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Association between daily level of objective physical activity and C-reactive protein in a representative national sample of adults with self-reported diagnosed arthritis or fibromyalgia

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Abstract

Purpose: Examine the association between physical activity and sedentary time with high sensitivity C-Reactive protein levels in adults with arthritis and fibromyalgia. We also investigated the level of physical activity that was associated with lower clinical levels of high sensitivity C-Reactive protein (< 3 mg/L).

Materials and methods: Observational design was used to evaluate the variables of interest based on the Canadian Health Measures Survey cycle 1 to 3 (2007 – 2012). Generalized adjusted additive models were used to explore the shape of the association between high sensitivity C-Reactive protein, daily physical activity, step count and sedentary time. High sensitivity C-Reactive protein was measured with blood samples. Physical activity, number of steps and sedentary time were objectively assessed using an Actical accelerometer.

Results: Daily moderate to vigorous physical activity and step count were significantly associated with lower high sensitivity C-Reactive protein levels, but daily light physical activity and sedentary time were not associated with high sensitivity C-Reactive protein levels, even after controlling for age, sex, daily smoking, body mass index, household income, level of education levels, marital status, work year, accelerometer wear time and season. Lower high sensitivity C-Reactive protein levels were associated with 1 to 150 minutes of daily moderate to vigorous physical activity and with daily step counts starting at 4000 in people with arthritis. Adults with fibromyalgia had lower levels of high sensitivity C-Reactive protein when engaging in 10 to 35 minutes of daily moderate to vigorous physical activity and in 5000 to 9000 daily steps.

Conclusions: Daily moderate to vigorous physical activity and step count were associated with high sensitivity C-Reactive protein levels that were below the clinical threshold. Given the positive outcomes of physical activity on health, adults with arthritis and fibromyalgia may benefit from these specific recommendations.

Introduction

Adults with arthritis and fibromyalgia present higher levels of inflammatory biomarkers leading to the development of pain and fatigue, and in turn results to a lower quality of life and physical disability [1–3]. Health care providers use these biomarkers in order to help them identify the progression of arthritis and fibromyalgia. Among these inflammatory biomarkers that are used by rheumatology specialists is high sensitivity C-Reactive protein (hsCRP). Indeed, hsCRP plays a role in the acute phase of inflammation and provides information about the inflammatory state in people with chronic arthritis and fibromyalgia [4]. Several studies have reported significantly higher levels of hsCRP in patients with arthritis and fibromyalgia compared to healthy controls subjects [5–7]. In fact, clinicians often use a level greater than 3 mg/l in hsCRP levels as a tool to help them with the diagnosis of arthritis [8] and is routinely used for clinical testing in patients with fibromyalgia [9]. Furthermore, a positive association has been found between hsCRP levels and fibromyagia symptoms severity [6, 7, 10, 11].

Physical activity (PA) and sedentary time (SED-time) are two modifiable factors that could play an important role in reducing the levels of hsCRP in adults with arthritis and fibromyalgia. In support of this concept, three studies examined the association between physical activity levels measured objectively using accelerometery with hsCRP in other populations [12–14]. Loprinzi et al. [12] reported that higher frequency of daily moderate to vigorous physical activity (MVPA) rather than total weekly MVPA accumulation was associated with C-Reactive protein levels in US adults. Ford et al. [14] observed that the amount of leisure-time physical activity was inversely associated with C-Reactive protein levels in the National Health and Nutrition Examination Survey (NHANES) cohort. However, Parsons et al. [13] found no evidence of a specific amount of PA that was associated with lower C-Reactive protein levels in British men. The authors concluded that longer duration of physical activity was not more important than shorter periods, however, MVPA seemed to have a greater importance. As for SED-time, a randomized control trial showed that physically active individuals had significantly lower C-Reactive protein levels compared to physically inactive subjects [15]. In addition, greater sitting time was positively associated with higher C-Reactive protein levels [16]. Moreover, SED-time measured objectively using a wearable activity monitor (Actigraph GT3X) for 7 consecutive days was positively associated with greater C-Reactive protein levels [17].

Taken together, to our knowledge, no data appears to be available on the relationship between PA and SED-time with hsCRP in patients with arthritis or fibromyalgia. Furthermore, no study has investigated the specific level of PA that is associated with hsCRP levels that are below the clinical cut-point of 3 mg/L in any population. Therefore, the aim of the present study was to examine the transversal association between objectively measured PA and SED-time with hsCRP levels in adults with arthritis and fibromyalgia. We also investigated the level of PA that was associated with lower clinical levels of hsCRP. We hypothesized that the higher daily levels of PA and lower daily time spent in sedentary behaviors in adults with arthritis and fibromyalgia will be associated with lower hsCRP levels (i.e., <3 mg/L). The shape of these associations should be not linear. This is the first study to identify a specific level of objectively measured PA that is associated with lower hsCRP levels in people with arthritis or fibromyalgia in a national representative sample.

Methods

Participants and Setting

Statistics Canada conducted the Canadian Health Measures Survey cycle 1 to 3 (2007 – 2012), from which the data were collected for the present study. Representative of approximately 96% of the Canadian population, participants were aged from 6 to 79 years and lived in private households at the time of the survey. This national survey collected data from ~10 000 respondents in five regional boundaries (British Columbia, the Prairies, Ontario, Quebec, and the Atlantic provinces). Data were collected in two stages [18]. First, sociodemographic and clinical data were collected during a household interview at the participant's home. Then, weight and height were measured, urinary samples were collected, and a spirometry test was conducted for evaluation of pulmonary function during a subsequent visit to a mobile examination center. Residents of Indian Reserves, Crown lands, institutions and certain remote regions, and full-time members of the Canadian Forces were excluded, as well as pregnant women and participants with functional limitation [18]. The present study included participants aged 18 to 79 years old with complete data for mental health and physical activity. All respondents provided written informed consent. The

Health Canada's Research Ethics Board provided ethical approval for CHMS in the analyses. More details about recruitment strategies and assessment tools have been previously published [19–22].

Measures

Sociodemographics

Sociodemographic and general health information were collected during an interview at the participants' home. Then, weight and height measurements were collected during a subsequent visit in a mobile clinic.

Diagnostic criteria for arthritis and fibromyalgia.

During the in-home interview, participants filled in a household questionnaire in order to establish their health profile. Regarding to our studied population, participants had to answer the following questions: "*Now, I'd like to ask about certain chronic health conditions which you may have. We are interested in "long-term conditions", which are expected to last or have already lasted 6 months or more and that have been diagnosed by a health professional. 'Do you have fibromyalgia?' 'Do you have arthritis, for example osteoarthritis, rheumatoid arthritis, gout or any other type, excluding fibromyalgia?'* Participants had to have been diagnosed by their doctor in order to answer 'yes' to one of the two first questions. For the third question, participants had to specify if their arthritis type was either rheumatoid arthritis, osteoarthritis or any other type of arthritis [23].

High sensitivity C-Reactive protein

During the mobile visit, subjects underwent testing for physical measurements conducted by laboratory technicians and phlebotomists. Blood samples were collected for the assessment of hsCRP protein levels and were then analyzed in the appropriate reference laboratory as previously described [24].

Physical activity and sedentary time

After the mobile examination centre visit, participants were asked to wear an Actical accelerometer (Phillips-Respironics, 17 grams, omnidirectional accelerometer) over their right hip on an elasticized belt during their waking hours for 7 consecutive days. The device started to collect data the day following the visit. The monitors were then posted to Statistics Canada. The data were validated by research assistants to determine if they were still within the manufacturer's calibration specifications. The Actical measures and records time-stamped acceleration in all directions, which indicates the intensity of physical activity. The digitized values are summed over an interval of one minute. Accelerometer data were in a count value per minute (cpm) and into steps accumulated per minute [25]. Studies demonstrated the validity and reliability of this device to measure physical activity in healthy adults, and used with our population of interest [21, 26, 27]. After each use, the monitor was checked to determine if it was still within the manufacturer's calibration specifications [28]. All data were blind to the respondents while they were wearing the device. A valid day was defined as 10 or more hours of wear time and respondents with 4 or more valid days were retained for analyses [21]. Accelerometer data were not included in the analyses if a participant had extreme counts (i.e., >20 000 cpm) [29]. The number of minutes per day spent in PA of different intensity levels was categorized using standard cpm for adults: MVPA (⩾ 1535 cpm), light physical activity (LPA) (100 to 1534 cpm) and SED-time (<100 cpm) [21]. Average minutes per day of MVPA and LPA, average steps per day, and average minutes per day of SED-time were separately used in the analyses. More details about the methods and measures have been previously published [21].

Data analysis

We used adjusted generalized additive models to explore the shape of the association between hsCRP, PA, number of steps and SED-time. Separate generalized additive models were fit for every combination of PA and SED-time and hsCRP. The generalized additive model is an extension of the generalized linear model in that one or more predictors may be specified using a smooth function [30]. It is a non-parametric model that permits nonlinear relationships to be modelled with flexibility without specifying the nonlinear functional form. This modelling framework is widely used to study the doses-response relationships between PA and health outcomes [31]. Predictions from generalized additive models were plotted with 95% confidence intervals. Adjusted covariates for all generalized additive models included sex, daily smoking (yes/no), household income (ranged from ≤15 000 to 100 000$), level of education (ranged from ≤high school to university), marital status (alone/couple), body mass index (BMI) and work year (work/non-work) [32–34]. The accelerometer wear time (i.e., 24 hours minus non-weartime [> 60 minutes with 0 counts]) and season of accelerometer assessment can also influence PA and sedentary behaviours

[35], therefore they were also included in the models. Since the hsCRP was not normally distributed, Poisson models were performed. To account for the complex, multistage probability sampling design, the weights provided by the Canadian Health Measures Survey were used in the analyses (i.e., activity monitor subsample weights combining cycle 1, 2 and 3). All analyses were performed using *survey* [36] and *mgcv* [30] packages in R version 3.3.

Results

Sample characteristics

Available accelerometer data of ~1220 participants with self-reported diagnosed arthritis and ~ 100 participants with self-reported diagnosed fibromyalgia from the 3 cycles in the current study represented respectively 15.35% and 1.63% of the Canadian population which are representative of the actual arthrtitis and fibromyagia prevalence in Canada [37, 38]. The mean of hsCRP for people with self-reported diagnosed arthritis was 3 mg/L (Standard error [SE] = 0.13, Median [Mdn] = 1.9), and 3 mg/L (SE = 0.4, Mdn = 2.5) for people with self-reported diagnosed fibromyalgia. The mean age of the participants with arthritis was 59.3 years old (SE = 0.43) and 53.5 years old (SE = 1.17) for the subjects with fibromyalgia. Sixty percent of the participants had arthritis and 94.1% of the participants who had fibromyalgia were women. Canadian Health Measures Survey participants with arthritis spent on average 14 (SE = 0.8, Mdn = 7.4), 195 (SE = 4.1, Mdn = 186.6) and 563 (SE = 4.5, Mdn = 572) minutes per day of MVPA, LPA and SED-time, respectively. Participants with fibromyalgia spent on average 9 (SE = 1.5, Mdn 7.1), 194.9 (SE = 9.5, Mdn = 193.9) and 543 (SE = 12.6, Mdn = 535.4) minutes per day of MVPA, LPA and SED-time, respectively. Table 1 shows weighted characteristics of the participants included in the analyses. The estimated regression coefficients for all models are reported in the table 2 and 3.

Shape of traversal associations between high sensitivity C-Reactive protein and physical activity

Our results suggested that higher daily MVPA and step count were significantly associated with lower hsCRP level in adults having a self-reported diagnosis of arthritis as well as in adults with self-reported diagnosis of fibromyalgia. On the other hand, LPA and SED-time were not associated with hsCRP levels in the two studied populations. Fig 1 and Fig 2 present adjusted generalized additive model results from adjusted models of hsCRP as a function of each daily MVPA duration and number of steps for both participants with self-reported diagnosed arthritis and fibromyalgia. The lines show the smoothed function from adjusted generalized additive model for PA variables, and the shaded area indicates the 95% confidence intervals. Each model was adjusted for age, sex, education, wear time, season, income, and current smoking status. All four plots indicated nonlinear associations between hsCRP levels and daily MVPA and number of steps, respectively. All figures indicate a line at 3.0 mg/l, which represents the clinical threshold of hsCRP considered to be clinically elevated [39]. For the arthritic population, approximately 1 to 150 minutes of daily MVPA was significantly related with lower levels of hsCRP 3.0mg/l starting around 4000 daily steps. Seven thousand five hundred steps per day were associated with the lowest levels of hsCRP, though a slight increase from 7500 and 15000 steps was observed.

In Fig 3, lower levels of hsCRP were noted in participants with fibromyalgia who engaged in 10 to 35 minutes of daily MVPA, with 15 minutes being associated with the lowest level. Interestingly, between 15 minutes and 35 minutes, the curve increased, but remained under the clinically threshold. In Fig 4, participants engaging in 5000 to 9000 and more than 13500 steps per day showed lower levels of hsCRP. The daily number of steps associated with the lowest level of hsCRP was approximately 7500.

Sedentary time was not significantly associated with hsCRP. In adults with self-reported arthritis, the models explained 11.4% of the variance in the MVPA-hsCRP association and 11.9% in the steps-hsCRP association. In adults with self-reported fibromyalgia, the models explained 32.6% of the variance in the MVPA-high sensitivity C-Reactive protein association, and 45.5% in the step-hsCRP association. More detailed information about the weighted estimated regression coefficients for physical activity modalities and hsCRP association with arthritis and fibromylagia are in reported in table 2 and 3.

Discussion

This study investigated the transversal association between daily PA levels and hsCRP levels in a representative national sample of adults with self-reported diagnosed of arthritis or fibromyalgia. Results showed a non-linear pattern between two physical activity modalities (i.e., MVPA and steps) with hsCRP levels and this was independent of SED-time in the two studied populations. This is the first study to identify a specific level of objectively measured PA that is associated with lower hsCRP levels in people with arthritis or fibromyalgia in a

national representative sample. Lower hsCRP levels were observed from the first MVPA minute until 150 minutes in people with arthritis. Our results are in line with the findings of Loprinzi et al. (2015) who found that participants engaging in a higher frequency of MVPA (# of days of ≥ 30 min/day of MVPA) was strongly associated with lower C-Reactive protein levels than the total weekly MVPA volume in US adults. These findings are also similar with the study of Parson et al. [13] who showed that longer bouts of PA are not necessarily more important than shorter ones. Furthermore, our findings suggested that SED-time was not related to hsCRP levels. This finding differs from what has been previously found in the literature. That is, three studies have previously found a positive association with sedentary time and hsCRP levels [15–17]. However, the studied population in these investigations were either young or old participants with an active or inactive lifestyle, or adults with type 2 diabetes, which may explain the different results.

Canadian Health Measures Survey participants with fibromyalgia were associated with smaller amount of MVPA levels and step counts with levels of hsCRP. This finding is consistent with the study from Bernard et al. [40] who stated that the nationally representative sample of women with self-reported fibromyalgia actually spent significantly less time in MVPA than the controls. Therefore, it supports the idea that different populations could need different physical activity modalities in order to gain benefits from PA and not necessarily need to meet national PA guidelines, which recommend 30 minutes of MVPA [41]. In addition, LPA was not associated with lower hsCRP levels in both populations in the present study. This suggests that a higher intensity in PA may be required in order to find a significant correlation with hsCRP.

These findings offer some insights that have important implications for health care providers dealing with people having arthritis or fibromyalgia. Indeed, the PA modalities correlated with lower hsCRP levels become interesting health indicators that may be used by health professionals with the planning of intervention programs. For example, walking may be one PA that could be recommended to these populations since it has been shown to be beneficial in individuals with arthritis or fibromyalgia [42]. In addition, a report showed that patients with arthritis may benefit from an exercise intervention [37]. Therefore, results from the present study provide support in favour of PA as a health promotion tool for people with arthritis and fibromyalgia. It should also be note that short bouts of PA appear to have a similar effect as longer ones. This is important for the arthritic population since they engage in lower duration of PA compared to people without the illness [43].

Strengths and limitations

Our study has a few limitations. First, we were not able to analyze the results within the different classifications of arthritis because arthritis classification varied between cycle 1, 2, and 3 or to control the presence of another rheumatic and musculoskeletal disease. Second, participants having a temporary immune condition have been included in the blood sample collection, which could have altered hsCRP results [44]. Third, the CRP level could be more pronounced among large sample of FI patients [45]. Consequently, the identified PA dose could vary for this population. Finally, the self-reported diagnostic of arthritis or fibromylagia might be associated with higher risk of misclassification of participants. Thus, false positive adults could be included in arthritis or fibromylagia groups. However, this is the first study to explore the relationship between objectively measure PA modalities and hsCRP levels in a representative national sample of adults with self-reported diagnosed arthritis or fibromyalgia.

Conclusion

In conclusion, every daily MVPA minutes until 150 minutes or daily steps counts starting at 400 could be associated with lower CRP level in people with arthritis. Individuals with fibromyalgia had lower levels of hsCRP when engaging in 10 to 35 minutes of daily MVPA and in 5000 to 9000 daily steps. Our findings give us a better understanding of a potential prescription of PA in these populations that could be used by health care professionals. Further research may want to investigate the specific type of PA that could optimize the benefits for people having these two chronic conditions.

Table 1 Weighted means and ratio among participants

	Arthritis	Fibromyalgia
Age (years) – Mean (M) (SE)	59.3 (0.43)	53.5 (1.17)
Sex % (N)		
Men	39.9 (1 532 818)	5.9 (23 904)
Women	60.1 (2 311 598)	94.1 (383601)
Current daily smoker % (N)		
Yes	16.2 (62 2065)	19.4 (78 898)
No	83.8 (3 222 211)	80.6 (328 607)
Education % (N)		
< than high school diploma	15.5 (597 461)	12.9 (52 742)
College or uni or bach	28.9 (1 112 373)	29.2 (118 788)
Workschool	15.1 (52 250)	16.3 (66 252)
Other	40.4 (1 552 332)	41.6 (169 723)
Household incomes (CAN dollars) % (N)		
≥ 10 000	21.7 (832 768)	14.7 (59 770)
≤ 20 000	10.2 (394 460)	16.4 (66 611)
20 000 < 40 000	22.3 (857 040)	18.3 (74 722)
40 000 < 60 000	22.5 (863954)	18.1 (73 879)
60 000 < 80 000	13.6 (523 906)	22.2 (90 505)
80 000 < 100 000	9.7 (372 287)	10.3 (42 016)
Marital status % (N)		
Alone	32.9 (1 235 218)	28.8 (117 189)
Couple	67.1 (2 579 197)	71.2 (290 316)
Work year % (N)		
No work	48.8 (1 874 457)	43.3 (176 441)
Work	51.2 (1 969 959)	56.7 (231 064)
Self-reported chronic disease % (N)		
Yes	64.1 (2 463 113)	84.7 (345 030)
No	35.9 (1 381 303)	15.3 (62 476)
Body mass index (kg/m2) (SE)	28 (0.2)	28 (0.7)
MVPA (min/day) – M (SE)	14 (0.8)	9 (1.5)
LPA (min/day) – M (SE)	195 (4.0)	195 (9.4)
Sedentary (min/day) – M (SE)	563 (4.5)	543 (12.6)
Step count – M (SE)	6 694.1 (148.53)	6 056.9 (313.14)
Wear time (hour/day) – M (SE)	12 (0.09)	12 (0.2)
C-Reactive Protein (mg/L) – M (SE)	3 (0.13)	3 (0.4)

Table 2 Weighted estimated regression coefficients for physical activity and high sensitivity C-Reactive protein association in arthritis

	edf	*Ref df*	*Chi sq.*	*p-value*	*Adjusted R2*	*Deviance explained (%)*
MVPA (min/day)	2.5	3.1	13.3	0.0053**	0.12	11.4
LPA (min/day)	2.4	3.1	2.5	0.6	0.11	10.8
Steps (per day)	3.5	9	30.5	3,61E***	0.12	11.9
Sedentary behavior (min/day)	3.9	4.8	7.8	0.1	0.11	11.2

Table 3 Weighted estimated regression coefficients for physical activity and high sensitivity C-Reactive protein association in fibromyalgia

	edf	*Ref df*	*Chi sq.*	*p-value*	*Adjusted R2*	*Deviance explained (%)*
MVPA (min/day)	2.7	3.3	9.7	00282*	0.2	32.6
LPA (min/day)	1	1	0.6	0.425	0.1	22.1
Steps (per day)	4.2	9	27.5	5,19E***	0.3	45.5
Sedentary behavior (min/day)	1	1	1.09	0.296	0.1	25.3

Table 4 Weighted estimated regression coefficients for physical activity and high sensitivity C-Reactive protein association in fibromyalgia

	M	*SE*	*Mdn*	*IQR*
Age (years)	59.3	0.43	60	17
CRP (mg/L)	3.0	0.1	1.9	3.1
BMI (kg/m2)	28.0	0.2	27.1	6.7
MVPA (min/day)	13.6	0.9	7.4	16.7
LPA (min/day)	195.4	4.1	186.6	102.3
Sed (min/day)	563.8	4.5	572	118.5
Wear (min/day)	12.9	0.09	13.0	2.6

Table 5 Weighted means among participants with self-reported diagnosed fibromyalgia

	M	*SE*	*Mdn*	*IQR*
Age (years)	53.5	1.2	55	14
CRP (mg/L)	3.6	0.4	2.5	4.1
BMI (kg/m2)	28.1	0.8	27.1	6.6
MVPA (min/day)	8.9	1.5	7.1	8.4
LPA (min/day)	194.9	9.5	193.9	64.9
Sed (min/day)	543.2	12.6	535.2	126.0
Wear (min/day)	12.5	0.2	12.4	2.3

Fig 1 Associations between C-reactive protein level and moderate-vigorous physical activity in people with self-reported arthritis

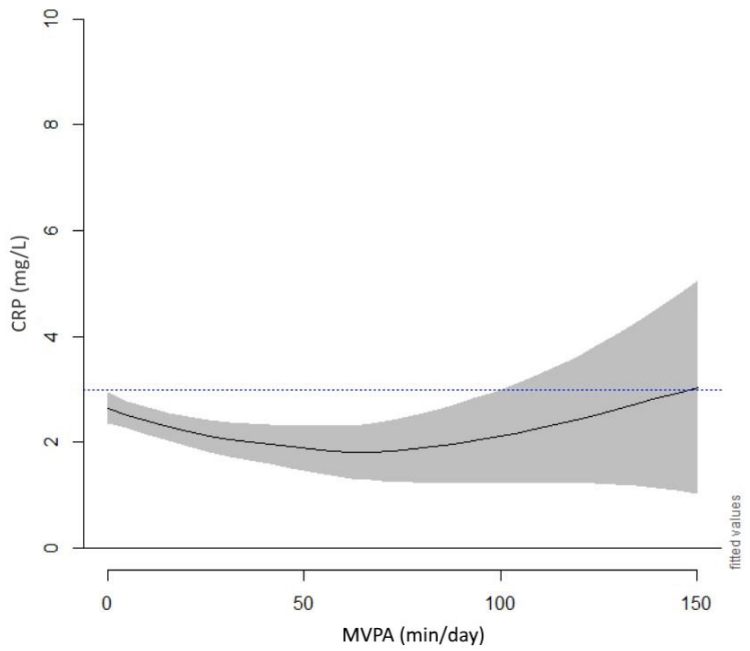


Fig 2 Associations between C-reactive protein level and daily steps in people with self-reported arthritis

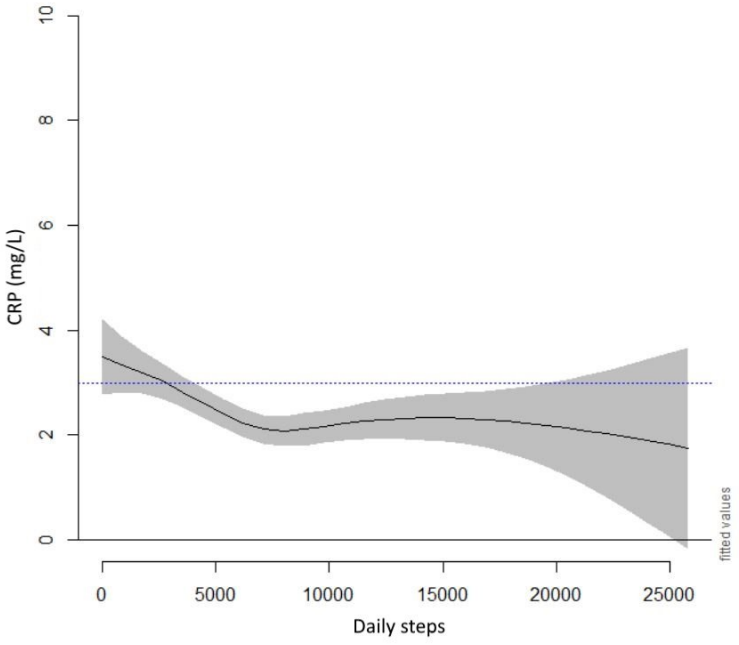


Fig 3 Associations between C-reactive protein level and moderate-vigorous physical activity in people with self-reported fibromyalgia

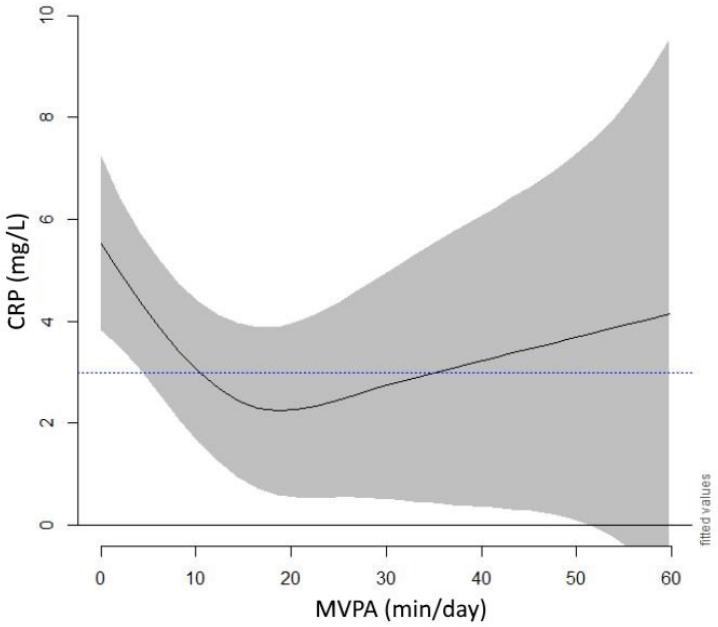
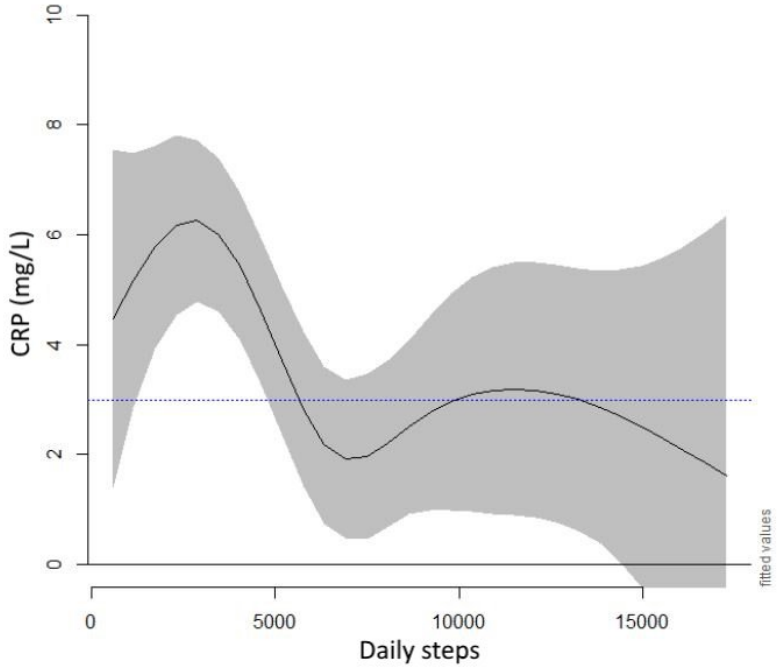


Fig 4 Associations between C-reactive protein level and daily steps in people with self-reported fibromyalgia



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