxidant effects of regular PA might diminish the processes contributing to central sensitization.³⁵⁻³⁷ Other proposed mechanisms in humans include the activation of opioid and serotonin pathways³⁸ or involvement of endocannabinoid system³⁹ induced from regular PA which could exert analgesic effects. While further research is needed to elucidate how much and what type of PA can induce such changes to modulate pain, our results suggest that PA between 300-600 mins per week may be sufficient for spinal conditions and upper extremity pain, with PA exceeding 750 min associated with higher likelihood of shoulder pain.

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Association of PA and lower extremity pain

The association of PA to lower extremity pain was different than what was observed for upper extremity and spine conditions. Our results suggest PA exceeding 450 min was associated with higher odds of MSK-pain in lower extremity. These findings may be partially explained by higher amounts of PA are likely to involve greater use of the lower extremity. In the United States, it has been reported that walking is the most popular form of exercise followed by biking, yard work, strength training, dancing, and running, which are activities that commonly place physical demands through the lower extremity.⁴⁰ Running is one of the most popular exercises in the world and has been shown to result in lower extremity pain in multiple anatomical locations with nearly all (94.7% of runners) reporting experience of pain at least once after running.⁴¹

We also observed that greater PA was associated with a higher number of sites of MSKpain in the lower extremity. A dose response was observed: 450-600 min was associated with pain in three anatomical regions, 600-750 min with pain in four anatomical regions, 750-900 min with five anatomical regions, and 900+ min with six anatomical regions. The optimal PA level to reduce pain in those with existing musculoskeletal lower extremity pain is unknown. A prior study reported that a minimum of 45 total moderate-vigorous min per week was sufficient to elicit improved or sustained high function with lower-extremity symptoms regardless of age, gender, body mass index, or presence of knee osteoarthritis.⁴² Our findings of PA ranging from 150-450 min not increasing the odds of having pain in the lower extremities suggest this range might be appropriate to be safe and promote other health benefits.

Clinical implication

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While the WHO 2020 guidelines on PA recommend 150-300 min of moderate-intensity PA, or 75-150 min of vigorous-intensity PA, or some equivalent combination of moderateintensity and vigorous-intensity aerobic PA per week for optimal health outcomes,¹⁰ the current study suggests that more PA beyond the WHO recommendation may be necessary to decrease the odds of developing pain particularly in the upper extremity. Our findings suggest a target of 300-450 min of PA per week could be optimal for preventing pain in the upper extremity without clear associated higher rate of lower extremity pain. Recognizing concerns on higher prevalence of pain in low back, neck, and thoracic spine increased during the COVID-19 pandemic,¹⁷ PA target of the higher target of 450 min of PA may not be advisable for those with increased concern for lower extremity pain.

Limitation

While our findings are derived from a large-scale multinational study of participants, we do note potential limitations. Self-report of PA and MSK-pain are limited by reporting bias and inaccuracy including risk for over-reporting level of PA.^{43 44} The cross-sectional study design limits our understanding between PA and the etiology of MSK-pain. We are limited in ability in discriminating the types of PA to report of MSK-pain by anatomical locations. Further prospective cohort or interventional studies may further elucidate the best form and dose of PA to address MSK-pain by anatomical location and specific musculoskeletal injury, and additionally investigate the role of MSK-pain intensity instead of using a binary (yes/no) classification.

CONCLUSION

Our findings suggest that PA time above the WHO recommendations may prevent pain in multiple locations such as neck, thoracic spine, low back, and in the upper extremities. Especially, undertaking PA for 300-450 min per week may be most beneficial. However, selective individuals who are prone to injuries or suffer from existing degenerative changes in lower extremities may need to be more cautious when exercising above 450 min per week.

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Data Availability Statement: Data are available upon reasonable request

Ethics Statements

-Ethics approval: This study was approved by the ethics committee of the lead university (Goethe University Frankfurt) and also locally from the partners in the participating countries.

-Digital informed consent was obtained from all subjects involved in the study.

Authors Contribution: HCR/AT: data collection, interpretation, drafting and critical revision of the manuscript, LM, KH, LV, DG: data collection, critical revision of the manuscript, JW: conception/design, data collection, interpretation, critical revision of the manuscript

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Table 1. Association of PA with MSK-Pain by Anatomical Locations

		Dose of WHO Guideline-Based PA											
Location of	150-300 min		300-450 min		450-600 min		600-750 min		750-900 min		900+ min		
MSK-Pain	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted O	
	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI	
Neck/Cervical	0.89	0.99	0.76	0.89	0.66	0.78	0.62	0.75	0.63	0.82	0.59	0.78	
	(0.79-1.01)	(0.87-1.12)	(0.67-0.88)	(0.77-1.03)	(0.57-0.76)	(0.67-0.91)	(0.52-0.74)	(0.62-0.90)	(0.52-0.77)	(0.67-1.00)	(0.52-0.67)	(0.68-0.8	
Shoulder	0.87	0.92	0.87	0.94	0.83	0.93	0.80	0.88	1.10	1.27	0.98	1.16	
Shoulder	(0.75-1.00)	(0.79-1.06)	(0.74-1.02)	(0.79-1.10)	(0.71-0.99)	(0.79-1.11)	(0.66-0.98)	(0.72-1.08)	(0.90-1.34)	(1.04-1.56)	(0.85-1.13)	(1.00-1.3	
Upper arm	0.77	0.98	0.60	0.81	0.56	0.76	0.62	0.81	0.89	1.23	0.73	1.01	
opp u ann	(0.60-1.00)	(0.76-1.27)	(0.44-0.81)	(0.60-1.11)	(0.41-0.77)	(0.54-1.05)	(0.42-0.89)	(0.55-1.19)	(0.63-1.28)	(0.85-1.80)	(0.56-0.94)	(0.77-1.3	
Elbow	0.73	0.77	0.64	0.70	0.95	0.99	0.92	0.93	0.90	0.94	1.19	1.30	
	(0.54-0.97)	(0.57-1.03)	(0.46-0.89)	(0.50-0.98)	(0.70-1.30)	(0.72-1.37)	(0.64-1.32)	(0.64-1.37)	(0.60-1.34)	(0.62-1.42)	(0.93-1.53)	(0.99-1.7	
Forearm	0.91 (0.65-1.28)	1.08 (0.76-1.52)	0.53 (0.34-0.82)	0.63 (0.40-0.99)	0.72 (0.47-1.07)	0.85 (0.55-1.30)	0.80 (0.50-1.29)	0.96 (0.59-1.55)	0.74 (0.43-1.26)	0.90 (0.52-1.54)	0.98 (0.70-1.36)	1.17	
	0.86	1.07	0.57	0.74	0.63	0.81	0.79	1.00	0.71	0.95	0.86	(0.82-1.6	
Wrist	0.80	(0.86-1.34)	(0.43-0.74)	(0.57-0.98)	(0.03) (0.48-0.82)	(0.62-1.07)	(0.58-1.06)	(0.74-1.37)	(0.50-0.99)	(0.67-1.34)	(0.70-1.07)	(0.91-1.4	
	0.68	0.81	0.43-0.74	0.57	0.47	0.62-1.07)	0.60	0.74	0.60	0.77	0.57	<u>0.91-1.4</u> 0.74	
Hand	(0.53-0.88)	(0.62-1.05)	(0.32-0.61)	(0.40-0.79)	(0.34-0.66)	(0.41-0.83)	(0.41-0.87)	(0.50-1.09)	(0.40-0.91)	(0.50-1.18)	(0.44-0.75)	(0.56-0.9	
	0.85	0.91	0.63	0.72	0.65	0.71	0.80	0.93	0.71	0.81	0.75	0.84	
Fingers	(0.66-1.10)	(0.70-1.19)	(0.46-0.86)	(0.52-0.99)	(0.47-0.86)	(0.51-0.99)	(0.56-1.14)	(0.65-1.34)	(0.48-1.07)	(0.53-1.22)	(0.58-0.98)	(0.64-1.1	
	0.75	0.77	0.83	0.90	0.71	0.78	0.69	0.74	0.54	0.64	0.63	0.77	
Thoracic spine	(0.63-0.90)	(0.64-0.93)	(0.69-1.02)	(0.74-1.10)	(0.58-0.88)	(0.63-0.97)	(0.54-0.89)	(0.57-0.97)	(0.40-0.73)	(0.47-0.87)	(0.52-0.76)	(0.63-0.9	
D.1	0.85	0.98	0.74	0.88	0.60	0.74	1.04	1.18	0.69	0.88	0.78	0.90	
Ribs	(0.59-1.21)	(0.68 - 1.42)	(0.49-1.11)	(0.58-1.34)	(0.38-0.95)	(0.46-1.17)	(0.66-1.62)	(0.73-1.88)	(0.39-1.22)	(0.50-1.57)	(0.54-1.11)	(0.62-1.3	
T	0.91	0.93	0.85	0.91	0.77	0.84	0.69	0.76	0.85	0.96	0.79	0.93	
Lower back	(0.80-1.03)	(0.82 - 1.06)	(0.73-0.97)	(0.78-1.05)	(0.67-0.90)	(0.72-0.97)	(0.57-0.82)	(0.63-0.91)	(0.71-1.03)	(0.79-1.16)	(0.70-0.90)	(0.81-1.0	
A la daman	0.70	0.94	0.45	0.61	0.68	0.97	0.67	0.89	0.91	1.33	0.60	0.82	
Abdomen	(0.52-0.95)	(0.69 - 1.28)	(0.31-0.67)	(0.41-0.91)	(0.48-0.97)	(0.68-1.40)	(0.44-1.02)	(0.57-1.37)	(0.60-1.38)	(0.87-2.05)	(0.44-0.83)	(0.59-1.1-	
Pelvis/Gluteals	1.00	1.11	0.77	0.86	0.92	1.13	1.02	1.15	0.96	1.19	1.10	1.37	
Pervis/Giulears	(0.78-1.28)	(0.86-1.43)	(0.57-1.03)	(0.64-1.17)	(0.69-1.23)	(0.84-1.52)	(0.74-1.41)	(0.81-1.62)	(0.67-1.39)	(0.82-1.73)	(0.86-1.40)	(1.06-1.7	
Hip	1.06	1.05	0.93	0.96	1.05	1.09	0.93	0.97	1.24	1.37	0.97	1.17	
mp	(0.87-1.30)	(0.85-1.29)	(0.74-1.17)	(0.76-1.21)	(0.84-1.32)	(0.87-1.38)	(0.71-1.22)	(0.73-1.29)	(0.94-1.63)	(1.03-1.81)	(0.79-1.18)	(0.95-1.4	
Groin	0.94	1.04	0.72	0.80	0.98	1.05	1.08	1.20	1.31	1.40	1.28	1.40	
GIUII	(0.65-1.34)	(0.72-1.49)	(0.47-1.10)	(0.52-1.23)	(0.65-1.46)	(0.69-1.59)	(0.69-1.71)	(0.75-1.91)	(0.83-2.10)	(0.87-2.27)	(0.92-1.79)	(0.99-1.9	
Thigh	0.99	1.13	0.87	0.99	1.24	1.41	1.39	1.59	1.60	1.82	1.37	1.51	
	(0.75-1.31)	(0.85-1.51)	(0.63-1.19)	(0.71-1.38)	(0.92-1.68)	(1.03-1.92)	(0.99-1.95)	(1.13-2.25)	(1.13-2.27)	(1.28-2.61)	(1.05-1.78)	(1.15-1.9	
Knee	1.02	1.08	1.04	1.10	1.17	1.25	1.12	1.22	1.43	1.55	1.16	1.30	
Trifee	(0.88-1.19)	(0.92-1.25)	(0.88-1.22)	(0.93-1.30)	(0.99-1.37)	(1.06-1.50)	(0.93-1.36)	(1.01-1.49)	(1.18-1.75)	(1.27-1.90)	(1.00-1.34)	(1.12-1.5	
Lower leg	0.77	0.93	0.82	1.04	1.02	1.31	1.14	1.43	0.95	1.22	1.03	1.34	
	(0.59-1.00)	(0.71-1.21)	(0.62-1.07)	(0.78-1.39)	(0.77-1.34)	(0.98-1.73)	(0.83-1.55)	(1.04-1.97)	(0.66-1.36)	(0.85-1.77)	(0.81-1.31)	(1.04-1.7	
Ankle/Achilles	1.09	1.14	1.19	1.24	1.42	1.47	1.48	1.55	1.70	1.79	1.69	1.85	
	(0.87-1.36)	(0.90-1.43)	(0.93-1.52)	(0.96-1.59)	(1.12-1.81)	(1.14-1.88)	(1.12-1.94)	(1.17-2.06)	(1.28-2.26)	(1.34-2.40)	(1.37-2.08)	(1.49-2.3)	
Foot/Toes	1.22	1.28	1.12	1.25	1.08 (0.84-1.38)	1.24	1.10	1.26 (0.93-1.71)	1.23	1.50	1.17	1.53	
	(0.99-1.52)	(1.02-1.60)	(0.88-1.42)	(0.98-1.61)	(0.84-1.38)	(0.96-1.60)	(0.82-1.47)	(0.93-1./1)	(0.91-1.67)	(1.10-2.05)	(0.94-1.45)	(1.22-1.9)	

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Abbreviations: CI, Confidence Interval; MSK, Musculoskeletal; OR, Odds Ratio; PA, Physical Activity; WHO, World Health Organization Footnote: A group of participants who did not meet the WHO recommendations of PA (i.e. PA less than 150 min per week) was set as the reference group. The model was adjusted for sex, age, employment status, and depression risk.

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2	Number of	Dose of WHO Guideline-Based PA											
3 4	MSK-Pain	150-300 min		300-450 min		450-600 min		600-750 min		750-900 min		900+ min	
5	Locations	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
6 7 8	Minimum 1 location	1.06 (0.95-1.18)	1.10 (0.98-1.23)	1.04 (0.93-1.17)	1.12 (0.99-1.27)	1.01 (0.89-1.14)	1.11 (0.98-1.26)	0.92 (0.80-1.06)	1.04 (0.90-1.20)	1.09 (0.80-1.28)	1.28 (1.10-1.51)	1.05 (0.94-1.17)	1.30 (1.16-1.45)
9 10	Minimum 3 locations	0.89 (0.78-1.01)	0.97 (0.85-1.11)	0.80 (0.70-0.93)	0.90 (0.78-1.04)	0.80 (0.69-0.93)	0.93 (0.80-1.08)	0.86 (0.72-1.02)	1.00 (0.84-1.19)	0.93 (0.77-1.12)	1.12 (0.93-1.36)	0.88 (0.77-0.99)	1.08 (0.94-1.23)
11 12	Minimum 5 locations	0.76 (0.62-0.93)	0.84 (0.69-1.03)	0.65 (0.51-0.82)	0.75 (0.60-0.95)	0.61 (0.48-0.78)	0.73 (0.57-0.93)	0.74 (0.56-0.97)	0.85 (0.64-1.13)	0.87 (0.66-1.16)	1.09 (0.82-1.45)	0.83 (0.68-1.01)	1.06 (0.87-1.29)
13 14	Minimum 10 locations	0.70 (0.45-1.07)	0.76 (0.49-1.17)	0.32 (0.17-0.61)	0.36 (0.19-0.68)	0.57 (0.34-0.98)	0.64 (0.37-1.10)	0.64 (0.35-1.19)	0.67 (0.35-1.40)	0.62 (0.31-1.23)	0.70 (0.35-1.40)	0.61 (0.39-0.95)	0.67 (0.42-1.06)

Table 2. Association of PA with the Number of MSK-Pain Locations

Abbreviations: CI, Confidence Interval; MSK, Musculoskeletal; OR, Odds Ratio; PA, Physical Activity; WHO, World Health Organization Footnote: A group of participants who did not meet the WHO recommendations of PA (i.e. PA less than 150 min per week) was set as the reference group. The model was adjusted for sex, age, employment status, and depression risk. Tëssion no.

Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	
measurement		comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5-6
		(b) Describe any methods used to examine subgroups and interactions	5-6
		(c) Explain how missing data were addressed	5-6
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
	ļ	(e) Describe any sensitivity analyses	N/A
Results			

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	6
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	7-8
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	7-8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Association between physical activity and musculoskeletal pain: an analysis of international data from the ASAP survey

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Association between physical activity and musculoskeletal pain: an

analysis of international data from the ASAP survey

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ABSTRACT

Objective: To investigate the association of physical activity (PA) with musculoskeletal pain (MSK-pain).

Design: Cross-sectional study

Setting: 14 countries (Argentina, Australia, Austria, Brazil, Chile, France, Germany, Italy, the Netherlands, Singapore, South Africa, Spain, Switzerland, and the United States of America)

Participants: Individuals aged 18 or older living in participating countries.

Primary and secondary outcome measures: PA volumes were assessed with an adapted version of the Nordic Physical Activity Questionnaire-short (NPAQ-short). Prevalence of MSK-pain was captured by means of a 20-item checklist of body locations. Based on the WHO recommendation on PA, participants were classified as non-compliers (0-150 min/week), compliers (150-300 min/week), double compliers (300-450 min/week), triple compliers (450-600 min/week), quadruple compliers (600-750 min/week), quintuple compliers (750-900 min/week), and top compliers (more than 900 min/week). Multivariate logistic regression was used to obtain adjusted odds ratios of the association between PA and MSK-pain for each body location, correcting for age, sex, employment status, and depression risk.

Results: A total of 13,741 participants completed the survey. Compared to non-compliers, compliers had smaller odds of MSK-pain in one location (thoracic pain, OR 0.77, CI 0.64-0.93). Double compliance was associated with reduced pain occurrence in six locations (elbow, OR 0.70, CI 0.50-0.98; forearm, OR 0.63, CI 0.40-0.99; wrist, OR 0.74, CI 0.57-0.98; hand, OR 0.57, CI 0.40-0.79; fingers, OR 0.72, CI 0.52-0.99; abdomen, OR 0.61, CI 0.41-0.91). Triple to top compliance was also linked with lower odds of MSK-pain (five locations in triple compliance, three in quadruple compliance, two in quintuple compliance, three in top compliance), but, at the same time, presented increased odds of MSK-pain in some of the other locations.

Conclusion: A dose of 300-450 min WHO-equivalent PA/week was associated with reduced MSK-pain. On the other hand, excessive doses of PA were associated with increased pain in certain body locations.

Strengths and Limitations of this study

- This is the first large-scale analysis of associations between MSK pain and PA considering multiple anatomical locations
- Large sample size enabled to investigate the associations between different degrees of compliance to physical activity recommended by WHO and MSK-pain
- Administration of the survey in 14 countries allowed participation of diverse populations
- Self-reported data may be subject to recall bias
- Cross-sectional observational design prohibits causal inference

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INTRODUCTION

Musculoskeletal pain (MSK-pain) is a common condition that can have negative physical, psychological, and social impacts.¹ A summary of previous epidemiological studies conducted with diverse techniques and populations revealed that MSK-pain affects between 13.5% and 47% of the general population with prevalence higher in women and increasing strongly with age.² Musculoskeletal conditions contribute to disability, especially in older age groups.² It has been reported that disability-adjusted life-years (DALYs), which reflects the years of life lost due to premature mortality and years of life lived with disability, increased by 62% between 1990 and 2016 around the world with 20% surge during the ten-year interval from 2006 to 2016.³ Most of the increased burden has derived from disability due to increased aging population affected by MSK conditions, , and the burden of MSK disorders is expected to increase even more in the future.⁴

Achieving sufficient physical activity (PA) is associated with a variety of positive health outcomes such as substantial risk reduction in all-cause mortality⁵ as well as multiple chronic diseases including type 2 diabetes and metabolic syndrome,⁶ cancer,⁶ and cardiovascular disease.⁷ In the light of these positive impacts, World Health Organization (WHO) recommends 150-300 min of moderate-intensity PA, or 75-150 min of vigorous-intensity PA, or aerobic PA with some combination of moderate and vigorous intensities.⁸ PA is also considered one of the most important strategies to prevent and manage MSK pain.⁹ However, compared to the number of studies investigating the association of PA with non-communicable disease, there seems to be a literature gap regarding MSK-pain. Furthermore, it is still less clear whether the amounts recommended by WHO are sufficient to elicit benefits in terms of addressing MSK-pain. The few available studies examining the relation of regular PA and MSK-pain tended to focus on

influence of PA for specific body locations or specific diagnoses such as low back pain, neck pain, or osteoarthritis and found inconsistent results.¹⁰ Other studies have evaluated the associations between PA and pain in occupational settings such as among physical therapists or teaching staff.^{11 12} Particularly, the interplay between the volume of PA and MSK-pain within the general population has been less explored.

The purpose of this study was to investigate the association of total PA with MSK-pain in a variety of anatomical locations including both upper and lower extremities. We hypothesize that greater time spent in PA than WHO recommendation would be associated with reduction of MSK-pain, but excess time performing PA might be associated with higher MSK-pain.

METHODS

Study Design

This article presents an explorative analysis of pre-pandemic baseline data on PA and MSK-pain assessed during the ASAP (Activity and Health during the SARS-CoV-2 Pandemic) survey. The survey was administered with results collected between April 3 and May 9, 2020, including participants from 14 countries (Argentina, Australia, Austria, Brazil, Chile, France, Germany, Italy, the Netherlands, Singapore, South Africa, Spain, Switzerland, and the United States of America (USA)).¹³⁻¹⁶ Ethical approval was obtained from the ethics committees of the study center and collaborating institutions. All participants provided digital informed consent.

Participants

Eligibility for participation in the ASAP survey was limited to individuals aged 18 or older living in participating countries. Recruitment was performed online using promotion by

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health-related organizations, mailing lists, and social media advertising (e.g. Facebook, Instagram, Twitter).

Questionnaire

To capture PA, the ASAP survey incorporated an adapted version of the Nordic Physical Activity Questionnaire-short (NPAQ-short). The instrument retrospectively assessed the amounts of moderate and combined moderate and vigorous activities (min/week) during leisure and occupational time. Moderate activities were defined as those that increase heart rate or breathing, and vigorous activities were defined as those that make heart racing, sweating, and shortness of breath. The questionnaire asked how much time participants spent in total on both moderate and vigorous PA on a typical week, and the time spent in all activities with a minimal duration of 10 minutes was asked to be added and entered in the form. The NPAQ-short has been shown to be reliable (test-retest reliability: rho = 0.80 to 0.82) and valid for observing compliance with the WHO recommendations on PA.¹⁷ The questionnaire was available in 7 different languages (Dutch, English, German, French, Italian, Brazilian-Portuguese, Spanish), and clarity and comprehensibility were validated by native speakers through forward and backward translation.

Prevalence of MSK-pain was captured by means of binary responses (yes/no) to an adapted 20-item checklist from a consensus statement on epidemiological injury reporting.¹⁸ Body locations were categorized as follows: neck/cervical spine, shoulder, upper arm, elbow, forearm, wrist, hand, fingers, thoracic spine, ribs, lower back, abdomen, pelvis/gluteal, hip, groin, thigh, knee, lower leg, ankle/Achilles tendon, foot/toe.

The English version of the ASAP survey can be found in Supplemental File 1.

Data Processing and Statistical Analysis

Self-reported PA was categorized as multiples of compliance with WHO guidelines which recommend 150-300 minutes/week of moderate activity, 75-150 minutes/week of vigorous activity, or any adequate combination of both.⁸ We used the formula (minutes of moderate-to-vigorous PA – minutes of vigorous PA) + minutes of vigorous PA *2 to classify participants as non-compliers (0-150 min/week), compliers (150-300 min/week), double compliers (300-450 min/week), triple compliers (450-600 min/week), quadruple compliers (600-750 min/week), quintuple compliers (750-900 min/week), and top compliers (more than 900 min/week).

For each body region, univariate logistic regression was conducted to calculate the unadjusted odds ratio (OR) of the association between pain (dependent variable) and PA. In a similar way, univariate logistic regression was then used to identify associations of pain (dependent variable) and potential confounding variables (sex, age, employment status, depression risk). Finally, multivariate logistic regression was performed including these confounding variables (if relevant) to obtain the adjusted ORs and 95% confidence interval (CI) of the association between the volume of PA and pain. All data analyses were conducted using SPSS 22 (SPSS INC., Armonk, NY, USA), and the significance level was set to $\alpha = 0.05$.

Patient and Public Involvement

Members of the target population without medical background were involved in the designing phase of the ASAP questionnaire. The questionnaire was face validated for each

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language with five non-academic individuals. Feedback on comprehension and clarity of the wording was used.

RESULTS

Valid datasets were identified for 13,741 participants (38 ± 15 years, minimum 18 and maximum 100, 59% females). The demographic data are summarized in the Table 1. 2604 individuals did not meet the WHO recommendation of PA while n=2735 belonged to 150-300 min group, n=1957 to 300-450 min group, n=1749 to 450-600 min group, n=1066 to 600-750 min group, n=849 to 750-900 min group, and n=2781 to 900+ min group. Comprehensive results are summarized in the Table 2 and 3.

Compared to inactive individuals, simple compliance was associated with reduced MSKpain in one body location (thoracic pain, OR 0.77, CI 0.64-0.93 Table 1). Double compliance increased the number of locations with less pain to six (elbow, OR 0.70, CI 0.50-0.98; forearm, OR 0.63, CI 0.40-0.99; wrist, OR 0.74, CI 0.7-0.98; hand, OR 0.57, CI 0.40-0.79; fingers, OR 0.72, CI 0.52-0.99; abdomen, OR 0.61, CI 0.41-0.91). Although higher amounts of PA were linked to lower pain levels to a variable degree (five body locations in triple compliance, three in quadruple compliance, two in quintuple compliance, three in top compliance), they also showed increased pain in other locations. Specifically, triple compliance was associated with higher pain in thigh (OR 1.41, CI 1.03-1.92), knee (OR 1.25, CI 1.06-1.50), and ankle/Achilles tendon (OR 1.47, CI 1.14-1.88). Quadruple compliance increased pain locations to four, quintuple compliance to six, and top compliance to seven.

Triple compliance was associated with lower odds to have a total of 5 or more (OR 0.75, CI 0.60-0.95) or 10 or more (OR 0.36, CI 0.19-0.68) pain locations, and quadruple compliance

was associated with lower odds to have 5 or more pain locations (OR 0.73, CI 0.57-0.93). However, quintuple and top compliances were associated with higher odds of having a minimum one pain location (OR 1.28, CI 1.10-1.51 and 1.30, CI 1.16-1.45 respectively).

DISCUSSION

The purpose of the present study was to understand the relation between PA and MSKpain. Previous research focused on the impact of PA on specific locations of MSK-pain (e.g., low back and neck¹⁹) or certain occupational settings.^{11 12} Our large-scale multinational study is novel in that it identified the associations between different degrees of compliance to PA recommended by WHO and multiple body locations in the general population after adjusting for multiple cofounding factors including age, which is known to be positively associated with MSK-pain prevalence.

Guideline compliance (150-300 min per week) was weakly associated with MSK pain, showing lower odds of having pain only in thoracic spine but higher odds in foot/toes. In contrast, double compliance (300-450 min per week) substantially increased the number of beneficial associations to six and thus seems to represent the optimal dose when PA is undertaken to prevent MSK. Finally, higher levels of PA (triple to top compliance) were associated with less odds of having pain in multiple upper body locations but paradoxically contributed to higher odds of lower extremity pain. Notably, participating in 300-600 min of PA per week was associated with lower odds of having pain in upper extremities, neck, and thoracic and lumbar spine. In contrast, participating in greater than 450 min of PA per week was associated with higher odds of having pain in the lower extremity.

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Time spent in PA and pain in neck, back, and upper extremity

A previous systematic review showed that there was limited evidence for no association between PA and neck pain.¹⁹ However, our study found that participating in PA between 450-900+ min was associated with lower odds of having pain in neck/cervical spine. Several epidemiological studies have demonstrated that certain postures sustained for prolonged duration combined with sedentary lifestyle were associated with neck pain.²⁰⁻²² Therefore, increased PA levels may be helpful to consider in those at risk for neck pain.

Association between PA and thoracic spine has been less explored,²³ but a recent observational study found that PA less than 150 min per week was associated with reduced thoracic mobility.²⁴ Our findings build on previous research in that PA less than 150 min per week is also associated with higher odds of having pain in the thoracic spine.

While it is generally accepted that PA and exercise are beneficial in the management of acute and chronic low back pain, a previous systematic review could not identify either positive or negative relationship.²⁵ One study suggested that the relationship between the level of activity and back pain might be explained by a U-shaped curve that suggests both low and excessive PA may increase the risk of low back pain.²⁶ Our findings partly support this concept as PA of 450-750 min was associated with lower odds of low back pain while lower or higher PA than that range did not have significant association.

PA in the range of 300-600 min was also associated with lower odds of having pain in several locations in the upper extremity such as elbow, forearm, wrist, hand, and fingers. PA exceeding 750 min was associated with higher odds of shoulder pain. The underlying mechanisms of how PA modulates pain are not completely understood, but several pathways have been proposed. Animal study findings suggest regular PA may act on the central nervous

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system (CNS) and alter rate of pain hypersensitivity, dysregulation of pain modulation, and development of chronic pain.²⁷⁻²⁹ In humans, it has been proposed that PA may intervene excitability and inhibition in the CNS,³⁰⁻³² and anti-inflammatory and antioxidant effects of regular PA might diminish the processes contributing to central sensitization.³³⁻³⁵ Other proposed mechanisms in humans include the activation of opioid and serotonin pathways³⁶ or involvement of endocannabinoid system³⁷ induced from regular PA which could exert analgesic effects. While further research is needed to elucidate how much and what type of PA can induce such changes to modulate pain, our results suggest that PA between 300-600 mins per week may be sufficient for spinal conditions and upper extremity pain, with PA exceeding 750 min associated with higher likelihood of shoulder pain.

Association of PA and lower extremity pain

The association of PA to lower extremity pain was different than what was observed for upper extremity and spine conditions. Our results suggest PA exceeding 450 min was associated with higher odds of MSK-pain in lower extremity. These findings may be partially explained by higher amounts of PA are likely to involve greater use of the lower extremity. In the United States, it has been reported that walking is the most popular form of exercise followed by biking, yard work, strength training, dancing, and running, which are activities that commonly place physical demands through the lower extremity.³⁸ Running is one of the most popular exercises in the world and has been shown to result in lower extremity pain in multiple anatomical locations with nearly all (94.7% of runners) reporting experience of pain at least once after running.³⁹

We also observed that greater PA was associated with a higher number of sites of MSKpain in the lower extremity. A dose response was observed: 450-600 min was associated with

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pain in three anatomical regions, 600-750 min with pain in four anatomical regions, 750-900 min with five anatomical regions, and 900+ min with six anatomical regions. The optimal PA level to reduce pain in those with existing musculoskeletal lower extremity pain is unknown. A prior study reported that a minimum of 45 total moderate-vigorous min per week was sufficient to elicit improved or sustained high function with lower-extremity symptoms regardless of age, gender, body mass index, or presence of knee osteoarthritis.⁴⁰ Our findings of PA ranging from 150-450 min not increasing the odds of having pain in the lower extremities suggest this range might be appropriate to be safe and promote other health benefits.

Clinical implication

While the WHO 2020 guidelines on PA recommend 150-300 min of moderate-intensity PA, or 75-150 min of vigorous-intensity PA, or some equivalent combination of moderateintensity and vigorous-intensity aerobic PA per week for optimal health outcomes,⁸ the current study suggests that more PA beyond the WHO recommendation may be necessary to decrease the odds of having pain particularly in the upper extremity. Our findings suggest a target of 300-450 min of PA per week could be optimal for preventing pain in the upper extremity without clear associated higher rate of lower extremity pain. Also, this range was associated with lower odds of having pain in multiple number of locations. Recognizing concerns on higher prevalence of pain in low back, neck, and thoracic spine increased during the COVID-19 pandemic,¹⁵ PA target of the higher target of 450 min of PA may not be advisable for those with increased concern for lower extremity pain. Furthermore, PA above 750 minutes was associated with having at least one pain location.

Limitation

While our findings derived from a large-scale multinational study of participants, we do note potential limitations. Self-report of PA and MSK-pain are limited by reporting bias and inaccuracy including risk for over-reporting level of PA.^{41 42} The cross-sectional study design limits our understanding between PA and the etiology of MSK-pain. Also, we are limited in ability in discriminating the types of PA to report of MSK-pain by anatomical locations. We were not able to distinguish or identify bilateral MSK-pain from our questionnaire as well. Furthermore, because a separate analysis was run for each body region, there is a risk of multiple testing problem. Since our analysis was explorative in nature, further prospective cohort or interventional studies are needed to elucidate the best form and dose of PA to address MSK-pain by anatomical location and specific musculoskeletal injury, and additionally investigate the role of MSK-pain intensity instead of using a binary (yes/no) classification.

CONCLUSION

Our findings showed that PA time above the WHO recommendations was associated with lower odds of having pain in multiple locations such as neck, thoracic spine, low back, and in the upper extremities. Especially, undertaking PA for 300-450 min per week was associated with reduced pain occurrence in six locations, elbow, forearm, wrist, hand, fingers, and abdomen.

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Ethics Statements

-Ethics approval: This study was approved by the University of Queensland Health and Behavioural Sciences, Low & Negligible Risk Ethics Sub-Committee, Ethics Committee of Karl Franzens University Graz, Research Ethics Committee of Fundación Instituto Superior de Ciencias de la Salud, Research Ethics Committee of the Universidade Cidade de São Paulo, Institutional Ethics Committee of the University of Santiago de Chile, Saint-Etienne University Hospital Ethical Committee, Ethics Committee of the Faculty of Psychology and Sports Sciences of Goethe University, Comitato di Ateneo per la Ricerca, Università degli Studi di Roma "Foro Italico", Medical Ethical Committee of Amsterdam UMC, Institutional Research Ethics Committee of Durban University of Technology, SingHealth Centralised Institutional Review Board, Cantonal Ethics Committee Northwest Switzerland, Ethics Committee of Universidad Politécnica de Madrid, and Partners Human Research Committee

-Digital informed consent was obtained from all subjects involved in the study.

Authors Contribution: HCR/AT: data collection, interpretation, drafting and critical revision of the manuscript, LM, KH, LV, DG: data collection, critical revision of the manuscript, JW: conception/design, data collection, interpretation, critical revision of the manuscript

Competing interests: None declared.

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Table 1. Demographic data of the participants by countries

Country	ARG	AUS	AUT	BRA	CHE	CHL	DEU	ESP	FRA	ITA	NLD	SGP	USA	ZAF	Others	Total
Sex (M/F)	429/494	56/248	192/546	620/948	115/212	471/766	696/1356	310/277	1200/1046	348/453	50/129	437/434	364/711	236/293	108/122	5632/8035
Age	37.1	41.6	27.3	34.2	37.3	31.5	40.4	43.0	43.3	38.5	47.5	40.1	43.1	32.4	40.0	38.3
(SD)	(15.4)	(14.1)	(9.6)	(10.6)	(11.5)	(13.6)	(16.3)	(13.4)	(16.9)	(15.3)	(14.0)	(12.1)	(14.0)	(14.3)	(13.5)	(15.1)
WHO-5	54.3	50.1	55.0	53.0	50.4	54.7	52.9	49.2	48.3	56.3	49.0	52.2	49.4	52.2	51.2	52.0
(SD)	(17.8)	(14.8)	(16.5)	(16.0)	(15.2)	(18.2)	(17.0)	(15.8)	(14.8)	(17.3)	(14.7)	(17.6)	(14.9)	(21.1)	(17.2)	(16.8)
Employment (Yes, %)	61.9	86.8	62.7	78.8	96.0	59.2	73.2	79.8	69.9	65.9%	77.1	88.8	84.1	53.7	85.0	72.8
MVPA	488.7	352.3	384.6	396.4	379.0	385.7	438.6	493.2	527.9	566.2	506.5	376.5	401.0	310.6	437.8	439.5
(SD)	(596.2)	(340.0)	(408.7)	(454.9)	(458.1)	(518.3)	(481.3)	(617.0)	(516.0)	(635.3)	(420.5)	(445.7)	(348.0)	(455.8)	(529.7)	(498.7)
VPA	218.7	121.3	141.4	202.0	130.6	153.9	146.9	188.4	234.7	247.2	200.2	171.0	195.9	144.1	203	186.4
(SD)	(338.0)	(152.4)	(206.5)	(305.7)	(152.6)	(287.9)	(226.5)	(295.2)	(343.3)	(350.1)	(225.7)	(302.4)	(230.0)	(272.7)	(275.6)	(288.8)

Abbreviations: F, Female; M, Male; MVPA, Moderate to Vigorous Physical Activity; SD, Standard Deviation; VPA, Vigorous Physical Activity, WHO-5, The 5item World Health Organization Well-Being Index

Country Abbreviations: ARG, Argentina; AUS, Australia; AUT, Austria; BRA, Brazil; CHE, Switzerland; CHL, Chile; DEU, Germany; ESP, Spain; FRA, France; ITA, Italy; NLD, Netherlands; SGP, Singapore; USA, United States of America; ZAF, South Africa mericā; ZAL, _

Adjusted OR

(95% CI)

0.78

(0.68 - 0.89)

1.16

(1.00-1.34)

1.01

(0.77 - 1.33)

1.30

(0.99-1.70)

1.17

(0.82 - 1.65)

1.15

(0.91 - 1.44)

0.74

(0.56 - 0.99)

0.84

(0.64 - 1.11)

0.77

(0.63 - 0.93)

0.90

(0.62 - 1.36)

0.93

(0.81 - 1.06)

0.82

(0.59-1.14)

1.37

(1.06 - 1.76)

1.17

(0.95 - 1.45)

1.40

(0.99-1.99)

1.51

(1.15 - 1.99)

1.30

(1.12 - 1.51)

1.34

(1.04 - 1.73)

1.85

(1.49-2.31)

1.53

(1.22 - 1.92)

Dose of WHO Guideline-Based PA Location of 150-300 min 300-450 min 600-750 min 750-900 min 900+ min 450-600 min MSK-Pain Crude OR Adjusted OR Crude OR (95% CI) 0.89 0.99 0.76 0.89 0.66 0.78 0.62 0.75 0.63 0.82 0.59 Neck/Cervical (0.79 - 1.01)(0.87 - 1.12)(0.67 - 0.88)(0.77 - 1.03)(0.57 - 0.76)(0.67 - 0.91)(0.52 - 0.74)(0.62 - 0.90)(0.52 - 0.77)(0.67 - 1.00)(0.52 - 0.67)0.87 0.92 0.87 0.94 0.83 0.93 0.80 0.88 1.10 1.27 0.98 Shoulder (0.75 - 1.00)(0.79 - 1.06)(0.74 - 1.02)(0.79 - 1.10)(0.71 - 0.99)(0.79 - 1.11)(0.66 - 0.98)(0.72 - 1.08)(0.90 - 1.34)(1.04 - 1.56)(0.85 - 1.13)0.77 0.98 0.60 0.81 0.56 0.76 0.62 0.81 0.89 1.23 0.73 Upper arm (0.63 - 1.28)(0.85 - 1.80)(0.60 - 1.00)(0.76 - 1.27)(0.44 - 0.81)(0.60 - 1.11)(0.41 - 0.77)(0.54 - 1.05)(0.42 - 0.89)(0.55 - 1.19)(0.56 - 0.94)0.77 0.64 0.70 0.95 0.99 0.92 0.93 0.90 0.94 1.19 0.73 Elbow (0.70 - 1.30)(0.54 - 0.97)(0.57 - 1.03)(0.46 - 0.89)(0.50-0.98)(0.72 - 1.37)(0.64 - 1.32)(0.64 - 1.37)(0.60 - 1.34)(0.62 - 1.42)(0.93 - 1.53)0.91 1.08 0.53 0.63 0.72 0.85 0.80 0.96 0.74 0.90 0.98 Forearm (0.65 - 1.28)(0.76 - 1.52)(0.34 - 0.82)(0.40 - 0.99)(0.47 - 1.07)(0.55 - 1.30)(0.50-1.29)(0.59-1.55)(0.43-1.26) (0.52 - 1.54)(0.70 - 1.36)0.86 1.07 0.57 0.74 0.63 0.81 0.79 1.00 0.71 0.95 0.86 Wrist (0.50 - 0.99)(0.70 - 1.07)(0.86 - 1.34)(0.43 - 0.74)(0.57 - 0.98)(0.48 - 0.82)(0.62 - 1.07)(0.58 - 1.06)(0.74 - 1.37)(0.67 - 1.34)(0.70 - 1.07)0.81 0.44 0.57 0.47 0.59 0.60 0.74 0.60 0.77 0.57 0.68 Hand (0.53 - 0.88)(0.62 - 1.05)(0.32 - 0.61)(0.34 - 0.66)(0.41 - 0.83)(0.41 - 0.87)(0.50 - 1.09)(0.40-0.91)(0.50 - 1.18)(0.44 - 0.75)(0.40-0.79)0.85 0.91 0.63 0.65 0.80 0.93 0.71 0.81 0.75 0.72 0.71 Fingers (0.66 - 1.10)(0.70 - 1.19)(0.46 - 0.86)(0.52 - 0.99)(0.47 - 0.86)(0.51-0.99)(0.56 - 1.14)(0.65 - 1.34)(0.48 - 1.07)(0.53 - 1.22)(0.58 - 0.98)0.75 0.77 0.83 0.90 0.71 0.78 0.69 0.74 0.54 0.64 0.63 Thoracic spine (0.63 - 0.90)(0.64 - 0.93)(0.74 - 1.10)(0.58 - 0.88)(0.63 - 0.97)(0.54 - 0.89)(0.57-0.97) (0.40 - 0.73)(0.47 - 0.87)(0.52 - 0.76)(0.69-1.02)0.85 0.98 0.74 0.88 0.60 0.74 1.04 1.18 0.69 0.88 0.78 Ribs (0.59 - 1.21)(0.68 - 1.42)(0.49-1.11)(0.58 - 1.34)(0.38 - 0.95)(0.66 - 1.62)(0.73 - 1.88)(0.39-1.22)(0.50 - 1.57)(0.54 - 1.11)(0.46 - 1.17)0.93 0.85 0.91 0.77 0.84 0.76 0.85 0.96 0.79 0.91 0.69 Lower back (0.80 - 1.03)(0.82 - 1.06)(0.73 - 0.97)(0.78 - 1.05)(0.67 - 0.90)(0.72 - 0.97)(0.57 - 0.82)(0.63 - 0.91)(0.71 - 1.03)(0.79 - 1.16)(0.70 - 0.90)0.94 0.45 0.61 0.89 0.91 1.33 0.60 0.70 0.68 0.97 0.67 Abdomen (0.52 - 0.95)(0.69-1.28)(0.31 - 0.67)(0.41 - 0.91)(0.48 - 0.97)(0.44 - 1.02)(0.57 - 1.37)(0.60 - 1.38)(0.87 - 2.05)(0.44 - 0.83)(0.68 - 1.40)1.00 1.11 0.77 0.86 0.92 1.13 1.02 1.15 0.96 1.19 1.10 Pelvis/Gluteals (0.78 - 1.28)(0.86 - 1.43)(0.57 - 1.03)(0.64 - 1.17)(0.69-1.23)(0.84 - 1.52)(0.81 - 1.62)(0.67 - 1.39)(0.82 - 1.73)(0.86 - 1.40)(0.74 - 1.41)1.06 1.05 0.93 0.96 1.05 1.09 0.93 0.97 1.24 1.37 0.97 Hip (0.87 - 1.30)(0.85 - 1.29)(0.74 - 1.17)(0.76 - 1.21)(0.84 - 1.32)(0.87 - 1.38)(0.71 - 1.22)(0.73 - 1.29)(0.94 - 1.63)(1.03 - 1.81)(0.79 - 1.18)1.04 0.72 0.80 0.98 1.05 1.08 1.20 1.31 1.28 0.94 1.40 Groin (0.65 - 1.34)(0.72 - 1.49)(0.47 - 1.10)(0.52 - 1.23)(0.65 - 1.46)(0.69-1.59)(0.69 - 1.71)(0.75 - 1.91)(0.83 - 2.10)(0.87 - 2.27)(0.92 - 1.79)0.87 0.99 1.24 1.59 1.82 0.99 1.13 1.41 1.39 1.60 1.37 Thigh (0.85 - 1.51)(0.71 - 1.38)(0.92 - 1.68)(1.03 - 1.92)(0.99 - 1.95)(1.13 - 2.25)(1.13-2.27)(1.28-2.61)(1.05 - 1.78)(0.75 - 1.31)(0.63 - 1.19)1.02 1.08 1.04 1.10 1.17 1.25 1.12 1.22 1.43 1.55 1.16 Knee (0.88 - 1.19)(0.92 - 1.25)(0.88 - 1.22)(0.93 - 1.30)(0.99-1.37)(1.06 - 1.50)(0.93 - 1.36)(1.01-1.49)(1.18 - 1.75)(1.27 - 1.90)(1.00-1.34)0.77 0.93 0.82 1.04 1.02 1.31 1.14 1.43 0.95 1.22 1.03 Lower leg (0.59-1.00)(0.71 - 1.21)(0.62 - 1.07)(0.78 - 1.39)(0.77 - 1.34)(0.98 - 1.73)(0.83 - 1.55)(1.04 - 1.97)(0.66-1.36) (0.85 - 1.77)(0.81 - 1.31)1.09 1.14 1.19 1.24 1.42 1.47 1.48 1.55 1.70 1.79 1.69 Ankle/Achilles (0.87 - 1.36)(0.90-1.43)(0.93 - 1.52)(0.96 - 1.59)(1.12 - 1.81)(1.14 - 1.88)(1.12 - 1.94)(1.17-2.06)(1.28-2.26) (1.34 - 2.40)(1.37 - 2.08)1.22 1.28 1.12 1.25 1.08 1.24 1.10 1.26 1.23 1.50 1.17 Foot/Toes (0.99-1.52)(0.93 - 1.71)(0.91 - 1.67)(0.94 - 1.45)(1.02 - 1.60)(0.88 - 1.42)(0.98-1.61)(0.84 - 1.38)(0.96 - 1.60)(0.82 - 1.47)(1.10-2.05)

Table 2. Association of PA with MSK-Pain by Anatomical Locations

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41 42 43

44

45 46 47

BMJ Open

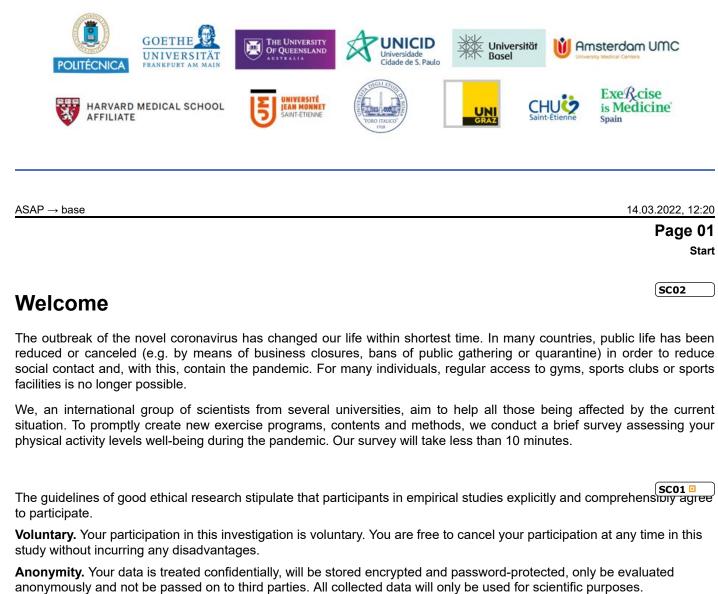
Abbreviations: CI, Confidence Interval; MSK, Musculoskeletal; OR, Odds Ratio; PA, Physical Activity; WHO, World Health Organization Footnote: A group of participants who did not meet the WHO recommendations of PA (i.e. PA less than 150 min per week) was set as the reference group. The model was adjusted for sex, age, employment status, and depression risk.

Table 3. Association of PA with the Number of MSK-Pain Locations

Number of		Dose of WHO Guideline-Based PA												
MSK-Pain	150-3	00 min	300-4	50 min	450-6	00 min	600-7	50 min	750-9	00 min	900-	+ min		
Locations	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR		
	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)		
Minimum	1.06	1.10	1.04	1.12	1.01	1.11	0.92	1.04	1.09	1.28	1.05	1.30		
1 location	(0.95-1.18)	(0.98-1.23)	(0.93-1.17)	(0.99-1.27)	(0.89-1.14)	(0.98-1.26)	(0.80-1.06)	(0.90-1.20)	(0.80-1.28)	(1.10-1.51)	(0.94-1.17)	(1.16-1.45)		
Minimum	0.89	0.97	0.80	0.90	0.80	0.93	0.86	1.00	0.93	1.12	0.88	1.08		
3 locations	(0.78-1.01)	(0.85-1.11)	(0.70-0.93)	(0.78-1.04)	(0.69-0.93)	(0.80-1.08)	(0.72-1.02)	(0.84-1.19)	(0.77-1.12)	(0.93-1.36)	(0.77-0.99)	(0.94-1.23)		
Minimum	0.76	0.84	0.65	0.75	0.61	0.73	0.74	0.85	0.87	1.09	0.83	1.06		
5 locations	(0.62-0.93)	(0.69-1.03)	(0.51-0.82)	(0.60-0.95)	(0.48-0.78)	(0.57-0.93)	(0.56-0.97)	(0.64-1.13)	(0.66-1.16)	(0.82-1.45)	(0.68-1.01)	(0.87-1.29)		
Minimum	0.70	0.76	0.32	0.36	0.57	0.64	0.64	0.67	0.62	0.70	0.61	0.67		
10 locations	(0.45-1.07)	(0.49-1.17)	(0.17-0.61)	(0.19-0.68)	(0.34-0.98)	(0.37-1.10)	(0.35-1.19)	(0.35-1.40)	(0.31-1.23)	(0.35-1.40)	(0.39-0.95)	(0.42-1.06)		

Abbreviations: CI, Confidence Interval; MSK, Musculoskeletal; OR, Odds Ratio; PA, Physical Activity; WHO, World Health Organization Footnote: A group of participants who did not meet the WHO recommendations of PA (i.e. PA less than 150 min per week) was set as the ref

Footnote: A group of participants who did not meet the WHO recommendations of PA (i.e. PA less than 150 min per week) was set as the reference group. The model was adjusted for sex, age, employment status, and depression risk.



Demographic information such as age or gender does not allow a clear conclusion to be drawn with regard to yourself.

Questions. If you still have questions about this study, you can find the contact details of the principal investigator of this study in the bottom of each page ('Imprint ASAP').

By participating in this survey (indicated by clicking the 'Participate'-button), I confirm that I am older than 18 years and have read and understood the informed consent.

Participate

Galley-proof base (ASAP) 14.03.2022, 12:20 Page 23 of 34

https://survey.studiumdigitale.uni-frankfurt.de/admin/preview.php?t=4o7... BMJ Open

 years Where do you live? [Please choose] Where do you work since the virus outbreak in your country? Remotely (Home office) Office/regular place of work 	SD01 -
 Male Female Non-binary I prefer not to say What is your age? years Where do you live? [Please choose] _ Where do you work since the virus outbreak in your country? Remotely (Home office) Office/regular place of work 	
 Female Non-binary I prefer not to say What is your age? years Where do you live? [Please choose] Where do you work since the virus outbreak in your country? Remotely (Home office) Office/regular place of work 	SD02 🗉
 Non-binary I prefer not to say What is your age? years Where do you live? [Please choose] Where do you work since the virus outbreak in your country? Remotely (Home office) Office/regular place of work 	SD02 =
 I prefer not to say What is your age? years Where do you live? [Please choose] Where do you work since the virus outbreak in your country? Remotely (Home office) Office/regular place of work 	SD02 🗉
What is your age? years Where do you live? [Please choose] V Where do you work since the virus outbreak in your country? Remotely (Home office) Office/regular place of work	SD02 🗉
 years Where do you live? [Please choose] Where do you work since the virus outbreak in your country? Remotely (Home office) Office/regular place of work 	SD02 =
Where do you live? [Please choose] Where do you work since the virus outbreak in your country? Remotely (Home office) Office/regular place of work	
 [Please choose] Where do you work since the virus outbreak in your country? O Remotely (Home office) O Office/regular place of work 	
 [Please choose] Where do you work since the virus outbreak in your country? O Remotely (Home office) O Office/regular place of work 	SD04 🗉
Where do you work since the virus outbreak in your country? Remotely (Home office) Office/regular place of work 	
O Office/regular place of work	
 Remotely (Home office) Office/regular place of work 	
 Remotely (Home office) Office/regular place of work 	SD03 •
O Office/regular place of work	
O both	
○ I do not have a formal employment.	
○ I do not want to tell.	
	Page 03
	Arbei
Do you currently work part-time or full-time?	SD05 •
O full-time	
O part-time	
I do not want to tell	
For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

	Page 04 KI
Have you had any symptoms beyond a minor respiratory tract infection since the virus	s outbreak in your
country? Only choose yes, if you had to stay in bed or reduce your regular movement behaviou	r due to these symptoms.
○ yes	
O no	
	Page 0
	Coron
Have you been diagnosed with the novel Coronavirus?	(KH02 🗉
Only choose "yes" if you have been diagnosed by a helathcare professional.	
⊖ yes	
O no	
O I do not want to tell	
	Page 0
	Einschraenkun
Please indicate the approximate number of days you have been limited in your ability t move freely due to restrictions of public life (e.g. prohibition of face-to-face contact, bu lockdowns).	
days	
	Page 0
	Erklaerun
From here, we will repeatedly ask how certain situations and conditions have changed in you of the novel coronavirus. For instance, if you just stated to be restricted in your ability to move please always compare the situation during these last 14 days to 14 typical days prior to the days, please compare these 30 days with 30 typical days prior to the outbreak.	e freely since 14 days,

Page 08 KAFrei

	KAFrei
Physical activities in	Leisure time
We would like to know	v, how physically active you have been in your free time (including commuting from and to work). derate and vigorous activities – light activities do not need to be reported.
	e those where your hearbeat increases and you breathe faster (e.g. brisk walking, cycling as a as a exercise, heavy gardening, running or recreational sports).
	those that get your heart racing, make you sweat and so short of breath that you find it difficult to , running, cycling at high speeds, cardio training, weigh-lifting or team sports such as football).
Moderate and vigoro	us activities
-	w much time do you spend in total on both moderate and vigorous physical activities?
Please sum all activitie 10 minutes.	es with a minimal duration of 10 minutes. Enter 0, if there was not at least one activity of more than
before the outbreak	Minutes per week.
since the outbreak	Minutes per week.
Vigorous activities o	
before the outbreak	Minutes per week.
since the outbreak	Minutes per week.
	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Page 09

KAJob

Physical activity in you	urioh			(KA10
			us on work/occupational tim e reported.	ne. Again, we only
Moderate activities are t	hose where your hearbea	at increases and you br	eathe faster (e.g. brisk walki	ing).
<u>Vigorous</u> activities are tl speak (e.g. repeated lifti		racing, make you swea	at and so short of breath tha	at you find it diffice
Moderate and vigorous	s activities			KA07 Rahm
			ate and vigorous physical act if there was not at least one	
before the outbreak	Minutes per	r week.		
since the outbreak	Minutes per	r week.		
Vigorous activities onl	v			KA08
How much of that time y	ou indicated above, do y	ou spend in total on vig	gorous physical activities of	only?
Please sum all activities 10 minutes. before the outbreak	with a minimal duration of Minutes per v		if there was not at least one	activity of more t
since the outbreak	Minutes per v	week.		
				Page
				Page
	pact of the restrictions i ivities such as shoppin		overall level of activity (no	Aktivitaetsn
			overall level of activity (nov	Aktivitaetsn
			overall level of activity (nor modest positive impact	Aktivitaetsn w includin g arso
light and very light act strongly negative	ivities such as shoppin slight negative	g, walking, etc.)	modest positive	Aktivitaetsn w including arso strongly positive
light and very light act strongly negative	ivities such as shoppin slight negative	g, walking, etc.)	modest positive	Aktivitaetsn w including arso strongly positive
light and very light act strongly negative	ivities such as shoppin slight negative	g, walking, etc.)	modest positive	Aktivitaetsn w including arso strongly positiv
light and very light act strongly negative	ivities such as shoppin slight negative	g, walking, etc.)	modest positive	Aktivitaetsn w including arso strongly positiv

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	Page 11 KA3
How did you engage in sport or exercise before the virus outbreak in your country?	(KA05 🗈
Multiple choice possible.	
Gym	
Sports club	
Self-organised outdoor (e.g. running, cycling in nature)	
Self-organised at home (e.g. cycle ergometer, dumbbells)	
others	
not at all	
How did you engage in sport or exercise since the virus outbreak in your country?	KA06
Multiple choice possible.	
self-organised outdoor (e.g. running, cycling in nature)	
self-organised at home (e.g. cycle ergometer, dumbbells)	
others	
not at all	

Pain

Please indicate whether you suffered from musculoskeletal pain before and/or since the virus outbreak. (WB13 •

The musculoskeletal system comprises all parts of the skeletal system with bones, muscles, ligaments, tendons, joints and their functions.

9 10 11		no pain	very light pain	light pain	moderate pain	strong pain	very strong pain
12 13 14	before outbreak	0	0	0	0	0	0
15 16 17	since outbreak	0	0	0	0	0	0

WB14 🗉 How much did pain interfere with your normal work (including both work outside the home and housework)?

21 22 23		no pain	not at all	a little bit	moderately	quite a bit	extremely	
24 25	before outbreak	0	0	0	0	0	0	
26 27 28	since outbreak	0	0	0	0	0	0	

2 3

Page 13

Checkliste

Multiple selections in both columns are possible.outbreakoutbreakI did not have pain.I	Please list all body regions where you had pain before (left boxe	es) and/or <u>side</u> (right boxes) the o	onset <mark>(WB</mark>
I did not have pain. I Neck/cervical spine I Shoulder I Upper arm I Elbow I Forearm I Wrist I Hand I Fingers I Thoracic spine/upper back I Sternum/Ribs I Lumbar spine/lower back I Hip I Groin I Thigh I Knee I Lower leg I Ankle/achilles tendon I	Multiple coloctions in both columns are possible		sin
Neck/cervical spine			
Shoulder Upper arm Elbow Forearm Forearm Wrist Hand Fingers Thoracic spine/upper back Sternum/Ribs Lumbar spine/lower back Pelvis/buttock Hip Groin Thigh Knee Lower leg Ankle/achilles tendon			
Upper armElbowForearmWristHandFingersThoracic spine/upper backSternum/RibsLumbar spine/lower backAbdomenPelvis/buttockHipGroinThighKneeLower legAnkle/achilles tendon			
Elbow Flow Forearm Wrist Hand Fingers Thoracic spine/upper back <t< td=""><td></td><td></td><td></td></t<>			
Forearm Image: Series and Series an		_	
WristHandFingersThoracic spine/upper backSternum/RibsLumbar spine/lower backAbdomenPelvis/buttockHipGroinThighKneeLower legAnkle/achilles tendon		_	
HandIFingersIThoracic spine/upper backISternum/RibsILumbar spine/lower backIAbdomenIPelvis/buttockIHipIGroinIThighIKneeILower legIAnkle/achilles tendonI		_	
Fingers Thoracic spine/upper back Sternum/Ribs Lumbar spine/lower back Abdomen Pelvis/buttock Hip Groin Thigh Knee Lower leg Ankle/achilles tendon		_	
Thoracic spine/upper back Sternum/Ribs Lumbar spine/lower back Abdomen Pelvis/buttock Hip Groin Thigh Knee Lower leg Ankle/achilles tendon		_	
Sternum/Ribs I Lumbar spine/lower back I Abdomen I Pelvis/buttock I Hip I Groin I Thigh I Knee I Lower leg I Ankle/achilles tendon I			
Lumbar spine/lower backIAbdomenIPelvis/buttockIHipIGroinIThighIKneeILower legIAnkle/achilles tendonI			
Abdomen I Pelvis/buttock I Hip I Groin I Thigh I Knee I Lower leg I Ankle/achilles tendon I			
Pelvis/buttock Hip Groin Thigh Knee Lower leg Ankle/achilles tendon			_
HipIIGroinIIThighIIKneeIILower legIIAnkle/achilles tendonII			_
Groin Image: Constraint of the second se			
Thigh Image: Constraint of the second seco		—	
Knee Image: Constraint of the second secon			
Lower leg Image: Comparison of the second	-		
Ankle/achilles tendon			
	-		
	Foot/toes		L

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Page 14

WHO5

2 3 4							WHO5
5 6	Please indicate for each of the five statements which of the novel coronavirus.	n is closest to	o how you	have bee	en feeling <u>l</u>	<u>before</u> the	Sourceak
7 8 9 10 11 12 13		all the time	most of the time	a little more than half of the time	a little less than half of the time	every now and then	at no time
14	Before the outbreak						
15 16 17	I have felt cheerful and in good spirits	0	0	0	0	0	0
18 19	I have felt calm and relaxed	0	0	0	0	0	0
20 21	I have felt active and vigorous	0	0	0	0	0	0
22 23	I woke up feeling fresh and rested	0	0	0	0	0	0
24 25 26	my daily life has been filled with things that interest me	0	0	0	0	0	0
27 28 29	Please indicate for each of the five statements which	in closest t	- hou vou	have her	n fooling (oinee the	WB11
30 31	of the novel coronavirus.	i is closest to	o now you	nave bee	in reening s	since the	outpreak
32 33 34 35 36 37		all the time	most of the time	a little more than half of the time	a little less than half of the time	every now and then	at no time
38 39	Since the outbreak						
40 41	I have felt cheerful in good spirits	0	\frown			_	
42 43		0	0	0	0	0	0
	I have felt calm and relaxed	0	0	0	0	0	0
44 45	I have felt calm and relaxed I have felt active and vigorous	0		0	0	0 0 0	0 0 0
45 46 47			0	-	0	0	0 0 0
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	Page 17 TP2
How much time per week would you like to spend for such a training program?	TP02
Minutes per training session/workout	
How often would you like to exercise?	TP04 🗉
O daily	
O 4-6 times a week	
O 3-4 times a week	
O 1-2 times a week	
Which type of exercise would you like to perform?	(TP03 •
Multiple choice possible.	
Strength	
Coordination/Balance	
Cognition	
Flexibility/Stretching	
Relaxation	
no preference	
	Page 18
Thank you for participating!	(EN04
You are welcome to visit us on our homepage as well as on Facebook and Instagram:	EN05
Homepage Facebook Instagram	
Please feel free to share this survey with your family, work colleagues and friends! Thank you!	

Last Page

Thank you for participating!

Your answers have been saved, you can now close the browser window.

Imprint ASAP – 2020

12 von 12

Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5-6
		(b) Describe any methods used to examine subgroups and interactions	5-6
		(c) Explain how missing data were addressed	5-6
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	6
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	7-8
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	7-8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Association between physical activity and musculoskeletal pain: an analysis of international data from the ASAP survey

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Association between physical activity and musculoskeletal pain: an

analysis of international data from the ASAP survey

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ABSTRACT

Objective: To explore the association of physical activity (PA) with musculoskeletal pain (MSK-pain).

Design: Cross-sectional study

Setting: 14 countries (Argentina, Australia, Austria, Brazil, Chile, France, Germany, Italy, the Netherlands, Singapore, South Africa, Spain, Switzerland, and the United States of America)

Participants: Individuals aged 18 or older

Primary and secondary outcome measures: PA volumes were assessed with an adapted version of the Nordic Physical Activity Questionnaire-short (NPAQ-short). Prevalence of MSK-pain was captured by means of a 20-item checklist of body locations. Based on the WHO recommendation on PA, participants were classified as non-compliers (0-150 min/week), compliers (150-300 min/week), double compliers (300-450 min/week), triple compliers (450-600 min/week), quadruple compliers (600-750 min/week), quintuple compliers (750-900 min/week), and top compliers (more than 900 min/week). Multivariate logistic regression was used to obtain adjusted odds ratios of the association between PA and MSK-pain for each body location, correcting for age, sex, employment status, and depression risk.

Results: A total of 13,741 participants completed the survey. Compared to non-compliers, compliers had smaller odds of MSK-pain in one location (thoracic pain, OR 0.77, CI 0.64-0.93). Double compliance was associated with reduced pain occurrence in six locations (elbow, OR 0.70, CI 0.50-0.98; forearm, OR 0.63, CI 0.40-0.99; wrist, OR 0.74, CI 0.57-0.98; hand, OR 0.57, CI 0.40-0.79; fingers, OR 0.72, 0.52-0.99; abdomen, OR 0.61, 0.41-0.91). Triple to top compliance was also linked with lower odds of MSK-pain (five locations in triple compliance, three in quadruple compliance, two in quintuple compliance, three in top compliance), but, at the same time, presented increased odds of MSK-pain in some of the other locations.

Conclusion: A dose of 300-450 min WHO-equivalent PA/week was associated with lower odds of MSK-pain in six body locations. On the other hand, excessive doses of PA were associated with higher odds of pain in certain body locations.

Strengths and Limitations of this study

- This is the first large-scale analysis of associations between MSK pain and PA considering multiple anatomical locations
- Large sample size enabled to investigate the associations between different degrees of compliance to physical activity recommended by WHO and MSK-pain
- Administration of the survey in 14 countries allowed participation of diverse populations
- Self-reported data may be subject to recall bias
- Cross-sectional observational design prohibits causal inference

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INTRODUCTION

Musculoskeletal pain (MSK-pain) is a common condition that can have negative physical, psychological, and social impacts.[1] A summary of previous epidemiological studies conducted with diverse techniques and populations revealed that MSK-pain affects between 13.5% and 47% of the general population, with prevalence higher in women and increasing strongly with age.[2] Musculoskeletal conditions contribute to disability, especially in older age groups.[2] It has been reported that disability-adjusted life-years (DALYs), which reflects the years of life lost due to premature mortality and years of life lived with disability, increased by 62% between 1990 and 2016 around the world with 20% surge during the ten-year interval from 2006 to 2016.[3] Most of the increased burden has derived from disability due to increased aging population affected by MSK conditions, , and the burden of MSK disorders is expected to increase even more in the future.[4]

Achieving sufficient physical activity (PA) is associated with a variety of positive health outcomes such as substantial risk reduction in all-cause mortality[5] as well as multiple chronic diseases including type 2 diabetes and metabolic syndrome,[6] cancer,[6] and cardiovascular disease.[7] In the light of these positive impacts, World Health Organization (WHO) recommends 150-300 min of moderate-intensity PA, or 75-150 min of vigorous-intensity PA, or aerobic PA with some combination of moderate and vigorous intensities.[8] PA is also considered one of the most important strategies to prevent and manage MSK-pain.[9] However, compared to the available evidence on the association of PA with non-communicable disease, there seems to be a fewer number of studies on the topic of PA and MSK-pain. . Furthermore, it is still less clear whether the amounts recommended by WHO are sufficient to elicit benefits in terms of addressing MSK-pain. The few available studies examining the relation of regular PA

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and MSK-pain tended to focus on influence of PA for specific body locations or specific diagnoses such as low back pain, neck pain, or osteoarthritis and found inconsistent results.[10] Other studies have evaluated the associations between PA and pain in occupational settings such as among physical therapists or teaching staff.[11,12] Particularly, the interplay between the volume of PA and MSK-pain within the general population has been less explored.

The purpose of this study was to explore the association of total PA with presence of MSK-pain in a variety of anatomical locations including both upper and lower extremities. We hypothesized that greater time spent in PA than WHO recommendation would be associated with the absence of MSK-pain in more body regions, but that excess time performing PA might be associated with the presence of MSK-pain in more body regions.

METHODS

Study Design

This article presents an explorative analysis of pre-pandemic baseline data on PA and MSK-pain assessed during the ASAP (Activity and Health during the SARS-CoV-2 Pandemic) survey. The survey was administered with results collected between April 3 and May 9, 2020, including participants from 14 countries (Argentina, Australia, Austria, Brazil, Chile, France, Germany, Italy, the Netherlands, Singapore, South Africa, Spain, Switzerland, and the United States of America (USA)).[13-16] Ethical approval was obtained from the ethics committees of the study center and collaborating institutions. All participants provided digital informed consent.

Participants

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Eligibility for participation in the ASAP survey was limited to individuals aged 18 or older living in participating countries. Recruitment was performed online using promotion by health-related organizations, mailing lists, and social media advertising (e.g. Facebook, Instagram, Twitter).

Questionnaire

To capture PA, the ASAP survey incorporated an adapted version of the Nordic Physical Activity Questionnaire-short (NPAQ-short). The instrument retrospectively assessed the amounts of moderate and combined moderate and vigorous activities (min/week) during leisure and occupational time. Moderate activities were defined as those that increase heart rate or breathing, and vigorous activities were defined as those that make heart racing, sweating, and shortness of breath. The questionnaire asked how much time participants spent in total on both moderate and vigorous PA on a typical week, and the time spent in all activities with a minimal duration of 10 minutes was asked to be added and entered in the form. The NPAQ-short has been shown to be reliable (test-retest reliability: rho = 0.80 to 0.82) and valid for observing compliance with the WHO recommendations on PA.[17] The questionnaire was available in 7 different languages (Dutch, English, German, French, Italian, Brazilian-Portuguese, Spanish), and clarity and comprehensibility were validated by native speakers through forward and backward translation.

Prevalence of MSK-pain was captured by means of binary responses (yes/no) to an adapted 20-item checklist from a consensus statement on epidemiological injury reporting.[18] Body locations were categorized as follows: neck/cervical spine, shoulder, upper arm, elbow,

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forearm, wrist, hand, fingers, thoracic spine, ribs, lower back, abdomen, pelvis/gluteal, hip, groin, thigh, knee, lower leg, ankle/Achilles tendon, foot/toe.

The English version of the ASAP survey can be found in Supplemental File 1.

Data Processing and Statistical Analysis

Self-reported PA was categorized as multiples of compliance with WHO guidelines which recommend 150-300 minutes/week of moderate activity, 75-150 minutes/week of vigorous activity, or any adequate combination of both.[8] We used the formula (minutes of moderate-to-vigorous PA – minutes of vigorous PA) + minutes of vigorous PA *2 to classify participants as non-compliers (0-150 min/week), compliers (150-300 min/week), double compliers (300-450 min/week), triple compliers (450-600 min/week), quadruple compliers (600-750 min/week), quintuple compliers (750-900 min/week), and top compliers (more than 900 min/week). In addition to the assessment of PA, participants were asked where they worked in multiple choices which also included a 'no employment' option, and the answers to this question were used to categorize participants into being employed or not employed for our analysis. Also, the WHO-Well-Being Index (WHO-5) was used to capture depression risk as validated by previous research.[19]

For each body region, univariate binary logistic regression was conducted to calculate the unadjusted odds ratio (OR) of the association between pain (dependent variable: yes/no) and PA. In a similar way, univariate binary logistic regression was then used to identify associations of pain (dependent variable) and potential confounding variables (sex, age, employment status, depression risk). Finally, multivariate binary logistic regression was performed including these confounding variables (if relevant) to obtain the adjusted ORs and 95% confidence interval (CI)

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of the association between the volume of PA and pain (dependent variable). As participants may have a strongly varying number of pain locations and as the impact of pain on the individual may vary with the number of affected body regions, additional analyses, using the same procedures as described above (binary logistic regression corrected for confounders), were performed to obtain adjusted OR for pain in only one, at least 3, 5, or 10 body locations.

All data analyses were conducted using SPSS 22 (SPSS INC., Armonk, NY, USA), and the significance level was set to $\alpha = 0.05$.

Patient and Public Involvement

Members of the target population without medical background were involved in the designing phase of the ASAP questionnaire. The questionnaire was face validated for each language with five non-academic individuals. Feedback on comprehension and clarity of the Lich wording was used.

RESULTS

Valid datasets were identified for 13,741 participants (38 ± 15 years, minimum 18 and maximum 100, 59% females). The demographic data are summarized in the Table 1. 2604 individuals did not meet the WHO recommendation of PA while n=2735 belonged to 150-300 min group, n=1957 to 300-450 min group, n=1749 to 450-600 min group, n=1066 to 600-750 min group, n=849 to 750-900 min group, and n=2781 to 900+ min group. Comprehensive results are summarized in the Table 2 and 3.

Compared to inactive individuals, simple guideline compliance was associated with lower odds of suffering from MSK-pain in one body location (thoracic pain, OR 0.77, CI 0.64-

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> 0.93 Table 1). Double compliance was associated with lower odds of suffering from MSK-pain in six locations (elbow, OR 0.70, CI 0.50-0.98; forearm, OR 0.63, CI 0.40-0.99; wrist, OR 0.74, CI 0.7-0.98; hand, OR 0.57, CI 0.40-0.79; fingers, OR 0.72, CI 0.52-0.99; abdomen, OR 0.61, CI 0.41-0.91). Although higher amounts of PA were associated with lower odds of suffering from MSK-pain in variable numbers of locations (five body locations in triple compliance, three in quadruple compliance, two in quintuple compliance, three in top compliance), they were also associated with higher odds of suffering from MSK-pain in other locations. Specifically, triple compliance was associated with presence of MSK-pain in thigh (OR 1.41, CI 1.03-1.92), knee (OR 1.25, CI 1.06-1.50), and ankle/Achilles tendon (OR 1.47, CI 1.14-1.88). Quadruple compliance increased pain locations to four, quintuple compliance to six, and top compliance to seven.

> Triple compliance was associated with lower odds to have a total of 5 or more (OR 0.75, CI 0.60-0.95) or 10 or more (OR 0.36, CI 0.19-0.68) pain locations, and quadruple compliance was associated with lower odds to have 5 or more pain locations (OR 0.73, CI 0.57-0.93). However, quintuple and top compliances were associated with higher odds of having a minimum one pain location (OR 1.28, CI 1.10-1.51 and 1.30, CI 1.16-1.45 respectively).

DISCUSSION

The purpose of the present study was to explore the relation between PA and MSK-pain. Previous research focused on the impact of PA on specific locations of MSK-pain (e.g., low back and neck[20]) or certain occupational settings.[11,12] Our large-scale multinational study is novel in that it identified the associations between different degrees of compliance to PA recommended by WHO and multiple body locations in the general population after adjusting for multiple

cofounding factors including age, which is known to be positively associated with MSK-pain prevalence.

Guideline compliance (150-300 min per week) was weakly associated with MSK pain, showing lower odds of having pain only in thoracic spine but higher odds in foot/toes. In contrast, double compliance (300-450 min per week) substantially increased the number of locations that were associated with lowers odds of MSK-pain to six and thus seems to represent the optimal dose when PA is undertaken to prevent MSK. Finally, higher levels of PA (triple to top compliance) were associated with less odds of having pain in multiple upper body locations but paradoxically contributed to higher odds of having lower extremity pain. Notably, participating in 300-600 min of PA per week was associated with lower spine. In contrast, participating in greater than 450 min of PA per week was associated with higher odds of having pain in the lower extremity.

Time spent in PA and pain in neck, back, and upper extremity

A previous systematic review showed that there was limited evidence for no association between PA and neck pain.[20] However, our study found that participating in PA between 450-900+ min was associated with lower odds of having pain in neck/cervical spine. Several epidemiological studies have demonstrated that certain postures sustained for prolonged duration combined with sedentary lifestyle were associated with neck pain.[21-23] Therefore, increased PA levels may be helpful to consider in those at risk for neck pain.

Association between PA and thoracic spine has been less explored,[24] but a recent observational study found that PA less than 150 min per week was associated with reduced

thoracic mobility.[25] Our findings build on previous research in that PA less than 150 min per week is also associated with higher odds of having pain in the thoracic spine.

While it is generally accepted that PA and exercise are beneficial in the management of acute and chronic low back pain, a previous systematic review could not identify either positive or negative relationship.[26] One study suggested that the relationship between the level of activity and back pain might be explained by a U-shaped curve that suggests both low and excessive PA may increase the risk of low back pain.[27] Our findings partly support this concept as PA of 450-750 min was associated with lower odds of low back pain while lower or higher PA than that range did not have significant association.

PA in the range of 300-600 min was also associated with lower odds of having pain in several locations in the upper extremity such as elbow, forearm, wrist, hand, and fingers. PA exceeding 750 min was associated with higher odds of shoulder pain. The underlying mechanisms of how PA modulates pain are not completely understood, but several pathways have been proposed. Animal study findings suggest regular PA may act on the central nervous system (CNS) and alter rate of pain hypersensitivity, dysregulation of pain modulation, and development of chronic pain.[28-30] In humans, it has been proposed that PA may intervene excitability and inhibition in the CNS,[31-33] and anti-inflammatory and antioxidant effects of regular PA might diminish the processes contributing to central sensitization.[34-36] Other proposed mechanisms in humans include the activation of opioid and serotonin pathways[37] or involvement of endocannabinoid system[38] induced from regular PA which could exert analgesic effects. While further research is needed to elucidate how much and what type of PA can induce such changes to modulate pain, our results suggest that PA between 300-600 mins per

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week may be sufficient for spinal conditions and upper extremity pain, with PA exceeding 750 min associated with higher likelihood of shoulder pain.

Association of PA and lower extremity pain

The association of PA to lower extremity pain was different than what was observed for upper extremity and spine conditions. Our results suggest PA exceeding 450 min was associated with higher odds of MSK-pain in lower extremity. These findings may be partially explained by higher amounts of PA are likely to involve greater use of the lower extremity. In the United States, it has been reported that walking is the most popular form of exercise followed by biking, yard work, strength training, dancing, and running, which are activities that commonly place physical demands through the lower extremity.[39] Running is one of the most popular exercises in the world and has been shown to result in lower extremity pain in multiple anatomical locations with nearly all (94.7% of runners) reporting experience of pain at least once after running.[40]

We also observed that greater PA was associated with a higher number of sites of MSKpain in the lower extremity. A dose response was observed: 450-600 min was associated with pain in three anatomical regions, 600-750 min with pain in four anatomical regions, 750-900 min with five anatomical regions, and 900+ min with six anatomical regions. The optimal PA level to reduce pain in those with existing musculoskeletal lower extremity pain is unknown. A prior study reported that a minimum of 45 total moderate-vigorous min per week was sufficient to elicit improved or sustained high function with lower-extremity symptoms regardless of age, gender, body mass index, or presence of knee osteoarthritis.[41] Our findings of PA ranging from

150-450 min not increasing the odds of having pain in the lower extremities suggest this range might be appropriate to be safe and promote other health benefits.

Clinical implication

While the WHO 2020 guidelines on PA recommend 150-300 min of moderate-intensity PA, or 75-150 min of vigorous-intensity PA, or some equivalent combination of moderateintensity and vigorous-intensity aerobic PA per week for optimal health outcomes,[8] the current study suggests that more PA beyond the WHO recommendation may be necessary to decrease the odds of having pain particularly in the upper extremity. Our findings suggest a target of 300-450 min of PA per week could be optimal for preventing pain in the upper extremity without clear associated higher rate of lower extremity pain. Also, this range was associated with lower odds of having pain in multiple number of locations. Recognizing concerns on higher prevalence of pain in low back, neck, and thoracic spine increased during the COVID-19 pandemic,[15] PA target of the higher target of 450 min of weekly exercise may be helpful in this population. Our results suggest exceeding 450 min of PA may not be advisable for those with increased concern for lower extremity pain. Furthermore, PA above 750 minutes was associated with having at least one pain location.

Limitation

While our findings derived from a large-scale multinational study of participants, we do note potential limitations. Self-report of PA and MSK-pain are limited by reporting bias and inaccuracy including risk for over-reporting level of PA.[42,43] The cross-sectional study design limits our understanding between PA and the etiology of MSK-pain. Also, we are limited in

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ability in discriminating the types of PA to report of MSK-pain by anatomical locations. We were not able to distinguish or identify bilateral MSK-pain from our questionnaire as well. Furthermore, because a separate analysis was run for each body region, there is a risk of multiple testing problem. Since our analysis was explorative in nature, further prospective cohort or interventional studies are needed to elucidate the best form and dose of PA to address MSK-pain by anatomical location and specific musculoskeletal injury, and additionally investigate the role of MSK-pain intensity instead of using a binary (yes/no) classification.

CONCLUSION

Our findings showed that PA time above the WHO recommendations was associated with

lower odds of having pain in multiple locations such as neck, thoracic spine, low back, and in the

upper extremities. Especially, undertaking PA for 300-450 min per week was associated with

reduced pain occurrence in six locations, elbow, forearm, wrist, hand, fingers, and abdomen.

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Data Availability Statement: Data are available upon reasonable request

Ethics Statements

-Ethics approval: This study was approved by the University of Queensland Health and Behavioural Sciences (202000693), Ethical committee of the University of Graz (GZ. 39/62/63 ex 2019/20), Research Ethics Committee of Fundación Instituto Superior de Ciencias de la Salud (DEPINV CODE: 11/20), Research Ethics Committee of the Universidade Cidade de São Paulo (CAAE: 30555320.0.0000.0008), Institutional Ethics Committee of the University of Santiago de Chile (nº 123/2020), Saint-Etienne University Hospital Ethical Committee (IORG0007394; IRBN492020/CHUSTE), Ethics Committee of the Faculty of Psychology and Sports Sciences of Goethe University Frankfurt (no. 2020-13), Comitato di Ateneo per la Ricerca, Università degli Studi di Roma "Foro Italico" (CAR 43/2020), Medical Ethical Committee of Amsterdam UMC (2020.192), Institutional Research Ethics Committee of Durban University of Technology (IREC 042/20), SingHealth Centralised Institutional Review Board (2020/2287), Cantonal Ethics Committee Northwest Switzerland (2020-01058), Ethics Committee of Universidad Politécnica de Madrid (20200507-1), and Partners Human Research Committee (2020P000963)

-Digital informed consent was obtained from all subjects involved in the study.

Authors Contribution: HCR/AT: data collection, interpretation, drafting and critical revision of the manuscript, LM, KH, LV, DG: data collection, critical revision of the manuscript, JW: conception/design, data collection, interpretation, critical revision of the manuscript

Competing interests: None declared.

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Table 1. Demographic data of the participants by countries

Country	ARG	AUS	AUT	BRA	CHE	CHL	DEU	ESP	FRA	ITA	NLD	SGP	USA	ZAF	Others	Total
Sex (M/F)	429/494	56/248	192/546	620/948	115/212	471/766	696/1356	310/277	1200/1046	348/453	50/129	437/434	364/711	236/293	108/122	5632/8035
Age	37.1	41.6	27.3	34.2	37.3	31.5	40.4	43.0	43.3	38.5	47.5	40.1	43.1	32.4	40.0	38.3
(SD)	(15.4)	(14.1)	(9.6)	(10.6)	(11.5)	(13.6)	(16.3)	(13.4)	(16.9)	(15.3)	(14.0)	(12.1)	(14.0)	(14.3)	(13.5)	(15.1)
WHO-5	54.3	50.1	55.0	53.0	50.4	54.7	52.9	49.2	48.3	56.3	49.0	52.2	49.4	52.2	51.2	52.0
(SD)	(17.8)	(14.8)	(16.5)	(16.0)	(15.2)	(18.2)	(17.0)	(15.8)	(14.8)	(17.3)	(14.7)	(17.6)	(14.9)	(21.1)	(17.2)	(16.8)
Employment (Yes, %)	61.9	86.8	62.7	78.8	96.0	59.2	73.2	79.8	69.9	65.9%	77.1	88.8	84.1	53.7	85.0	72.8
MVPA	488.7	352.3	384.6	396.4	379.0	385.7	438.6	493.2	527.9	566.2	506.5	376.5	401.0	310.6	437.8	439.5
(SD)	(596.2)	(340.0)	(408.7)	(454.9)	(458.1)	(518.3)	(481.3)	(617.0)	(516.0)	(635.3)	(420.5)	(445.7)	(348.0)	(455.8)	(529.7)	(498.7)
VPA	218.7	121.3	141.4	202.0	130.6	153.9	146.9	188.4	234.7	247.2	200.2	171.0	195.9	144.1	203	186.4
(SD)	(338.0)	(152.4)	(206.5)	(305.7)	(152.6)	(287.9)	(226.5)	(295.2)	(343.3)	(350.1)	(225.7)	(302.4)	(230.0)	(272.7)	(275.6)	(288.8)

Abbreviations: F, Female; M, Male; MVPA, Moderate to Vigorous Physical Activity; SD, Standard Deviation; VPA, Vigorous Physical Activity, WHO-5, The 5item World Health Organization Well-Being Index

Country Abbreviations: ARG, Argentina; AUS, Australia; AUT, Austria; BRA, Brazil; CHE, Switzerland; CHL, Chile; DEU, Germany; ESP, Spain; FRA, France; ITA, Italy; NLD, Netherlands; SGP, Singapore; USA, United States of America; ZAF, South Africa

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Table 2. Association of PA with MSK-Pain by Anatomical Locations

					Dos	e of WHO Gu	ideline-Bas	ed PA				
Location of		-300 min	300-4	450 min	450-6	00 min	600-7	'50 min	750-9	00 min	900	+ min
MSK-Pain	Ciude Oi		Crude OR	Adjusted OR								
	(95% CI		(95% CI)									
Neck/Cervio	cal 0.89	0.99	0.76	0.89	0.66	0.78	0.62	0.75	0.63	0.82	0.59	0.78
	(0.79-1.0)		(0.67-0.88)	(0.77-1.03)	(0.57-0.76)	(0.67-0.91)	(0.52-0.74)	(0.62-0.90)	(0.52-0.77)	(0.67-1.00)	(0.52-0.67)	(0.68-0.89)
Shoulder	0.87	0.92	0.87	0.94	0.83	0.93	0.80	0.88	1.10	1.27	0.98	1.16
	(0./5-1.00		(0.74-1.02)	(0.79-1.10)	(0.71-0.99)	(0.79-1.11)	(0.66-0.98)	(0.72-1.08)	(0.90-1.34)	(1.04-1.56)	(0.85-1.13)	(1.00-1.34)
Upper arm	$1 \qquad 0.77$	0.98	0.60	0.81	0.56	0.76	0.62	0.81	0.89	1.23	0.73	1.01
	(0.00-1.00		(0.44-0.81)	(0.60-1.11)	(0.41-0.77)	(0.54-1.05)	(0.42-0.89)	(0.55-1.19)	(0.63-1.28)	(0.85-1.80)	(0.56-0.94)	(0.77-1.33)
Elbow	0.73	0.77	0.64	0.70	0.95	0.99	0.92	0.93	0.90	0.94	1.19	1.30
	(0.54-0.97		(0.46-0.89)	(0.50-0.98)	(0.70-1.30)	(0.72-1.37)	(0.64-1.32)	(0.64-1.37)	(0.60-1.34)	(0.62-1.42)	(0.93-1.53)	(0.99-1.70)
Forearm	0.91	1.08	0.53	0.63	0.72	0.85	0.80	0.96	0.74	0.90	0.98	1.17
	(0.65-1.28		(0.34-0.82)	(0.40-0.99)	(0.47-1.07)	(0.55-1.30)	(0.50-1.29)	(0.59-1.55)	(0.43-1.26)	(0.52-1.54)	(0.70-1.36)	(0.82-1.65)
Wrist	0.86	1.07	0.57	0.74	0.63	0.81	0.79	1.00	0.71	0.95	0.86	1.15
	(0.70-1.07		(0.43-0.74)	(0.57-0.98)	(0.48-0.82)	(0.62-1.07)	(0.58-1.06)	(0.74-1.37)	(0.50-0.99)	(0.67-1.34)	(0.70-1.07)	(0.91-1.44)
Hand	0.68	0.81	0.44	0.57	0.47	0.59	0.60	0.74	0.60	0.77	0.57	0.74
	(0.53-0.88		(0.32-0.61)	(0.40-0.79)	(0.34-0.66)	(0.41-0.83)	(0.41-0.87)	(0.50-1.09)	(0.40-0.91)	(0.50-1.18)	(0.44-0.75)	(0.56-0.99)
Fingers	0.85	0.91	0.63	0.72	0.65	0.71	0.80	0.93	0.71	0.81	0.75	0.84
	(0.66-1.10		(0.46-0.86)	(0.52-0.99)	(0.47-0.86)	(0.51-0.99)	(0.56-1.14)	(0.65-1.34)	(0.48-1.07)	(0.53-1.22)	(0.58-0.98)	(0.64-1.11)
Thoracic spi	ine 0.75	0.77	0.83	0.90	0.71	0.78	0.69	0.74	0.54	0.64	0.63	0.77
	(0.03-0.90		(0.69-1.02)	(0.74-1.10)	(0.58-0.88)	(0.63-0.97)	(0.54-0.89)	(0.57-0.97)	(0.40-0.73)	(0.47-0.87)	(0.52-0.76)	(0.63-0.93)
Ribs	0.85	0.98	0.74	0.88	0.60	0.74	1.04	1.18	0.69	0.88	0.78	0.90
	(0.59-1.2)		(0.49-1.11)	(0.58-1.34)	(0.38-0.95)	(0.46-1.17)	(0.66-1.62)	(0.73-1.88)	(0.39-1.22)	(0.50-1.57)	(0.54-1.11)	(0.62-1.36)
Lower bac	k 0.91	0.93	0.85	0.91	0.77	0.84	0.69	0.76	0.85	0.96	0.79	0.93
Lower oue	(0.80-1.03		(0.73-0.97)	(0.78-1.05)	(0.67-0.90)	(0.72-0.97)	(0.57-0.82)	(0.63-0.91)	(0.71-1.03)	(0.79-1.16)	(0.70-0.90)	(0.81-1.06)
Abdomen	0.70	0.94	0.45	0.61	0.68	0.97	0.67	0.89	0.91	1.33	0.60	0.82
	(0.52-0.93		(0.31-0.67)	(0.41-0.91)	(0.48-0.97)	(0.68-1.40)	(0.44-1.02)	(0.57-1.37)	(0.60-1.38)	(0.87-2.05)	(0.44-0.83)	(0.59-1.14)
Pelvis/Glute	als 1.00	1.11	0.77	0.86	0.92	1.13	1.02	1.15	0.96	1.19	1.10	1.37
T etvis/ Giuce	(0.78-1.20		(0.57-1.03)	(0.64-1.17)	(0.69-1.23)	(0.84-1.52)	(0.74-1.41)	(0.81-1.62)	(0.67-1.39)	(0.82-1.73)	(0.86-1.40)	(1.06-1.76)
Hip	1.06	1.05	0.93	0.96	1.05	1.09	0.93	0.97	1.24	1.37	0.97	1.17
	(0.87-1.30		(0.74-1.17)	(0.76-1.21)	(0.84-1.32)	(0.87-1.38)	(0.71-1.22)	(0.73-1.29)	(0.94-1.63)	(1.03-1.81)	(0.79-1.18)	(0.95-1.45)
Groin	0.94	1.04	0.72	0.80	0.98	1.05	1.08	1.20	1.31	1.40	1.28	1.40
	(0.65-1.34) ((0.47-1.10)	(0.52-1.23)	(0.65-1.46)	(0.69-1.59)	(0.69-1.71)	(0.75-1.91)	(0.83-2.10)	(0.87-2.27)	(0.92-1.79)	(0.99-1.99)
Thigh	0.99	1.13	0.87	0.99	1.24	1.41	1.39	1.59	1.60	1.82	1.37	1.51
Imgn	(0.75-1.31		(0.63-1.19)	(0.71-1.38)	(0.92-1.68)	(1.03-1.92)	(0.99-1.95)	(1.13-2.25)	(1.13-2.27)	(1.28-2.61)	(1.05-1.78)	(1.15-1.99)
Knee	1.02	1.08	1.04	1.10	1.17	1.25	1.12	1.22	1.43	1.55	1.16	1.30
	(0.88-1.19		(0.88-1.22)	(0.93-1.30)	(0.99-1.37)	(1.06-1.50)	(0.93-1.36)	(1.01-1.49)	(1.18-1.75)	(1.27-1.90)	(1.00-1.34)	(1.12-1.51)
Lower leg	0.77	0.93	0.82	1.04	1.02	1.31	1.14	1.43	0.95	1.22	1.03	1.34
	(0.39-1.00		(0.62-1.07)	(0.78-1.39)	(0.77-1.34)	(0.98-1.73)	(0.83-1.55)	(1.04-1.97)	(0.66-1.36)	(0.85-1.77)	(0.81-1.31)	(1.04-1.73)
Ankle/Achil	les 1.09	1.14	1.19	1.24	1.42	1.47	1.48	1.55	1.70	1.79	1.69	1.85
	(0.87-1.30		(0.93-1.52)	(0.96-1.59)	(1.12-1.81)	(1.14-1.88)	(1.12-1.94)	(1.17-2.06)	(1.28-2.26)	(1.34-2.40)	(1.37-2.08)	(1.49-2.31)
Foot/Toes	1.22	1.28	1.12	1.25	1.08	1.24	1.10	1.26	1.23	1.50	1.17	1.53
1 1000 1003	(0.99-1.52) (1.02-1.60)	(0.88-1.42)	(0.98-1.61)	(0.84-1.38)	(0.96-1.60)	(0.82-1.47)	(0.93-1.71)	(0.91-1.67)	(1.10-2.05)	(0.94-1.45)	(1.22-1.92)

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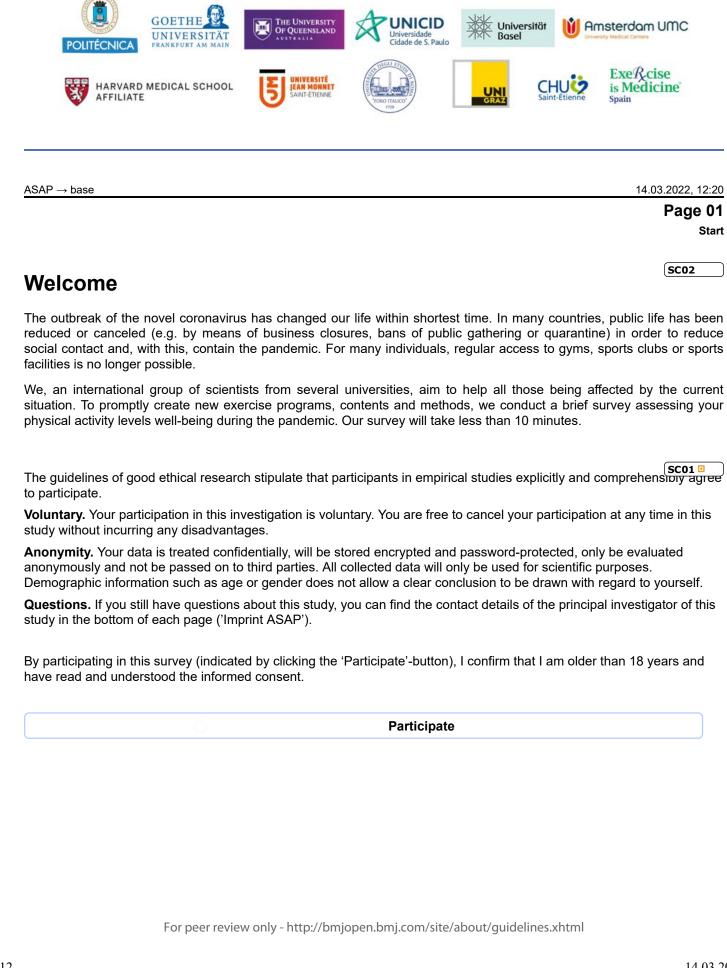
Abbreviations: CI, Confidence Interval; MSK, Musculoskeletal; OR, Odds Ratio; PA, Physical Activity; WHO, World Health Organization Footnote: A group of participants who did not meet the WHO recommendations of PA (i.e. PA less than 150 min per week) was set as the reference group. The model was adjusted for sex, age, employment status, and depression risk. The numbers in bold denote significant results, and the confidence interval that starts or ends with 1.0 derives from rounding the decimals.

Table 3. Association of PA with the Number of MSK-Pain Locations

Number of					Dos	e of WHO Gu	ideline-Bas	ed PA				
MSK-Pain	150-3	00 min	300-4	50 min	450-6	00 min	600-7	'50 min	750-9	000 min	900	+ min
Locations	Crude OR	Adjusted OR										
	(95% CI)											
Minimum	1.06	1.10	1.04	1.12	1.01	1.11	0.92	1.04	1.09	1.28	1.05	1.30
1 location	(0.95-1.18)	(0.98-1.23)	(0.93-1.17)	(0.99-1.27)	(0.89-1.14)	(0.98-1.26)	(0.80-1.06)	(0.90-1.20)	(0.80-1.28)	(1.10-1.51)	(0.94-1.17)	(1.16-1.45)
Minimum	0.89	0.97	0.80	0.90	0.80	0.93	0.86	1.00	0.93	1.12	0.88	1.08
3 locations	(0.78-1.01)	(0.85-1.11)	(0.70-0.93)	(0.78-1.04)	(0.69-0.93)	(0.80-1.08)	(0.72-1.02)	(0.84-1.19)	(0.77-1.12)	(0.93-1.36)	(0.77-0.99)	(0.94-1.23)
Minimum	0.76	0.84	0.65	0.75	0.61	0.73	0.74	0.85	0.87	1.09	0.83	1.06
5 locations	(0.62-0.93)	(0.69-1.03)	(0.51-0.82)	(0.60-0.95)	(0.48-0.78)	(0.57-0.93)	(0.56-0.97)	(0.64-1.13)	(0.66-1.16)	(0.82-1.45)	(0.68-1.01)	(0.87-1.29)
Minimum	0.70	0.76	0.32	0.36	0.57	0.64	0.64	0.67	0.62	0.70	0.61	0.67
10 locations	(0.45-1.07)	(0.49-1.17)	(0.17-0.61)	(0.19-0.68)	(0.34-0.98)	(0.37-1.10)	(0.35-1.19)	(0.35-1.40)	(0.31-1.23)	(0.35-1.40)	(0.39-0.95)	(0.42-1.06)

Abbreviations: CI, Confidence Interval; MSK, Musculoskeletal; OR, Odds Ratio; PA, Physical Activity; WHO, World Health Organization Footnote: A group of participants who did not meet the WHO recommendations of PA (i.e. PA less than 150 min per week) was set as the reference group. The model was adjusted for sex, age, employment status, and depression risk.

https://survey.studiumdigitale.uni-frankfurt.de/admin/preview.php?t=4o7... BMJ Open



		Page 0 s
Please indicate your	sex.	SD01 •
O Male		
O Female		
O Non-binary		
 I prefer not to say 		
What is your age?		SD02 🗉
years		
Where do you live?		SD04 🗉
[Please choose]	\checkmark	
 Remotely (Home of Office/regular place) both I do not have a for I do not want to te 	ce of work rmal employment.	
		Page 0
Do you currently wor	k part-time or full-time?	SD05 🗉
Do you currently wor	k part-time or full-time?	SD05 🗉
	k part-time or full-time?	SD05 🗉
O full-time		SD05 🖬
full-timepart-time		SD05 🖻

	Page 0
	oms beyond a minor respiratory tract infection since the virus outbreak in your
country? Only choose yes, if you h	nad to stay in bed or reduce your regular movement behaviour due to these symptoms.
O yes	
O no	
	Page 0 Coror
Have you been diagnose	d with the novel Coronavirus?
	ave been diagnosed by a helathcare professional.
O yes	
O no	
I do not want to tell	
	Page 0
	Einschraenku
	EXAMPLE A CALL STREET OF CARESTORY OF CAREST
days	
	Page 0
	Erklaeru
	dly ask how certain situations and conditions have changed in your country since the outpream or instance, if you just stated to be restricted in your ability to move freely since 14 days,
please always compare the	e situation during these last 14 days to 14 typical days prior to the outbreak. If you chose 30 se 30 days with 30 typical days prior to the outbreak.
please always compare the	

Page 08

K	Α	F	r	e	į

	KAFre
Physical activities in	leisure time
We would like to know	<i>i</i> , how physically active you have been in your free time (including commuting from and to work) derate and vigorous activities – light activities do not need to be reported.
	e those where your hearbeat increases and you breathe faster (e.g. brisk walking, cycling as a as a exercise, heavy gardening, running or recreational sports).
	those that get your heart racing, make you sweat and so short of breath that you find it difficult to running, cycling at high speeds, cardio training, weigh-lifting or team sports such as football).
Moderate and vigorou	us activities
On a typical week, how	w much time do you spend in total on both moderate and vigorous physical activities?
Please sum all activitie 10 minutes.	s with a minimal duration of 10 minutes. Enter 0, if there was not at least one activity of more than
before the outbreak	Minutes per week.
since the outbreak	Minutes per week.
Vigorous activities or	nly
10 minutes. before the outbreak	es with a minimal duration of 10 minutes. Enter 0, if there was not at least one activity of more than Minutes per week.
since the outbreak	Minutes per week.
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	i en peer review only integry on jopen on joen one about guidelines. And in

KAJob

Discourse of the taxet				KA10
	stions addressed free tir	me, the following two foc ctivities do not need to be	us on work/occupational t e reported.	ime. Again, we only
Moderate activities are t	hose where your hearb	eat increases and you br	eathe faster (e.g. brisk wa	alking).
<u>Vigorous</u> activities are th speak (e.g. repeated lifti		t racing, make you swea	at and so short of breath t	hat you find it diffice
Moderate and vigorous	s activities			KA07 Rahm
			ite and vigorous physical a if there was not at least on	
before the outbreak	Minutes p	er week.		
since the outbreak	Minutes p	er week.		
Vigorous activities only	V			KA08
10 minutes. before the outbreak	Minutes per	r week.		
since the outbreak	Minutes per			
		r week.		
		r week.		Page
		r week.		-
Please indicate the imp light and very light act	pact of the restrictions	s in public life on your o	overall level of activity (n	Page Aktivitaetsn now including arso
	pact of the restrictions	s in public life on your o	overall level of activity (n modest positive impact	Aktivitaetsn
light and very light act	pact of the restrictions ivities such as shoppi slight negative	s in public life on your o ng, walking, etc.)	modest positive	Aktivitaetsn now including arso strongly positiv
light and very light act strongly negative	pact of the restrictions ivities such as shoppi slight negative	s in public life on your o ng, walking, etc.)	modest positive	Aktivitaetsn now including arso strongly positiv

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	Раде 1 [,] ка
How did you engage in sport or exercise before the virus outbreak in your country?	KA05 🗉
Multiple choice possible.	
Gym	
Sports club	
Self-organised outdoor (e.g. running, cycling in nature)	
Self-organised at home (e.g. cycle ergometer, dumbbells)	
others	
not at all	
	KA06
How did you engage in sport or exercise since the virus outbreak in your country?	
Multiple choice possible.	
self-organised outdoor (e.g. running, cycling in nature)	
self-organised at home (e.g. cycle ergometer, dumbbells)	
others	

Pain

Please indicate whether you suffered from musculoskeletal pain before and/or since the virus outbreak. (WB13 •

The musculoskeletal system comprises all parts of the skeletal system with bones, muscles, ligaments, tendons, joints and their functions.

9 10 11		no pain	very light pain	light pain	moderate pain	strong pain	very strong pain
12 13 14	before outbreak	0	0	0	0	0	0
15 16 17	since outbreak	0	0	0	0	0	0

WB14 🗉 How much did pain interfere with your normal work (including both work outside the home and housework)?

21 22 23		no pain	not at all	a little bit	moderately	quite a bit	extremely
24 25	before outbreak	0	0	0	0	0	0
26 27 28	since outbreak	0	0	0	0	0	0

2 3

Page 13

Checkliste

Please list all body regions where you had pain <u>before</u> (le	ft boxes) and/or <u>side</u> (right boxes) the o	onset
	before	since
Multiple selections in both columns are possible.	outbreak	outbre
I did not have pain.		
Neck/cervical spine		
Shoulder		
Upper arm		
Elbow		
Forearm		
Wrist		
Hand		
Fingers		
Thoracic spine/upper back		
Sternum/Ribs		
Lumbar spine/lower back		
Abdomen		
Pelvis/buttock		
Hip		
Groin		
Thigh		
Knee		
Lower leg		
Ankle/achilles tendon		
Foot/toes		
Footiloes		

59

Page 14

is closest t all the time	o how you most of the time	a little more than half of the time	a little less than half of the time	every now and then	
		more than half of the	less than half of the	now and	at no tim
		more than half of the	less than half of the	now and	at no tim
O		ume	une	unen	at no tim
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0	~				
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0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
					WB11 🖸
is closest t	o how you	have bee	en feeling g	<u>since</u> the	outoreal
		more	a little		
all the	most of	of the	half of the	now and	
time	the time	time	time	then	at no tim
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0	0	0	0	0	0
0	0	0	0	0	0
0					0
					0
0	0	0	0	0	0
		is closest to how you all the most of time the time	is closest to how you have been a little more than half of the time the time of the time of the time the time the time	O O O O O O O O O Sis closest to how you have been feeling s a little more than half of the less than half of the time a little less than half of the less than half of the time O all the time most of the time O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O O <t< td=""><td>OOOOOOOOOOOOOOOOOStatistic closest to how you have been feeling since the more than half timea little less than half of the timea little less than half of the timeevery now and thenall the timemost of the timeOO</td></t<>	OOOOOOOOOOOOOOOOOStatistic closest to how you have been feeling since the more than half timea little less than half of the timea little less than half of the timeevery now and thenall the timemost of the timeOO

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			e the influend gyms, bans							
psychologic	cal well-b	eing								
strong negative influence O physical we) ell-being	0	0	0	no influence O	0	0	0	0	st po infl (w B
strong negative influence					no influence					st po infl
0	0	0	0	0	0	0	0	0	0	
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completely disagree			rather disagree				rather agree			to a
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Would you I	be interes in public	sted in a fr life?	ree online ex	ercise tra	aining prog	ram that y	you could u	se home-l	based des	
restrictions	be interes in public	sted in a fi life?	ree online ex	ercise tra	aining progi	ram that y	you could u	se home-l	based des	
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O yes	be interes in public	sted in a fi life?	ree online ex	ercise tra	aining prog	ram that y	you could u	se home-l	based des	Pa (TPO spite

	Page 17 TP2
How much time per week would you like to spend for such a training program?	(TP02 🗉
Minutes per training session/workout	
How often would you like to exercise?	(TP04 •
O daily	
 4-6 times a week 	
O 3-4 times a week	
 1-2 times a week 	
Which type of exercise would you like to perform?	(TP03 🗉
Multiple choice possible.	
Strength	
Coordination/Balance	
Flexibility/Stretching	
Relaxation	
no preference	
	Page 18 _{Code}
	EN04
Thank you for participating!	(EN05)
Thank you for participating! You are welcome to visit us on our homepage as well as on Facebook and Instagram:	
You are welcome to visit us on our homepage as well as on Facebook and Instagram:	

Last Page

Thank you for participating!

Your answers have been saved, you can now close the browser window.

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12 von 12

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Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5-6
		(b) Describe any methods used to examine subgroups and interactions	5-6
		(c) Explain how missing data were addressed	5-6
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	7
Main results	16	(<i>a</i>) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(b) Report category boundaries when continuous variables were categorized	7-8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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