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Effects of Recreational Exercise on Nonsteroidal Anti-inflammatory Drug Use: A Comprehensive Analysis of the NHANES Database

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Abstract

Introduction: *This study examines whether recreational physical activity is associated with reduced Non-Steroidal Anti Inflammatory Drugs (NSAIDs) use among adults. While NSAIDs effectively manage pain, they carry risks like gastrointestinal and cardiovascular side effects. Exercise, known for its anti-inflammatory effects, offers a non-pharmacological alternative. Physical activity reduces inflammation through anti-inflammatory cytokines, and lower visceral fat, and immune support, suggesting it may reduce NSAID need.*

Methods: *We performed a cross-sectional study using the 2017-2018 NHANES dataset, evaluating the association between NSAID use and recreational physical activity data. Statistical analysis with STATA 18.5 applied univariate and logistic regression modeling to assess associations between recreational exercise (moderate, vigorous, or both) and NSAID use in the last 30 days. Confounders, including age, gender, BMI, arthritis, and trouble sleeping, were adjusted using a multivariate analysis model.*

Key Findings: *5,145 adults who performed recreational activity in the last 30 days were evaluated for their use of NSAIDs. The adjusted analysis showed that, when controlling for age, gender, and BMI, individuals engaging in both moderate and vigorous exercise had significantly lower odds of NSAID use (OR 0.50, 95% CI: 0.32, 0.78). Additionally, arthritis (OR 3.89, 95% CI: 2.83, 5.34) and at least one comorbidity (OR 1.75, 95% CI: 1.15, 2.65) were linked to higher NSAID use. Additionally, having no trouble sleeping showed less likelihood of NSAID use (OR 0.34, 95% CI: 0.27, 0.41).*

Conclusion: *This study highlights that recreational moderate and vigorous exercise is associated with reduced NSAID use. Recognizing factors like arthritis and sleep quality that influence NSAID use helps improve pain management strategies, with exercise as an added benefit. Further research should explore exercise types and lasting effects on NSAID reduction.*

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Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) are used worldwide for pain management and account for 5-10% of annual prescriptions (Montuori et al., 2024). In the US, NSAIDs account for over 111 million prescriptions yearly and make up about 60%

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of the analgesic market due to their analgesic, anti-inflammatory, and antipyretic effects against conditions such as arthritis. (Laine, 2001) However, long-term NSAID use has been linked to gastrointestinal bleeding, cardiovascular events, and nephrotoxicity, with the elderly population being particularly susceptible. (Pirmohamed et al., 2004; Warden, 2010). Each year, NSAID-related side effects lead to approximately 103,000 hospitalizations and 16,500 deaths in the U.S., comparable to mortality rates from asthma, cervical cancer, and AIDS (Ussai et al., 2015). Given these risks, the utilization of alternative therapies that can have similar outcomes in pain control but with a lower risk of adverse effects is of paramount importance.

Physical activity is known for its anti-inflammatory effects (Pedersen & Saltin, 2015), offering a promising non-pharmacological approach to chronic pain management. Exercise reduces visceral fat, a significant source of chronic inflammation, and promotes anti-inflammatory cytokines like IL-10 and IL-1RA, which help regulate immune responses (Gleeson et al., 2011). Additionally, exercise induces cortisol and adrenaline release, amplifying its anti-inflammatory effects (Gleeson et al., 2011). Although exercise's anti-inflammatory benefits are well established, limited research has investigated whether it reduces the need for NSAIDs. Most studies focus on NSAIDs impacts on exercise, with some evidence suggesting that they may not effectively reduce muscle soreness or enhance performance and, at high doses, might hinder muscle adaptation in resistance-trained young adults (Cornu et al., 2020; Lilja et al., 2017). The potential of exercise alone to reduce NSAID reliance for pain management remains largely unexplored and requires further investigation.

This study aims to explore if recreational exercise is associated with reduced NSAID intake, through a logistic regression model using data from the 2017-2018 National Health and Nutrition Examination Survey (NHANES). Both moderate and vigorous recreational activities are analyzed to determine if exercise intensity impacts NSAID reliance. It was hypothesized that moderate to vigorous recreational activities may lower NSAID dependence due to exercise's anti-inflammatory effects. By identifying factors associated with NSAID use in active adults, this study has the potential to amplify the current knowledge of pain management, supporting public health initiatives that encourage physical activity as a means to reduce NSAID dependency and improve overall health.

Materials and Methods

This study employed a cross-sectional analysis to explore the association between recreational exercise and the use of NSAIDs in adults from the United States of America, utilizing data from the NHANES 2017-2018 dataset (NHANES, 2021). This survey includes approximately 9254 participants of all ages and encompasses diverse minority groups, such as Hispanics, non-Hispanic Blacks, and non-Hispanic Asians. The survey information is varied, including questionnaires about lifestyle and disease prevalence, physical examination, and laboratory data (Centers for Disease Control and Prevention, 2024). The analysis used demographic and health-related variables to build a logistic regression model examining the predictors of NSAID use. Participants were adults aged 18 and older, with complete data for moderate or vigorous recreational exercise and NSAID use. Individuals with missing or incomplete data for the variables of interest were excluded. The missing data had no specific pattern, so a complete case analysis was performed. In total, 5,846 observations were included in the analysis.

The primary independent variable was recreational exercise, categorized into 4 groups: no moderate or vigorous exercise, only moderate exercise, only vigorous exercise, and both moderate and vigorous exercise. In this survey, moderate recreational activity was defined as any recreational activity that caused a slight increase in heart rate or breathing for at least 10 minutes, while vigorous recreational activity was defined as any recreational activity that caused a significant increase in heart rate or breathing for at least 10 minutes (Centers for Disease Control and Prevention, 2021). The dependent variable was NSAID use, measured as a binary outcome. In the NHANES data set, NSAID use was a binary variable with "yes" indicating that a participant had used any form of NSAIDs in the last 30 days. Doses and specifications of the type of NSAIDs used were not provided in the dataset and therefore could not be specified in the multivariate model.

A forward selection strategy was employed to include the additional variables of gender, age, Body Mass Index (BMI), arthritis, gout, at least one comorbidity, and trouble sleeping. Arthritic diseases were added separately as they are important risk factors of NSAID use, and it is not specified in the data set if they are included in the at least 1 comorbidity variable. Additionally, the variable "at least 1 comorbidity" explores polypharmacy, not included as a separate variable in the data set. These variables were selected for their clinical relevance and potential to confound the relationship between exercise and NSAID use, ensuring a comprehensive adjustment

in the analysis. The relationship of these variables is shown in Figure 1.

Statistical analysis was done using STATA 18.5™ BE. Univariate analysis used logistic regression to assess the relationship between each independent variable and NSAID use. Variables with clinical relevance were added to the multivariate model in a stepwise fashion, assessing the model's chi-square likelihood ratio for each one of the selected variables. A multivariate logistic regression was then conducted to identify variables associated with NSAID use, with odds ratios (OR) and 95% confidence intervals (CI) calculated for each variable. A p-value less than 0.05 was considered significant. Sensitivity analyses of the final multivariate model were evaluated using a goodness-of-fit test and the area under the curve (AUC) to determine its predictive accuracy. Multicollinearity was assessed, and variables with a Variance Inflation Factor (VIF) higher than five were considered for removal if these altered the significance of the exercise variable. further detail on STATA commands found in supplementary material.

Results

A total of 5,846 participants were included in the study. Of these, 701 were excluded due to missing data, resulting in 5,145 participants analyzed in the final dataset. The following characteristics were seen in the 342 (6%) participants that used NSAIDs: mean age 57 (SD 15), female 59.6%, mean BMI 31.97 (SD 7.47), at least one comorbidity (87.7%), and with trouble sleeping (50.3%). The level of exercise in the overall population: participants that didn't engage in moderate or vigorous exercise (67.3%), only moderate (21.3%), only vigorous (4.1%), and in both (7.3%). The comorbidities were arthritis (62.9%), gout (1.8%), and both (6.4%). Baseline characteristics are described further in Table 1.

Unadjusted models (Table 2) showed a significant association between participants who performed both moderate and vigorous exercise with lower NSAIDs use, compared to those who did not perform moderate or vigorous exercise, [0.74 OR (95% CI: 0.57, 0.96), 0.38 OR (95% CI: 0.22, 0.66)] $p < 0.05$, respectively, with this association being more significant for participants who performed both exercise modalities at the same time, 0.29 OR (95% CI: 0.19, 0.45), $p<0.05$.

In the adjusted model (Table 2), the association between participants who engaged in both moderate and vigorous exercise with lower NSAID use remained significant compared to those who did not perform moderate or vigorous exercise after adjustment for gender, age, and body mass index, 0.50 OR (95% CI: 0.32, 0.78), $p <0.02$. Participants who had arthritis had higher odds for NSAID use compared to those who did not have arthritis, 3.89 OR (95% CI: 2.83, 5.34), $p <0.001$, and those with at least one comorbidity had higher odds for NSAID use compared to those who had none, 1.75 OR (95% CI: 1.15, 2.65), p-value <0.009. Visual representations of all odd ratios present in the multivariate analysis are present in Figure 2.

In the sensitivity analysis, a goodness-of-fit test was conducted to assess the model's fit to the data. The p-value of 0.6918 failed to reject the null hypothesis of good fit, indicating that the model adequately represents the observed data. Additionally, the AUC was calculated to evaluate the model's predictive performance. With an AUC of 0.7640, the model has a 76.40% probability of correctly classifying a positive or negative instance. To assess multicollinearity, VIF was calculated for the final multivariate model. The mean VIF obtained was 3.23, indicating an acceptable multicollinearity level. However, upon examining individual variables, age and BMI were found to have VIF values exceeding 5, suggesting high collinearity. To evaluate the impact of these variables, a second multivariate model was constructed without age and BMI. A comparison of the two models revealed that removing these variables did not significantly alter the significance of the exercise variable. Therefore, considering the clinical relevance of age and BMI, these were retained in the final model.

Discussion

The present study indicates that engaging in both moderate and vigorous recreational exercise is significantly associated with lower NSAIDs use. Large population-based cohort studies consistently demonstrate an inverse association between markers of systemic inflammation and physical activity or fitness levels, while data from several small-scale intervention studies support the notion that exercise training reduces inflammation (Beavers et al., 2010; Metsios et al., 2020). Additionally, an interventional study suggests that NSAIDs do not effectively prevent exercise-induced pain or inflammation, which may explain the reduced use of these medications among individuals who engage in regular exercise (Roberts et al., 2024). Supporting the well-established anti-inflammatory effects of physical activity, regular exercise may help reduce the need for pain medication.

After adjusting the model, both arthritis and gout were significantly associated with increased NSAID use, consistent with the chronic management of these conditions. This highlights the need for alternative pain management strategies that could reduce NSAID dependency in those with chronic conditions. Another significant variable was that participants

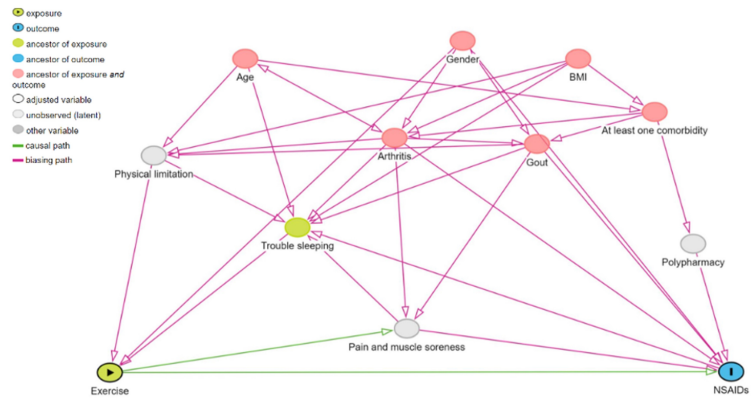

Figure 1: *Direct Acyclic Graph describing the clinical relationship for the covariates that were included in the multivariate analysis.*

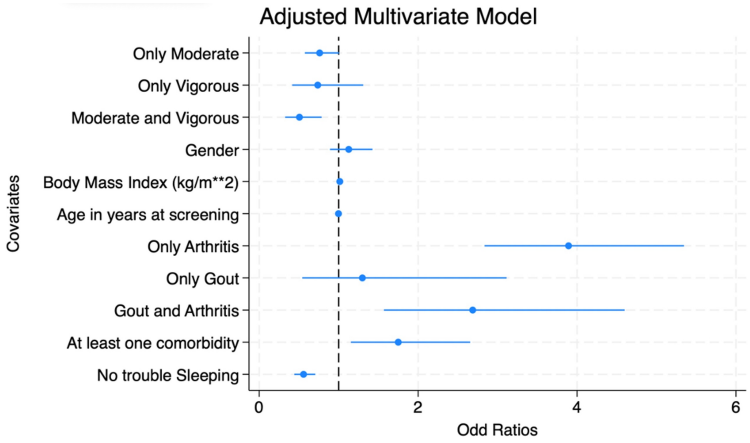

Figure 2: *Forest plot of the multivariate model.*

	NSAID used in last 30 days		
Sample Characteristic	**No n(%)**	**Yes n(%)**	**Total n(%)**
Number of participants - n (%)	4,803 (93.4%)	342 (6.6%)	5,145 (100.0%)
Age in years at screening - Mean (SD)	50.754 (17.752)*	57.637 (14.558)*	51.211 (17.640)*
Sex			
Male - n (%)	2,343 (48.8%)	138 (40.4%)	2,481 (48.2%)
Female - n (%)	2,460 (51.2%)	204 (59.6%)	2,664 (51.8%)
Body mass index (kg/m^2) - Mean (SD)	29.692 (7.342)*	31.961 (7.747)*	29.842 (7.390)*
Level of recreational exercise			
Not moderate or vigorous - n (%)	2,515 (52.4%)	230 (67.3%)	2,745 (53.4%)
Only moderate - n (%)	1,121 (23.3%)	73 (21.3%)	1,194 (23.2%)
Only vigorous - n (%)	333 (6.9%)	14 (4.1%)	347 (6.7%)
Moderate and vigorous - n (%)	834 (17.4%)	25 (7.3%)	859 (16.7%)
Combined gout and arthritis			
No gout or Arthritis - n (%)	3,369 (70.1%)	99 (28.9%)	3,468 (67.4%)
Only arthritis - n (%)	1,152 (24.0%)	215 (62.9%)	1,367 (26.6%)
Only gout - n (%)	112 (2.3%)	6 (1.8%)	118 (2.3%)
Gout and Arthritis - n (%)	170 (3.5%)	22 (6.4%)	192 (3.7%)
At least one comorbidity			
No - n (%)	2,001 (41.7%)	42 (12.3%)	2,043 (39.7%)
Yes - n (%)	2,802 (58.3%)	300 (87.7%)	3,102 (60.3%)
Ever told doctor had trouble sleeping?			
No - n (%)	3,540 (73.7%)	170 (49.7%)	3,710 (72.1%)
Yes - n (%)	1,263 (26.3%)	172 (50.3%)	1,435 (27.9%)

*Mean (standard deviation)

Table 1: *NSAID used in the last 30 days.*

Variables	Odds ratio (95 %CI)	Standard error	P value
2.1 Unadjusted model			
atleast_mod*			
Only moderate	0.74 (0.57, 0.96)	0.098	0.028
Only vigorous	0.38 (0.22, 0.66)	0.106	0.001
Moderate and vigorous	0.29 (0.19, 0.45)	0.062	0.000
Age at years at screening	1.02 (1.01, 1.02)	0.003	0.000
Gender			
Female	1.46 (1.18, 1.80)	0.159	0.000
BodyMassIndexkgm2	1.04 (1.02, 1.05)	0.006	0.000
Combined arthritis and gout	1.88 (1.69, 2.11)	0.105	0.000
Trouble sleeping			
No	0.34 (0.27, 0.41)	0.036	0.000
At least one comorbidity			
Yes	5.40 (3.96, 7.37)	0.855	0.000
2.2 Adjusted model			
atlesat_mod			
Only moderate	0.76 (0.57, 1.00)	0.109	0.057
Only vigorous	0.73 (0.41, 1.30)	0.216	0.298
Moderate and vigorous	0.50 (0.32, 0.78)	0.113	0.002
Gender			
Female	1.12 (0.89, 1.42)	0.135	0.320
BodyMassIndexkgm2	1.01 (1.00, 1.02)	0.007	0.048
Age at years at screening	0.99 (0.98, 1.00)	0.004	0.601
Combined gout and arthritis			
Only arthritis	3.89 (2.83, 5.34)	0.629	0.000
Only gout	1.29 (0.54, 3.11)	0.579	0.558
Gout and arthritis	2.68 (1.56, 4.59)	0.736	0.000
Trouble sleeping			
No	0.55 (0.44, 0.70)	0.066	0.000
At least one comorbidity			
Yes	1.75 (1.15, 2.65)	0.372	0.009

*atleast_mod (at least moderate exercise): represents the level of recreational exercise

Table 2: *Unadjusted and adjusted models.*

without trouble sleeping had decreased NSAID use, this aligns with Korabelnikova et al (2020) study that explains that sleep disorders and headaches cause or exacerbate each other in a bidirectional manner that require this line of pharmacological approach. The relationship between sleep and physical activity may also play a role, as physical activity has been shown to improve sleep (Kline, 2014). The impact of sleep quality in this study suggests that improving both physical activity and sleep could collectively decrease dependence on pain medication. Addressing modifiable factors like sleep and physical activity ultimately leads to better pain management strategies and reduces the reliance on NSAIDs in chronic condition management.

Multicollinearity may affect other significant variables in the unadjusted model, such as gender, BMI, and age. Gender differences in NSAID use were observed, with women reporting higher usage than men, likely due to variation in pain perception influenced by biological factors like hormones and sociocultural differences in health-seeking behavior (Bartley & Fillingim, 2013; Dominick et al., 2003). Age and BMI are associated with higher NSAID use. This is consistent with prior literature, which found that adults and individuals with higher BMI are more susceptible to chronic pain and musculoskeletal conditions, such as osteoarthritis (Davis et al., 2017). Mechanical stress and joint deterioration in higher BMI individuals often increase inflammation and pain, commonly managed with NSAIDs (Li et al., 2020; Marcum & Hanlon, 2010).

The strengths of this study include the large, nationally representative sample from the NHANES 2017-2018 dataset, enhancing the generalizability of our findings to the broader U.S. population. However, limitations include the cross-sectional study design, restricting causal inference, and the self-reported nature of data, limiting control over survey responses. Another limitation is the variability in baseline characteristics among NSAID users (Table 1), which may introduce bias and affect group comparability, potentially impacting interpretation. Additionally, due to limited details on NSAIDs use, the effect of exercise on specific regimens or formulations is unknown. Information on specific recreational exercise types is also unavailable, and non-recreational physical activity is not included in our dataset. Likewise, we could not address the long term NSAID use since the dataset of past 30-day NSAIDs use does not sufficiently address this issue, which may lead to bias. Future studies should explore potential confounding factors such as comorbidities and sleep disorders more comprehensively to better understand their roles as mediators or modifiers in the relationship between exercise and NSAID use.

Conclusion

This study identifies an inverse relationship between recreational activities and NSAID use, suggesting that exercise may be associated with a reduction of NSAID use. Additionally, arthritis and gout are linked to increased NSAID use, while better sleep is associated with decreased use. However, future research is needed to explore the causality of this relationship, potentially utilizing longitudinal data and examining NSAID dosages and types of physical activity.

Abbreviations

NHANES: National Health and Nutrition Examination Survey
NSAID: Non-Steroidal Anti Inflammatory Drugs
BMI: Body Mass Index
AUC: Area Under the Curve
VIF: Variance Inflation Factor

Supplementary Materials

STATA codes

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Conflicts of Interest

The authors declare no conflict of interest.

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