Apathy and Physical Activity: A Systematic Review and Meta-Analysis

Ata Farajzadeh[1], Alexe Hébert[1], Ian M. Lahart[2], Martin Bilodeau[1], & Matthieu P. Boisgontier[1,3,*]

[1] School of Rehabilitation Sciences, Faculty of Health Sciences, University of Ottawa, Canada
[2] Faculty of Education, Health and Wellbeing, Institute of Human Sciences, University of Wolverhampton, Wolverhampton, UK
[3] Perley Health Centre of Excellence in Frailty-Informed Care, Ottawa, Canada

Abstract

Background. Patient motivation is essential for the success of their rehabilitation. Apathy, a state of primary motivational deficiency, may therefore hinder physiotherapists' interventions, such as those aimed at increasing patients' physical activity. This study aims to examine the negative relationship between apathy and physical activity and to identify the factors that influence this relationship.
Objective. This study aims to explore the negative association between apathy and physical activity, identifying factors influencing this relationship.
Methods. Six databases were searched for articles including both a measure of apathy and physical activity. Two reviewers screened articles for inclusion, assessed risk of bias, and extracted data from each study. Pearson product-moment correlations were pooled from eligible studies using the generic inverse pooling and random effects method to examine the relationship between apathy and physical activity.
Results. Twenty-eight articles were included in the systematic review and 22 studies (n = 12,541 participants) in the meta-analysis. Results showed a small negative correlation between apathy and physical activity ($r = -0.13$; 95% CI: -0.18 to -0.09; $p < 0.0001$). A subgroup meta-analysis revealed that the correlation was statistically significant in patients with Parkinson's disease and in older adults who were healthy, depressed, fallers, or had mild cognitive impairment. A meta-regression suggested an effect of age, with older age being associated with a stronger correlation between apathy and physical activity.
Conclusions. Our results suggest that higher levels of apathy are associated with lower levels of physical activity and that this negative association is strengthened with aging. Therefore, apathy could be a limiting factor to exercise therapy and may have prognostic implications in patients whose condition requires physical activity.

Key words

Apathy, Exercise, Health, Motivation

Cite this article:

Farajzadeh A, Hébert A, Lahart IM Bilodeau M, Boisgontier MP. (2024). Apathy and physical activity : A systematic review and meta-analysis. *MedRxiv.*

Data & Code:

https://doi.org/10.5281/zenodo.10929857

***Author for correspondence:**

Matthieu P. Boisgontier
Email: matthieu.boisgontier@uottawa.ca

In the early 1990s, apathy began to be considered a syndrome rather than a mere symptom of another condition, and was defined as a state of primary motivational impairment characterized by reduced goal-directed behaviors (e.g., lack of productivity, effort, initiative, and perseverance), reduced goal-directed cognitions (e.g., lack of interest in learning new things, in new experiences, lack of concern about one's personal and health problems, reduced socialization), and reduced emotional concomitances of behavior (e.g., flat affect, emotional indifference)[1,2]. To date, the dominant theoretical frameworks still consider three subtypes of apathy: behavioral, cognitive, and emotional[3,4], with a fourth subtype, social apathy, recently proposed but requiring further research[5]. Levy and Dubois[6] proposed that behavioral apathy is related to difficulties in elaborating the plan of actions necessary for behavior. Cognitive apathy is the inability to self-activate thoughts or self-initiate actions. Emotional apathy is the inability to establish the linkage between emotional signals and behavior[6].

Apathy occurs across a wide range of neurological and psychiatric disorders[7], including dementia (54%)[8], schizophrenia (47-53%)[9-11], Parkinson's disease (40%)[12], and stroke (33%)[13]. Apathy has also been observed in healthy young adults (1.5%)[14] and older adults with normal cognitive function (2-7%)[15-19]. Apathy is associated with lower cognitive performance in older adults with normal cognitive functioning[16], cognitive decline (mild cognitive impairment)[17], transition to dementia[20,21], and dementia severity[22,23]. Therefore, apathy could be considered a marker of impending cognitive decline and future risk for dementia[16]. Moreover, apathy has been associated with frailty[24], functional decline[25-28], poorer quality of life[14,19,29], higher mortality[30,31], and higher healthcare costs[32].

In addition, some studies suggest that apathy can negatively affect physical activity[23-36], which includes exercise, sports, active travel (cycling, walking), household chores, and work-related physical activity[37]. This potential effect of apathy is worth investigating since physical activity is now widely recognized as one of the top contributors to physical and mental health, improving cognitive functioning[38], and reducing rates of cardiovascular disease[39], cancer[40], hypertension[41], diabetes[42], obesity[43], depression[44], and functional dependence[44,45]. Despite these benefits, over one in four adults fails to meet the recommended levels of physical activity[37]. While the motivational impairment that defines apathy is likely to reduce the engagement in physical activity, there are some discrepancies in the literature, with multiple articles showing no evidence of such relationship[46,47] or even supporting the opposite association[48].

The main objective of this study was to conduct a systematic review and meta-analysis of the direct relationship between apathy and physical activity. We hypothesized that levels of apathy would be negatively associated with levels of physical activity. In addition, we examined whether this association was influenced by apathy measures, physical activity measures (i.e., accelerometers, pedometers, questionnaires), physical activity outcome (e.g., total physical activity, moderate or vigorous physical activity, steps per day), health status, age, and gender.

Methods

Search Strategy

This review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[49]. Potential studies were identified by searching the MEDLINE (via PubMed), PsycINFO, Web of Science, Embase, SPORTDiscus, and CINHAL databases. The search terms used to identify relevant studies were variants of physical activity (e.g., physical activity, physical education, training, physical fitness, exercise, sport, walk) and apathy (e.g., abulia, apathetic, amotivation, avolition, neuropsychiatric inventory, NPI, emotional indifference, frontal lobe personality scale, Lille apathy rating scale, LARS, dementia apathy interview and rating, DAIR, frontal system behavior scale, FrSBe, key behaviors change inventory, KBCI, apathy evaluation scale, apathy scale, irritability apathy scale, and IAS). Articles were searched up to November 2023 with no limitation on the start date. A filter was used to limit the search to studies published in English. To reduce literature bias, this systematic review was pre-registered in PROSPERO (CRD42023492162)[50].

Eligibility Criteria and Study Selection

Inclusion Criteria

To be included in this systematic review, articles had to 1) be published in a peer-reviewed journal, 2) be written in English, 3) report original data collected from human participants, 4) include at least one self-reported measure of apathy and at least one measure of physical activity, and 5) formally test the association between these two variables. The physical activity measure could be a self-reported measure of the level of physical activity or device-based measure (e.g., accelerometry). Cohort studies, baseline data from clinical trials, and cross-sectional studies were included in this review.

Exclusion Criteria

Studies were excluded if they were 1) published as a book chapter, study protocol, or conference abstract, or 2) based on laboratory-based measures of physical fitness (e.g., maximal muscle force, $\dot{V}O_2$ max) and not on a measure of physical activity.

Study Selection

Functional Articles were screened using the Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia), a web-based collaborative software platform that streamlines the production of systematic reviews. After duplicates were removed, titles and abstracts were independently reviewed by two reviewers who authored this article (AF, AH) according to the inclusion and exclusion criteria using a systematic four-step process. Step 1: Articles that did not report original empirical data were excluded (e.g., reviews, meta-analyses, protocols, commentaries, technical reports, case studies). Step 2: Articles that did not involve human participants were excluded. Step 3: Articles that did not assess both apathy and physical activity were excluded. Step 4: Articles that did not formally test the association between apathy and physical activity, and for which the corresponding author did not provide this information in response to our email request, were excluded. If there was any doubt at any step, the full text was further reviewed. In addition, reference screening and forward citation tracking were performed on the articles remaining after these four steps. Disagreements between the two reviewers (AF, AH) were resolved by consensus among four reviewers (AF, AH, MB, MPB).

Data Extraction

Data extracted from the selected articles included first author's name, article title, publication year, number of participants, number of men and women, mean age and range, health status, type of apathy measure, level of apathy, type of physical activity measure and outcome, level of physical activity, as well as statistical estimates, and significance of the association between apathy and physical activity.

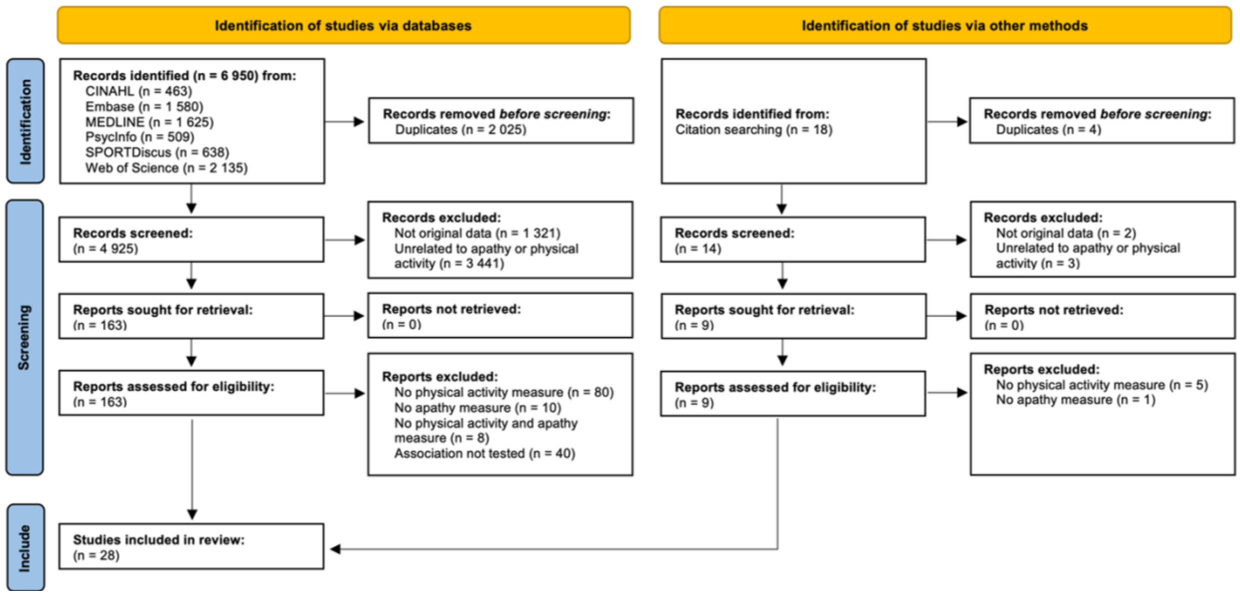

Figure 1. PRISMA 2020 flow diagram.

Bias Assessment

The included studies were assessed for methodological quality using 10 questions from the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies[51]. Two reviewers (AF, AH) independently answered these questions for each study, with a third reviewer (MPB) involved in case of disagreement.

Meta Analysis

All analyses were conducted in RStudio integrated development environment (IDE) (2023.06.1+524, "Mountain Hydrangea" release) for R software environment[52] using the 'meta'[53], 'metasens'[54], and 'metafor'[55] R packages.

Main Meta Analysis

In the main meta-analysis, we pooled Pearson product-moment correlations from eligible studies to examine the relationship between apathy and physical activity. Correlations were pooled using the generic inverse pooling method via the 'metacor' function in the R 'meta' package[53]. This function automatically performs a necessary Fisher's z-transformation on the original, untransformed correlations prior to pooling. The 'metacor' function also reconverts the pooled association back to its original form for ease of interpretation. We anticipated considerable between-study heterogeneity, and therefore, used a random-effects model to pool correlations. The restricted maximum likelihood (RML) estimator[56] was used to calculate the heterogeneity variance Tau^2. In addition to Tau^2, to quantify between study heterogeneity, we report the I^2 statistic, which provides the percentage of variability in the correlations that is not caused by sampling error[57]. The I^2 statistic was interpreted as: 0-40%, may not be important; 30-60%, may represent moderate heterogeneity; 50-90%, may represent substantial heterogeneity; and 75-100%, may represent considerable heterogeneity. To reduce the risk of false positives, we used a Knapp-Hartung adjustment[58] to calculate the confidence interval around the pooled association. We also report the prediction interval, which provides a range within which we can expect the associations of future studies to fall based on the current evidence. If significant, the pooled correlation was interpreted using Cohen's conventions[59]: r ≈ -0.10, small negative correlation; r ≈ -0.30, moderate negative correlation; r ≈ -0.50, large negative correlation.

Publication Bias Assessment

Publication bias was assessed using a funnel plot, which is a scatter plot of the studies' effect size expressed as the Fisher's z transformed correlation on the x-axis against a measure of their standard error (which is indicative of precision of the study's effect size) on the y-axis. When there is no publication bias, the data points in a funnel plot should form a roughly symmetrical, upside-down funnel. Studies in the top part of the plot, which have lower standard errors, are expected to lie closely together, and not far away from the pooled effect size. In the lower part of the plot, studies have higher standard errors, the funnel "opens up", and effect sizes are expected to scatter more heavily to the left and right of the pooled effect. Egger's regression was used to formally test funnel plot's asymmetry[60]. The Rücker's limit meta-analysis method[61], which explicitly includes the heterogeneity variance in the model, was used to compute bias-corrected estimate of the true effect size.

Another method used to assess publication bias was p-curve analysis[59]. When the null hypothesis is true (i.e., there is no true effect), p-values are assumed to follow a uniform distribution: highly significant effects (e.g., p = 0.01) are as likely as barely significant effects (e.g., p = 0.049). However, when the null hypothesis is false (i.e., there is a true effect in our data), p-values are assumed to follow a right-skewed distribution: highly significant effects are more likely than barely significant effects. A left-skewed distribution would suggest that some studies used statistical tests to find significant results in ways that may not be reproducible or generalizable (i.e., p-hacking).

Secondary Meta-Analysis, Subgroup Meta-Analyses, and Meta-Regressions

A secondary meta-analysis was conducted using the same approach, but based on Spearman's rho values, to further test the relationship between apathy and physical activity.

Subgroup meta-analyses were conducted to examine the differences in correlations between studies including participants with different health conditions and using different types of physical activity outcomes, and apathy measures.

Meta-regressions were conducted to examine if the average age of participants or the proportion of women in a study predicted the reported correlation between apathy and physical activity. Another meta-regression was used as a sensitivity analysis to examine whether the quality of the studies affected the correlation.

Results

Literature Search

The primary search identified 6,950 potentially relevant articles from the six databases (Figure 1), including 2,025 duplicates. Of the 4,925 articles screened, 3,441 were unrelated to apathy or physical activity. Disagreement occurred in 31 cases, all of which were resolved by consensus. Of the 1,484 remaining articles, 1,321 were excluded in step 1 because they did not report original data. No articles were excluded in step 2 as all articles involved human participants. We excluded 98 articles in step 3 because they did not include a measure of apathy (k = 10), physical activity (k = 80), or both (k = 8). To increase the completeness of our review, we emailed the corresponding authors of articles that did not formally test the association between the apathy and physical activity, and asked for the Pearson correlation estimate of this

Table 1. Characteristics of the studies included in the systematic review.

Study (Year)	N (# women)	Mean age (SD/range)	Health status	Mean apathy (SD or range)	Mean physical activity (SD or range; measure)	Correlation	p-value	Quality score
Abrantes (2012)	45 (15)	66.1(7.6)	Parkinson's disease	10.7 (6.8; AS)	n.a. (IPAQ-SF)	r = −0.25	0.098‡	9
Ayari (2023)	23 (16)	78 (7)	Cognitive impairment	0.17 (NPI-apathy subscale)	451.08 MET-min/week (IPAQ-SF)	r = −0.48	0.020‡	9
Farholm (2017)	106 (65)	45.7 (11.9)	Mental illness	n.a. (S-AES)	39.3(52.3, min/day; IPAQ-SF) 44.9(34.2; min/day; wrist accelero.)	ρ = −0.49 ρ = −0.39	<0.001 <0.01	9
Friedmann (2015)	40 (29)	80.72 (9.3)	Cognitive impairment	17.1 (0.6; AES)	107.4 (10.4; kcal/day; chest accelero.)	r = −0.04†	0.821	10
Gorzkowska (2020)	134 (61)	65.2 (9.2)	Parkinson's disease	n.a. (AS)	n.a. (IPAQ, MLTPAQ)	n.a.	<0.05	9
Groeneweg-Koolhoven (2016)	266 (n.a.)	n.a. (>60)	Depressed older adults	n.a. (AS)	n.a. (IPAQ)	B = −0.9 β = −0.1 OR = 0.5 r = −0.12†	0.05	9
Grool (2014)	4354 (2548)	76 (5.4)	Older adults	n.a. (dichotomized; GDS-apathy subscale)	n.a. (ad-hoc questionnaire)	r = −0.05†	<0.001	7
Hamre (2021)	101 (21)	55.5 (11.4)	Stroke	28.0 (7.8; AES)	2.1 (0.3; HUNT-derived questions)	B = −0.02 r = −0.32†	0.001	10
Hashimoto (2016)	213 (114)	68.9 (7.5)	Older adults	n.a. (AS)	n.a. (modified BHPAQ) Leisure (5-point scale) work (5-point scale) sport (< vs. ≥ 4 MET-h/week)	 OR = 0.59 n.a. n.a.	 <0.05 >0.05 >0.05	6
Henstra (2018)	243 (161)	75.8 (7.0)	Older adult fallers	n.a. (dichotomized; GDS-apathy subscale)	n.a. (ad-hoc questionnaire)	r = −0.15†	0.016	9
Henstra (2019a)	380 (247)	69 (11)	Healthy and depressed older adults	n.a. (dichotomized; AS)	2231 (1989; MET-min/week; IPAQ)	B = −59.8 r = −0.17†	<0.001	6
Henstra (2019b)	2893 (1416)	73.3 (6.6)	Older adults	n.a. (dichotomized; GDS-apathy subscale)	135.4 (80.8; LAPAQ)	r = −0.06†	<0.001	10
Henstra (2022)	394 (278)	69.3 (6.9)	Healthy and depressed older adults	n.a. (AS)	n.a. (IPAQ; low vs. moderate vs. high)	r = −0.17†	<0.001	6
Ersöz Hüseyinsinoğlu (2017)	85 (35)	64.7 (10.2)	Stroke	31.4 (11.9; AES)	2646.5 (1235.6; daily step; pedo.) 1.8 (1.0 distance count; pedo.) 425.9 (541; MET-min/week; IPAQ-SF)	ρ = −0.15 ρ = 0.01 ρ = −0.11	0.42 0.92 0.29	10
Ishimaru (2020)	43 (35) 20 (14)	90.2 (6.4) 87.5 (6.1)	Severe Alzheimer Moderate Alzheimer	n.a. (NPI-Apathy subscale) n.a. (NPI-Apathy subscale)	73.5 (39.1; counts/min; wrist accelero.) 92.1 (27.9; counts/min; wrist accelero.)	ρ = −0.71 n.a.	>0.05 >0.05	9
Ito (2020)	60 (22)	63.7 (14.4)	Stroke	n.a. (dichotomized; AS)	5772(2805; daily steps; pedo.)	r = −0.32†	0.013	7
Ito (2021)	101 (36)	64.5 (13.5)	Stroke	10.6 (6.7; AS)	6184 (2914; daily steps; pedo.)	B = 0.48 β = 0.05 r = 0.05†	0.64	8
Knak (2020)	67 (32)	41 (10)	Myotonic dystrophy	13 (15.9; AES)	485(144; min/week; hip accelero.) 441(382; min/week; IPAQ-SF)	β = −4.36 r = −0.17†	0.16 n.a.	8
Krell-Roesch (2023)	3222 (1433)	79.2 (65.6)	Healthy and MCI older adults	188 (6; NPI-Apathy subscale)	6.5 (3.9) (NHIS/MHS PAQ)	OR = 0.89 r = −0.32†	<0.001	8
Lemij (2023)	239 (239)	74.7 (4.4)	Cancer	n.a. (AS)	28.9 (35; MET-h/week; NHST II)	β = −0.43 r = −0.08†	0.236	9
Miura (2014)	32 (22)	67.8 (7.4)	Parkinson's disease	n.a. (AS)	n.a. (dichotomized; ad-hoc questions)	r = −0.12†	0.510	7
Ng (2021)	121 (47)	64.48 (8.2)	Parkinson's disease	8.7 (6.28; AS)	161.2 (89.5; PASE)	r = −0.23	0.011‡	8
Ringen (2018)	83 (26)	40 (11.7)	Mental illness	22.0 (6.4; AES)	3.5 (2.7; h/week; HUNT questions)	r = −0.24†	0.028	10
Rios Romenets (2015)	33 (14)	63.8 (9.2)	Parkinson disease	27.8 (7.4; AS)	n.a. (yes vs. no; CCHS questions) n.a. (h/week; CCHS derived questions)	ρ = −0.31 r = −0.18	>0.05 0.316‡	10
Sacheli (2018)	17 (4)	62.7 (6.1) 68.8 (4.7)	Parkinson's disease Parkinson's disease	7.8 (2.9; AS) 15.5 (7.1; AS)	Active: 476.3 (63.1; diary min/week) Sedentary: 104.2 (63.1; diary min/week)	 r = −0.40†	 0.011‡	 8
Talamonti (2022)	41 (26)	66.93 (5.3)	Healthy older adults	n.a. (GDS-apathy subscale)	n.a. (dichotomized; ad-hoc questions)	r = −0.25	0.67	7
Vanner (2008)	43 (31)	53.7 (10.2)	Multiple sclerosis	30.8 (9.3; AES)	10.6 (57.9; PADS)	r = −0.278	0.071	9
Yao (2015)	317 (180)	64.5 (10.2)	Healthy older adults	467 (113; AS)	n.a. (modified BHPAQ) Leisure (5-point scales) work (5-point scales) sport (dichotomized; MET-h/week)	 β = −0.25 β = −0.05 β = −0.09	 <0.001 >0.05 >0.05	8

Notes. Accelero. = accelerometer, AES = Apathy Evaluation Scale, AS = Apathy Scale, B = unstandardized regression coefficient, BHPAQ = Baecke questionnaire on Habitual Physical Activity, CCHS = Canadian Community Health Survey, GDS = Geriatric Depression Scale, HUNT = Nord-Trøndelag Health Study, IPAQ = International Physical Activity Questionnaire, LAPAQ = LASA Physical Activity Questionnaire, MCI = Mild Cognitive Impairment, MLTPAQ = Minnesota Leisure Time Physical Activity Questionnaire, n.a. = not available, NHIS/MHS PAQ = National Health Interview Survey and the Minnesota Heart Survey Physical Activity Questionnaire, NHST II = Nurses' Health Study II Activity and Inactivity Questionnaire, NPI = Neuropsychiatric Inventory Questionnaire, OR: Odds Ratio, PADS = Physical Activity Disability Scale, PASE = Physical Activity Scale for the Elderly, pedo. = pedometer, r = Pearson's correlation coefficient, S-AES = Short Apathy Evaluation Scale, β = standardized regression coefficient, ρ = Spearman's correlation coefficient. †When Pearson's correlation coefficient (r) was not reported in an article, but the exact p-value and sample size (n) were available and it was possible to know the sign of the correlation based on the information provided in the article, the r value was computed using an ad-hoc R code. ‡When exact p-values were not reported in an article, but the sample size (n) and Pearson's correlation coefficient I were available, the exact p-value was computed using an ad-hoc R code. For the studies that reported a relative p-value < 0.001 instead of an exact p-value, we used a p-value of 0.0009 to estimate an approximate r value.

association and the sample size used to calculate it or the raw data for the physical activity and apathy measures so we could compute it ourselves. Forty-two corresponding authors were contacted. Six of these authors replied: one author provided their raw data[62], one author provided their Pearson's correlation coefficient[63], and four authors replied that they would contact their co-authors but did not get back to us[64-67]. We excluded 138 articles in step 4 because the article did not formally test the association between apathy and physical activity, and the corresponding author did not respond to our email request. Based on reference screening and forward citation tracking, the principal reviewer (AF) identified three studies[68-70] that assessed both physical activity and apathy, but one of them did not formally test their association[68]. However, the corresponding author of the latter article[68] did provide us with the Pearson's correlation value in response to our email request. As a result, a total of 28 articles were included in our systematic review. Two of these articles, published by the same group, had similar methods, and partly overlapping recruitment periods, suggesting that some participants may have been included in both studies[47,71]. Quality score of studies ranged from 6 to 10 out of 10, with a mean ± SD of 8.4 ± 1.2 (Table 1).

Descriptive Results

Participants

The 28 articles identified by the systematic review included a total of 13,716 participants aged 30 to 95 years, including 7,167 women, 6,283 men, and 266 participants whose gender and sex was not reported. The studies investigated populations with stroke (k = 4)[47,48,71,72], multiple sclerosis (k = 1)[33], Parkinson's disease (k = 6)[36,68,70,73-75], mental illness (k = 2)[76,77], cancer (k = 1)[78], myotonic dystrophy (k = 1)[46], Alzheimer's disease (k = 1)[35], depression (k = 3)[69,79,80], cognitive impairment (k = 3)[62,63,81], as well as healthy older adults (k = 9)[34,79-86] (Table 1).

Apathy

In 14 of the 28 studies, apathy was assessed using the Apathy Scale (k = 13)[36,47,68-71,73-75,78-80,84] or its shorter version [12-item Apathy Scale (k = 1)[34]]. This scale consists of 14 questions rated on a Likert scale ranging from 0 (not at all) to 3 (a lot). The total score on the 14-item Apathy Scale ranges from 0 to 42, with higher scores indicating more severe apathy. In clinical settings, a patient with a score ≥ 16 is considered apathetic[87]. Apathy was also assessed using the Apathy Evaluation Scale (k = 6)[33,46,48,63,72,77] or its shorter version [12-item Apathy Evaluation Scale (k = 1)[76]]. This scale consists of 18 items assessing the cognitive, emotional, and behavioral aspects of apathy, rated on a Likert scale ranging from 1 (not at all) to 4 (a lot). The total score ranges from 18 to 72, with higher scores indicating more severe apathy. In clinical setting, a patient with a score ≥ 37 is considered apathetic[88]. The other measures that were used are the apathy subscale of the Geriatric Depression Scale (k = 4)[82,83,85,86] and the apathy subscale of the Neuropsychiatric Inventory Questionnaire (k = 3)[35,62,81].

Eighteen studies reported mean levels of apathy (Table 1). The Apathy Scale-based studies revealed a range from 8.7[36] to 27.8[68], while the Apathy Evaluation Scale studies reported levels between 13.0[46] and 31.4[48].

Physical Activity

Twenty-four studies assessed physical activity using a self-reported measure (Table 1). Five of these questionnaire-based studies used the short form of the International Physical Activity Questionnaire (IPAQ-SF)[46,48,62,73,76], which consists of 6 items assessing time spent in light (i.e., walking), moderate (e.g., carrying light loads, cycling at moderate speed, doubles tennis), and vigorous physical activity (e.g., digging, fast cycling, heavy lifting, aerobics)

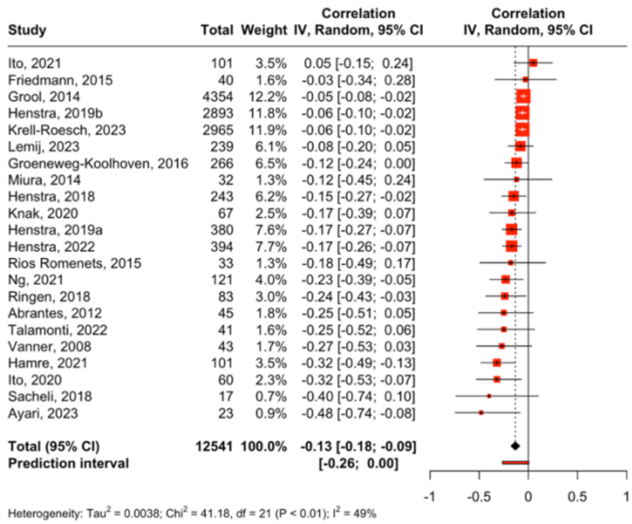

Figure 1. Main meta-analysis. Correlation between apathy and physical activity based on Pearson's r values (k = 22, n = 12,541). CI = confidence interval, IV = inverse variance.

over the last 7 days[89]. The other questionnaires used to assess physical activity were: the long form version of the IPAQ (IPAQ-LF) (k = 4)[69,70,79,80], the modified Baecke Habitual Physical Activity Questionnaire (BHPAQ) (k = 2)[34,84], the Minnesota Leisure Time Physical Activity Questionnaire (k = 1)[70], the Longitudinal Aging Study Amsterdam Physical Activity Questionnaire (LAPAQ) (k = 1)[83], the National Health Interview Survey and the Minnesota Heart Survey Physical Activity Questionnaire (NHIS/MHS PAQ) (k = 1)[81], the Nurses' Health Study II Activity and Inactivity Questionnaire (NHST II Activity) (k = 1)[78], Physical Activity Disability Scale (PADS) (k = 1)[33], the Nord-Trøndelag Health Study-derived questions (HUNT) (k = 2)[72,77], the Canadian Community Health Survey-derived questionnaire (CCHS) (k = 1)[68], and the Physical Activity Scale for the Elderly (PASE) (k = 1)[36].

Physical activity was also assessed with devices such as accelerometers measuring accelerations in three dimensions (k = 4)[35,46,63,76] and pedometers measuring the number of steps (k = 3)[47,48,71] (Table 1). These devices were worn at the hip (k = 2)[46,48], chest (k = 1)[63], wrist (k = 2)[35,76], or pocket (k = 1)[47], and one study did not report where the device was worn[71]. Studies based on accelerometer-derived measures used an ActiGraph device (ActiGraph, LLC, Pensacola, FL, USA)[46,63], the Polar M200 (Polar Electro Oy, Kempele, Finland)[76], or the Micro Motionlogger Watch (Ambulatory Monitoring, Ardsley, NY, USA)[35]. The pedometers used were the Omron Walking Style Pro 2.0 (Omron Healthcare, Kyoto, Japan)[48], or the Yamasa EX-300 (Yamasa, Choshi, Japan)[47]. One study did not specify the pedometer that was used[71].

To assess physical activity, the studies used the following outcomes: score from a questionnaire (e.g., PASE, PADS, BHPAQ ; k = 11)[33,34,36,68,72,75,81-85], METmin/week (k = 7)[34,48,69,78-80,84], steps per day (k = 3)[47,48,71], time per day or week (k = 8)[46,68,70,73,74,76,77,86], counts per minute (k = 1)[35], kilocalories per day (k = 1)[63]. Four studies used multiple physical activity outcomes (k = 4)[34,48,68,84].

Association Between Physical Activity and Apathy

Among the 28 articles included in the systematic review, five reported correlation coefficients of the association between physical activity and apathy. Specifically, two articles reported at least one Pearson's r correlation coefficient[33,73] and three other articles reported at least one Spearman's rho[35,48,76]. When a correlation coefficient was not reported, but the exact p value (or t value) and sample size were available and it was possible to know the sign of the correlation, which was the case for 11 studies[46,47,63,69,71,72,74,75,77,78,82], the Pearson's r value was computed using an ad-hoc R code. For the studies that reported a relative p-value < 0.001 instead of an exact p-value, we used a p-value of 0.0009 to estimate an approximate r value[79,80,81,83,85]. Through email correspondence

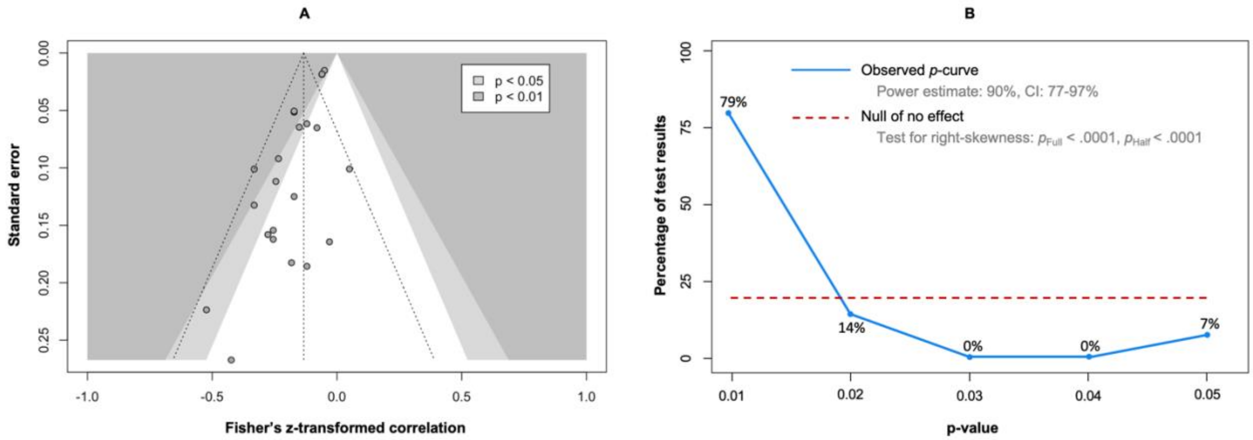

Figure 3. Publication bias assessment. Contour-enhanced funnel plot of the main meta-analysis (A). The vertical dashed line represents the average effect size. The two other dashed lines represent the idealized funnel-shape that studies are expected to follow. P-curve analysis (B). The blue line indicates the distribution of the analyzed p-values. The red dotted line illustrates a uniform distribution of the p-values, indicating the absence of a true effect.

with the authors, we obtained three additional Pearson's r values[36,62,68] and one additional Spearman's rho value[68]. Furthermore, one Pearson's r value was calculated based on publicly available data[86]. In total, 22 Pearson's r values from 22 studies[33,36,46,47,62,63,68,69,71-75,77-79,80,81-83,85,86] and seven Spearman's rho values from four studies[35,48,68,76] were used in the meta-analysis (Table 1). When exact p-values were not reported in an article, but the sample size (n) and Pearson's correlation coefficient I were available, the exact p-value was computed using an ad-hoc R code.

The remaining 3 studies did not report a correlation coefficient and were therefore not included in the meta-analysis. Two of these studies reported showed a significant negative association between physical activity and apathy based on odds ratios (84) or standardized beta coefficient (β) (34). The third study reported only a relative p-value > 0.05 (70).

Meta Analysis

Main Meta Analysis

Our meta-analysis of 22 studies (n = 12,541) based on Pearson's r revealed a statistically significant small negative correlation between apathy and physical activity (r = -0.13; 95% confidence interval [95% CI]: -0.18 to -0.09; p < 0.0001; Table 2; Figure 2). Further supporting this result, between-study statistical heterogeneity could be considered moderate (Tau^2 = 0.0038, 95% CI: 0.0003 to 0.0167; I^2 = 49.0%, 95% CI: 16.4 to 68.9%), and the prediction interval ranged from r = -0.26 to 0.00, suggesting that the correlation is expected to be negative for a future study.

Publication Bias Assessment

Overall, the funnel plot of the studies' effect size expressed as the Fisher's z transformed correlation against a measure of their standard error shows an asymmetrical pattern (Figure 3A), with more studies on the left of the vertical dashed line representing the average effect size. In addition, if the missing studies were imputed

Table 2. Results of the main, secondary, and subgroup meta-analyses.

	k	N	cor.	95% CI	I^2 (%)	p
Main: Pearson's r values						< .0001
Apathy and physical activity	22	12,541	-.13	[-.18 to -.09]	49	
Main: Rücker's limit method						.0065
Apathy and physical activity	22	12,541	-.08	[-.14 to -.02]	49	
Secondary: Spearman's rho value						.043
Apathy and physical activity	4	543	-.40	[-.68 to -.02]	82	
Subgroup: Health status						< .0001
Older adults (healthy, depression, falls, or MCI)	10	11,599	-.10	[-.15 to -.05]	50	
Parkinson's disease	5	248	-.22	[-.31 to -.14]	0	
Stroke	3	262	-.20	[-.64 to .34]	9	
Cancer	1	239	-.08	[-.20 to .05]		
Severe mental illness	1	83	-.24	[-.43 to -.03]		
Myotonic dystrophy	1	67	-.17	[-.39 to .07]		
Multiple sclerosis	1	43	-.27	[-.53 to .03]		
Subgroup: Physical activity outcome						< .0001
Score	7	6,398	-.14	[-.23 to -.04]	56	
MET-min/week	6	1,347	-.15	[-.22 to -.08]	0	
Active time	5	241	-.22	[-.30 to -.14]	0	
Steps/day	2	161	-.13	[-.99 to .98]	81	
Frequency	1	4,354	-.05	[-.08 to -.02]		
Kcal/day	1	40	-.03	[-.34 to .28]		
Subgroup: Apathy measure						< .0001
Apathy Scale (AS)	11	1,688	-.15	[-.20 to -.10]	0	
Apathy Evaluation Scale (AES)	5	334	-.23	[-.35 to -.11]	0	
GDS	4	12,541	-.06	[-.10 to -.02]	22	
NPI	2	2,988	-.23	[-1.00 to .99]	77	

Notes. 95% CI = 95% confidence interval, Cor. = Correlation estimate, GDS = Apathy subscale of the Geriatric Depression Scale, I2 = Percentage of variability in the correlations that is not caused by sampling error, k = Number of studies, MCI = Mild Cognitive Impairment, MET = Metabolic equivalent, N = number of participants, NPI = Apathy subscale of the Neuropsychiatric Inventory Questionnaire.

in the right part of the plot to increase the symmetry, most of these studies would lie in the non-significance region (in white), which suggests that the asymmetry in the funnel plot may be caused by publication bias rather other potential causes, such as different study procedures and between-study heterogeneity. Egger's regression test confirmed that the data in the funnel plot was asymmetric (b = -1.44, 95% CI: -1.97 to -0.91, p = 3.1 x 10-5). However, the bias-corrected estimate of the true effect size, calculated using Rücker's limit meta-analysis method, showed that the small correlation reported in the main analysis would remain significant even if such publication bias was present in our data set (r = -0.08; 95% CI: -0.14 to -0.02; p = 0.0065).

The 29 correlation values (Pearson's r or Spearman's rho) were provided to the p-curve analysis (Figure 3B). The observed p-curve included 14 statistically significant results ($p < 0.05$), 13 of which were highly significant ($p < 0.025$), and was visually right-skewed. The other 15 results were excluded because they had a $p > 0.05$. The p-value of the right-skewness test was < 0.001 for both the half curve (curve of p values ≤ 0.025) and the full curve (curve of p values < 0.05), confirming that the p-curve was right-skewed and suggesting that the effect of our meta-analysis is true, i.e., that the effect we estimated is not an artifact caused by selective reporting (e.g., p-hacking) in the literature[90]. In addition, the statistical power of the studies that were included in the p-curve analysis was 90% (90% CI: 77 to 97%), suggesting that approximately 90% of the significant results are expected to be replicable.

Secondary Meta-Analysis

Results of the secondary meta-analysis based on Spearman's rho values (k = 4, n = 543) were consistent with those based on Pearson's r as they showed a statistically significant moderate to large negative correlation between apathy and physical activity (r = -0.40; 95% CI: -0.68 to -0.02; p = 0.043) (Figure 4). However, we observed substantial to considerable between-study statistical heterogeneity (between-cluster Tau^2 = 0.09, 95% CI: 0.01 to 0.97; I^2 = 82.0%; 95% CI: 64.1 to 91.0%), and the prediction interval ranged from r = -0.87 to 0.45, indicating that a moderate to large positive correlation cannot be ruled out for future studies.

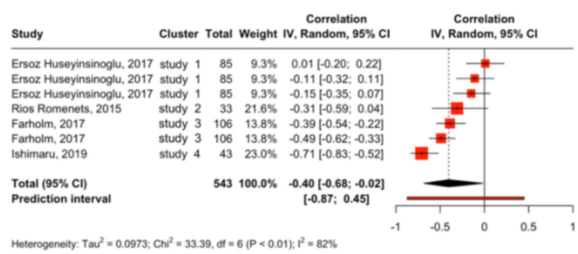

Figure 4. Secondary meta-analysis. Correlation between apathy and physical activity based on Spearman's rho values (k = 7, n = 437). CI = confidence interval, IV = inverse variance.

Subgroup Meta-Analyses

The test of subgroup differences between health status was possible between studies comprising

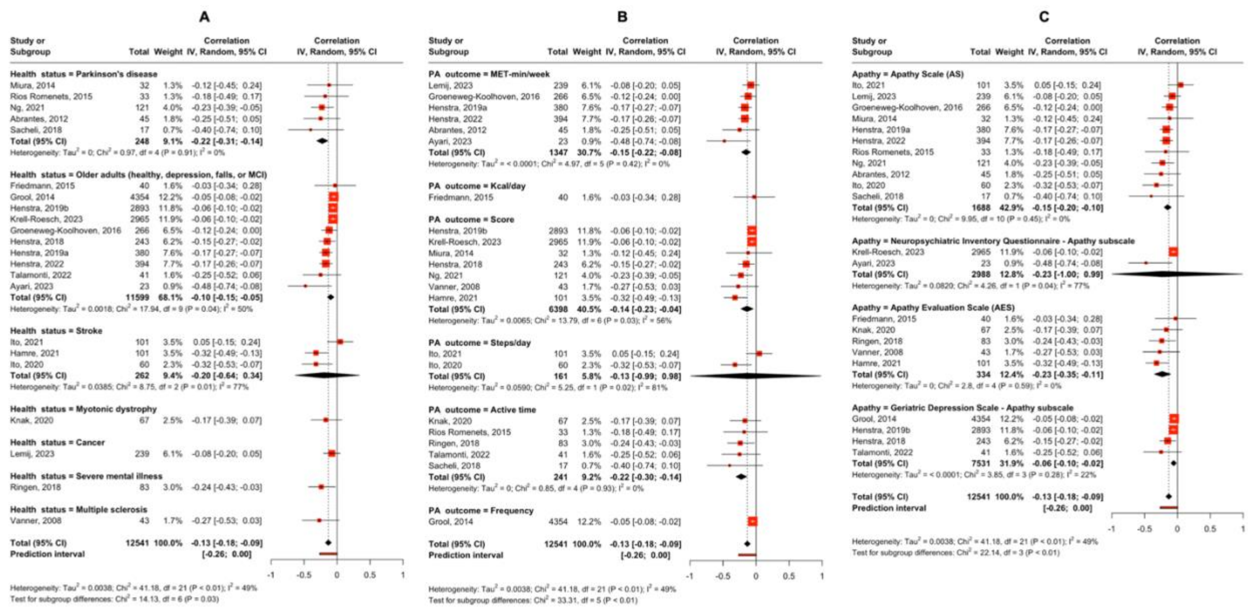

Figure 5. Subgroup meta-analyses. Differences according to health status (A), physical activity outcome (B), and apathy measure (C). CI = confidence interval, IV = inverse variance, MCI = mild cognitive impairment, PA = physical activity.

older adults who were healthy, depressed, fallers, or had mild cognitive impairment (k = 10), people with Parkinson's Disease (k = 5), and stroke survivors (k = 3). We found statistical difference between these studies (p < 0.0001) (Table 2; Figure 5A). The relationship between apathy and physical activity was statistically significant in studies that included older adults who were healthy, depressed, fallers, or had mild cognitive impairment (r = -0.10; 95% CI: -0.15 to -0.05) or patients with Parkinson's disease (r = -0.22; 95% CI: -0.31 to -0.14), but not in studies that included stroke survivors (r = -0.20; 95% CI: -0.64 to -0.34). However, statistical power was lacking in the latter (k = 3) and other health status (k = 1).

The test of subgroup differences between physical activity outcomes was possible between studies using a score from a questionnaire (k = 7), MET-min/week (k = 6), active time per day or week (k = 5), and steps per day (k = 2) (Table 2; Figure 5B). We found statistical difference between these studies (p < 0.0001). The relationship between apathy and physical activity was statistically significant in studies using a score (r = -0.14; 95% CI: -0.23 to -0.04), MET-min/week (r = -0.15; 95% CI: -0.22 to -0.08), and active time (r = -0.22; 95% CI: -0.30 to -0.14), but not in studies that used the number of steps per day (r = -0.13; 95% CI: -0.99 to 0.98). However, statistical power was lacking in the latter (k = 2) and other physical activity outcomes (k = 1).

The test of subgroup differences between apathy measures was possible between studies using the Apathy Scale (k = 11), the Apathy Evaluation Scale (k = 5), the apathy subscale of the Geriatric Depression Scale (k = 4), and the apathy subscale of the Neuropsychiatric Inventory Questionnaire (k = 2) (Table 2; Figure 5C). The relationship between apathy and physical activity was statistically significant in studies using the Apathy Scale (r = -0.15; 95% CI: -0.20 to -0.10), Apathy Evaluation Scale (r = -0.23; 95% CI: -0.35 to -0.11), and Geriatric Depression Scale (r = -0.06; 95% CI: -0.10 to -0.02), but not in studies that used the Neuropsychiatric Inventory Questionnaire (r = -0.23; 95% CI: -1.00 to 0.99). However, statistical power was lacking in the latter apathy measure (k = 2).

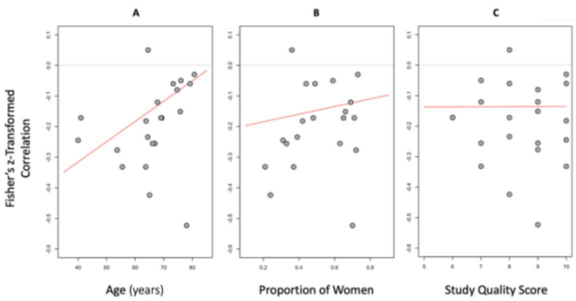

Figure 6. Meta-Regressions testing the influence of age (A), the proportion of women (B), and study quality score (C) on the correlation estimates of the main meta-analysis studies.

Meta-Regressions

Age statistically influenced the correlation values of the meta-analysis studies (k = 21; p = 0.003) (Figure 6A), with older samples being associated with more negative relationships between apathy and physical activity. Conversely, the proportion of women did not statistically influence the meta-analysis studies' correlation values (k = 21; p = 0.346) (Figure 6B).

Sensitivity Analysis

The meta-regression by quality score based on the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies[51] (k = 22) showed that a study's quality did not influence correlation values (p = 0.986) (Figure 6C).

Discussion

The main objective of this study was to conduct a systematic review and meta-analysis of the direct relationship between apathy and physical activity. In addition, we examined the influence of potential moderators.

The main meta-analysis based on Pearson's r values showed a small negative correlation between apathy and physical activity. The secondary analysis based on Spearman's rho values further supported these results. These results suggest that apathy is a potential risk factor for physical inactivity, which has been associated with functional independence[44,45] and quality of life[91,92]. Therefore, future studies should examine the potential moderating effect of physical activity on the association between apathy and physical functioning[24,79,83,93,94] or quality of life[93]. While some evidence suggests that apathy hinders engagement in physical activity[95], other evidence suggests that physical activity contributes to positive emotions, potentially mitigating apathy[73]. Therefore, the relationship between apathy and physical activity can potentially be bidirectional.

Our results suggest that the negative relationship between apathy and physical activity was mainly observed in people with Parkinson's disease and older adults who were healthy, depressed, fallers, or had mild cognitive impairment. Although there was no clear evidence of an association between apathy and physical activity in the other health conditions, such an association cannot be completely ruled out, as the lack of statistical significance could be explained by a lack of statistical power in these health conditions (e.g., stroke) or by the impossibility of comparing them with other health conditions in the subgroup meta-analysis, as they were only examined in a single study (e.g., cancer). The results also showed that the negative association between apathy and physical activity was observed only in studies using active time and questionnaires as a measure of physical activity outcome and the apathy scale for apathy assessment, although this may also be related to the low number of studies using other outcomes.

The results of this systematic review and meta-analysis should be considered in the light of two limitations. First, only articles published in English were included. Inclusion of articles published in other languages may have influenced the results. Second, due to the correlational nature of the meta-analyzed results, we cannot conclude a causal relationship between apathy and physical activity, nor can we exclude the possibility that this relationship is indirect, i.e., mediated by other factors.

Conclusion

The motivation required to adhere to prescribed rehabilitation exercises may be impaired in apathetic patients. In our meta-analysis of 12,541 participants, higher levels of apathy were associated with lower levels of physical activity. This detrimental effect was greater in older adults. These findings suggest that apathy may be a limiting factor in developing strategies for regular exercise, which is in the scope of practice of physiotherapists[100], and may have prognostic implications in patients whose condition requires physical activity.

Declarations

Data and Code Availability

According to good research practices[96], the dataset as wells as R and R Markdown scripts are freely available in Zenodo[97].

Authorship Contribution Statement

Based on the Contributor Roles Taxonomy (CRediT)[98,99] individual author contributions to this work are as follows: Ata Farajzadeh: Conceptualization, Methodology (systematic review), Formal Analysis; Investigation, Writing (Original Draft), Writing (Review and Editing). Alexe Hébert: Investigation. Ian M. Lahart: Methodology (meta-analysis), Formal Analysis, Writing (Review and Editing). Martin Bilodeau: Writing (Review and Editing), Supervision (AH). Matthieu P. Boisgontier: Conceptualization, Methodology, Formal Analysis, Data Curation, Visualization, Writing (Original Draft), Writing (Review and Editing), Supervision (AF and AH), Project Administration, Funding Acquisition.

Funding

Matthieu P. Boisgontier is supported by Natural Sciences and Engineering Research Council of Canada (NSERC; RGPIN-2021-03153), the Canada Foundation for Innovation (CFI 43661), and Mitacs. Ata Farajzadeh is supported by an Admission Scholarship, a Doctoral International Scholarship, and a Special Merit Scholarship from the University of Ottawa.

Conflict of Interest

The authors declare that there are no conflicts of interest related to the content of this article.

References

1. Marin RS. Differential diagnosis and classification of apathy. Am J Psychiatry. 1990;147(1):22-30. https://doi.org/10.1176/ajp.147.1.22

2. Marin RS. Apathy: a neuropsychiatric syndrome. J Neuropsychiatry Clin Neurosci. 1991;3(3):243-254. https://doi.org/10.1176/jnp.3.3.243

3. Robert P, Onyike CU, Leentjens AF, et al. Proposed diagnostic criteria for apathy in Alzheimer's disease and other neuropsychiatric disorders. Eur Psychiatry. 2009;24(2):98-104. https://doi.org/10.1016/j.eurpsy.2008.09.001

4. Costello H, Husain M, Roiser JP. Apathy and motivation: biological basis and drug treatment. Annu Rev Pharmacol Toxicol. 2024;64:313-338. https://doi.org/10.1146/annurev-pharmtox-022423-014645

5. Dickson SS, Husain M. Are there distinct dimensions of apathy? The argument for reappraisal. Cortex.

2022;149:246-256. https://doi.org/10.1016/j.cortex.2022.01.001

6. Levy R, Dubois B. Apathy and the functional anatomy of the prefrontal cortex-basal ganglia circuits. Cereb Cortex. 2006;16(7):916-928. https://doi.org/10.1093/cercor/bhj043

7. Le Heron C, Apps MAJ, Husain M. The anatomy of apathy: a neurocognitive framework for amotivated behaviour. Neuropsychologia. 2018;118(Pt B):54-67. https://doi.org/10.1016/j.neuropsychologia.2017.07.003

8. Leung DKY, Chan WC, Spector A, Wong GHY. Prevalence of depression, anxiety, and apathy symptoms across dementia stages: a systematic review and meta-analysis. Int J Geriatr Psychiatry. 2021;36(9):1330-1344. https://doi.org/10.1002/gps.5556

9. Mulin E, Leone E, Dujardin K, et al. Diagnostic criteria for apathy in clinical practice. Int J Geriatr Psychiatry. 2011;26(2):158-165. https://doi.org/10.1002/gps.2508

10. Yazbek H, Norton J, Capdevielle D, et al. The Lille Apathy Rating Scale (LARS): exploring its psychometric properties in schizophrenia. Schizophr Res. 2014;157(1-3):278-284. https://doi.org/10.1016/j.schres.2014.04.034

11. Faerden A, Finset A, Friis S, et al. Apathy in first episode psychosis patients: one year follow up. Schizophr Res. 2010;116(1):20-26. https://doi.org/10.1016/j.schres.2009.10.014

12. den Brok MG, van Dalen JW, van Gool WA, Moll van Charante EP, de Bie RM, Richard E. Apathy in Parkinson's disease: a systematic review and meta-analysis. Mov Disord. 2015;30(6):759-769. https://doi.org/10.1002/mds.26208

13. Zhang H, Feng Y, Lv H, Tang S, Peng Y. The prevalence of apathy in stroke patients: a systematic review and meta-analysis. J Psychosom Res. 2023;173:111478. https://doi.org/10.1016/j.jpsychores.2023.111478

14. Pardini M, Cordano C, Guida S, et al. Prevalence and cognitive underpinnings of isolated apathy in young healthy subjects. J Affect Disord. 2016;189:272-275. https://doi.org/10.1016/j.jad.2015.09.062

15. Hwang TJ, Masterman DL, Ortiz F, Fairbanks LA, Cummings JL. Mild cognitive impairment is associated with characteristic neuropsychiatric symptoms. Alzheimer Dis Assoc Disord. 2004;18(1):17-21. https://doi.org/10.1097/00002093-200401000-00004

16. Onyike CU, Sheppard JM, Tschanz JT, et al. Epidemiology of apathy in older adults: the Cache County Study. Am J Geriatr Psychiatry. 2007;15(5):365-375. https://doi.org/10.1097/01.JGP.0000235689.42910.0d

17. Geda YE, Roberts RO, Knopman DS, et al. Prevalence of neuropsychiatric symptoms in mild cognitive impairment and normal cognitive aging: population-based study. Arch Gen Psychiatry. 2008;65(10):1193-1198. https://doi.org/10.1001/archpsyc.65.10.1193

18. Lyketsos CG, Steinberg M, Tschanz JT, Norton MC, Steffens DC, Breitner JC. Mental and behavioral disturbances in dementia: findings from the Cache County Study on Memory in Aging. Am J Psychiatry. 2000;157(5):708-714. https://doi.org/10.1176/appi.ajp.157.5.708

19. Groeneweg-Koolhoven I, de Waal MW, van der Weele GM, Gussekloo J, van der Mast RC. Quality of life in community-dwelling older persons with apathy. Am J Geriatr Psychiatry. 2014;22(2):186-194. https://doi.org/10.1016/j.jagp.2012.10.024

20. Pink A, Stokin GB, Bartley MM, et al. Neuropsychiatric symptoms, APOE ε4, and the risk of incident dementia: a population-based study. Neurology. 2015;84(9):935-943. https://doi.org/10.1212/WNL.0000000000001307

21. Guercio BJ, Donovan NJ, Munro CE, et al. The Apathy Evaluation Scale: a comparison of subject, informant, and clinician report in cognitively normal elderly and mild cognitive impairment. J Alzheimers Dis. 2015;47(2):421-432. https://doi.org/10.3233/JAD-150146

22. Mega MS, Cummings JL, Fiorello T, Gornbein J. The spectrum of behavioral changes in Alzheimer's disease. Neurology. 1996;46(1):130-135. https://doi.org/10.1212/wnl.46.1.130

23. Lanctôt KL, Agüera-Ortiz L, Brodaty H, et al. Apathy associated with neurocognitive disorders: recent progress and future directions. Alzheimers Dement. 2017;13(1):84-100. https://doi.org/10.1016/j.jalz.2016.05.008

24. Ayers E, Shapiro M, Holtzer R, Barzilai N, Milman S, Verghese J. Symptoms of apathy independently predict incident frailty and disability in community-dwelling older adults. J Clin Psychiatry. 2017;78(5):e529-e536. https://doi.org/10.4088/JCP.15m10113

25. Clarke DE, Ko JY, Lyketsos C, Rebok GW, Eaton WW. Apathy and cognitive and functional decline in community-dwelling older adults: results from the Baltimore ECA longitudinal study. Int Psychogeriatr. 2010;22(5):819-829. https://doi.org/10.1017/S1041610209991402

26. Wadsworth LP, Lorius N, Donovan NJ, et al. Neuropsychiatric symptoms and global functional impairment along the Alzheimer's continuum. Dement Geriatr Cogn Disord. 2012;34(2):96-111. https://doi.org/10.1159/000342119

27. Musa Salech G, Lillo P, van der Hiele K, Méndez-Orellana C, Ibáñez A, Slachevsky A. Apathy, executive function, and emotion recognition are the main drivers of functional impairment in behavioral variant of frontotemporal dementia. Front Neurol. 2022;12:734251. https://doi.org/10.3389/fneur.2021.734251

28. Ishii S, Weintraub N, Mervis JR. Apathy: a common psychiatric syndrome in the elderly. J Am Med Dir Assoc. 2009;10(6):381-393. https://doi.org/10.1016/j.jamda.2009.03.007

29. Barone P, Antonini A, Colosimo C, et al. The PRIAMO study: a multicenter assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease. Mov Disord. 2009;24(11):1641-1649. https://doi.org/10.1002/mds.22643

30. Vilalta-Franch J, Calvó-Perxas L, Garre-Olmo J, Turró-Garriga O, López-Pousa S. Apathy syndrome in Alzheimer's disease epidemiology: prevalence, incidence, persistence, and risk and mortality factors. J Alzheimers Dis. 2013;33(2):535-543. https://doi.org/10.3233/JAD-2012-120913

31. Lansdall CJ, Coyle-Gilchrist ITS, Vázquez Rodríguez P, et al. Prognostic importance of apathy in syndromes associated with frontotemporal lobar degeneration. Neurology. 2019;92(14):e1547-e1557. https://doi.org/10.1212/WNL.0000000000007249

32. Kruse C, Maier F, Spottke A, et al. Apathy in patients with Alzheimer's disease is a cost-driving factor. Alzheimers Dement. 2023;19(7):2853-2864. https://doi.org/10.1002/alz.12915

33. Vanner EA, Block P, Christodoulou CC, Horowitz BP, Krupp LB. Pilot study exploring quality of life and barriers to leisure-time physical activity in persons with moderate to severe multiple sclerosis. Disabil Health J. 2008;1(1):58-65. https://doi.org/10.1016/j.dhjo.2007.11.001

34. Yao H, Takashima Y, Araki Y, Uchino A, Yuzuriha T, Hashimoto M. Leisure-time physical inactivity associated with cascular depression or apathy in community-dwelling elderly subjects: the Sefuri Study. J Stroke Cerebrovasc Dis. 2015;24(11):2625-2631. https://doi.org/10.1016/j.jstrokecerebrovasdis.2015.07.018

35. Ishimaru D, Tanaka H, Nagata Y, Takabatake S, Nishikawa T. Physical activity in severe dementia is associated with agitation rather than cognitive function. Am J Alzheimers Dis Other Demen. 2020;35:1533317519871397. https://doi.org/10.1177/1533317519871397

36. Ng SY, Chia NS, Abbas MM, et al. Physical activity improves anxiety and apathy in early Parkinson's disease: a longitudinal follow-up study. Front Neurol. 2021;11:625897. https://doi.org/10.3389/fneur.2020.625897

37. Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med. 2020;54(24):1451-1462. https://doi.org/10.1136/bjsports-2020-102955

38. Cheval B, Darrous L, Choi KW, et al. Genetic insights into the causal relationship between physical activity and cognitive functioning. Sci Rep. 2023;13(1):5310. https://doi.org/10.1038/s41598-023-32150-1

39. Wahid A, Manek N, Nichols M, et al. Quantifying the association between physical activity and cardiovascular disease and diabetes: a systematic review and meta-analysis. J Am Heart Assoc. 2016;5(9):e002495. https://doi.org/10.1161/JAHA.115.002495

40. Moore SC, Lee IM, Weiderpass E, et al. Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults. JAMA Intern Med. 2016;176(6):816-825. https://doi.org/10.1001/jamainternmed.2016.1548

41. Liu X, Zhang D, Liu Y, et al. Dose-response association between physical activity and incident hypertension: a systematic review and meta-analysis of cohort studies. Hypertension. 2017;69(5):813-820. https://doi.org/10.1161/HYPERTENSIONAHA.116.08994

42. Cheval B, Maltagliati S, Sieber S, et al. Why are individuals with diabetes less active? The mediating role of physical, emotional, and cognitive factors. Ann Behav Med. 2021;55(9):904-917. https://doi.org/10.1093/abm/kaaa120

43. Bleich SN, Vercammen KA, Zatz LY, Frelier JM, Ebbeling CB, Peeters A. Interventions to prevent global childhood overweight and obesity: a systematic review. Lancet Diabetes Endocrinol. 2018;6(4):332-346. https://doi.org/10.1016/S2213-8587(17)30358-3

44. Boisgontier MP, Orsholits D, von Arx M, et al. Adverse childhood experiences, depressive symptoms, functional dependence, and physical activity: a moderated mediation model. J Phys Act Health. 2020;17(8):790-799. https://doi.org/10.1123/jpah.2019-0133

45. van Allen Z, Orsholits D, Boisgontier MP. Funtional Limitations in stroke survivors: pre-stroke physical activity matters. Phys Ther. 2024.

46. Knak KL, Sheikh AM, Witting N, Vissing J. Physical activity in myotonic dystrophy type 1. J Neurol. 2020;267(6):1679-1686. https://doi.org/10.1007/s00415-020-09758-8

47. Ito D, Kawakami M, Narita Y, Yoshida T, Mori N, Kondo K. Cognitive function is a predictor of the daily step count in patients with subacute stroke with independent walking ability: a prospective cohort study. Arch Rehabil Res Clin Transl. 2021;3(3):100132. https://doi.org/10.1016/j.arrct.2021.100132

48. Ersöz Hüseyinsinoğlu B, Kuran Aslan G, Tarakci D, Razak Özdinçler A, Küçükoğlu H, Baybaş S. Physical activity level of ambulatory stroke patients: is it related to neuropsychological factors? Noro Psikiyatr Ars. 2017;54(2):155-161. https://doi.org/10.5152/npa.2016.12760

49. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372:n160. https://doi.org/10.1136/bmj.n160

50. Farajzadeh A, Hebert A, Bilodeau M, Boisgontier M. Apathy and physical activity: a systematic review. PROSPERO (CRD42023492162) [preregistration]; December 21, 2023. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023492162

51. National Institutes of Health. Quality assessment tool for observational cohort and cross-sectional studies [Internet]. 2014 (accessed online February 2024). https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools

52. R Core Team. R: A language and environment for statistical computing [Computer software]. Version 4.3.1. Vienna, Austria: Foundation for Statistical Computing; 2023. https://www.r-project.org

53. Schwarzer G. meta: general package for meta-analysis [R package]. Version 6.5-0; 2023. https://cran.rproject.org/web/packages/meta/meta.pdf

54. Schwarzer G, Carpenter RJ, Rücker G. metasens: advanced statistical methods to model and adjust for bias in meta-analysis [R package]. Version 1.5-2; 2023. https://cran.rproject.org/web/packages/metasens/metasens.pdf

55. Viechtbauer W. Conducting meta-analyses in R with the metafor package. J Stat Softw. 2010;36(3):1-48. https://cran.r-project.org/web/packages/metafor/metafor.pdf

56. Viechtbauer W. Bias and efficiency of metanalytic variance estimators in the random effects model. J Educ Behav Stat. 2005;30(3):261-293. https://doi.org/10.3102/10769986030003261

57. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539-1558. https://doi.org/10.1002/sim.1186

58. Knapp G, Hartung J. Improved tests for a random effects meta-regression with a single covariate. Stat Med. 2003;22(17):2693-2710. https://doi.org/10.1002/sim.1482

59. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed.; 1988.

60. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-634. https://doi.org/10.1136/bmj.315.7109.629

61. Simonsohn U, Nelson LD, Simmons JP. P-curve: a key to the file-drawer. J Exp Psychol Gen. 2014;143(2):534-547. http://doi.org/10.1037/a0033242

62. Ayari S, Abellard A, Sakrani S, et al. Comparison of dance and aerobic exercise on cognition and neuropsychiatric symptoms in sedentary older adults with cognitive impairment. Eur Geriatr Med. 2023;14(6):1289-1299. https://doi.org/10.1007/s41999-023-00849-z

63. Friedmann E, Galik E, Thomas SA, Hall PS, Chung SY, McCune S. Evaluation of a pet-assisted living intervention for improving functional status in assisted living residents with mild to moderate cognitive impairment: a pilot study. Am J Alzheimers Dis Other Demen. 2015;30(3):276-289. https://doi.org/10.1177/1533317514545477

64. Di Santo SG, Franchini F, Filiputti B, Martone A, Sannino S. The effects of COVID-19 and quarantine measures on the lifestyles and mental health of people over 60 at increased risk of dementia. Front Psychiatry. 2020;11:578628. https://doi.org/10.3389/fpsyt.2020.578628

65. Trumpf R, Haussermann P, Zijlstra W, Fleiner T. Circadian aspects of mobility-related behavior in patients with dementia: an exploratory analysis in acute geriatric psychiatry. Int J Geriatr Psychiatry. 2023;38(6):e5957. https://doi.org/10.1002/gps.5957

66. Galik E, Resnick B, Hammersla M, Brightwater J. Optimizing function and physical activity among nursing home residents with dementia: testing the impact of function-focused care. Gerontologist. 2014;54(6):930-943. https://doi.org/10.1093/geront/gnt108

67. Arbour-Nicitopoulos KP, Duncan MJ, Remington G, Cairney J, Faulkner GE. The utility of the health action process approach model for predicting physical activity intentions and behavior in schizophrenia. Front Psychiatry. 2017;8:135. https://doi.org/10.3389/fpsyt.2017.00135

68. Rios Romenets S, Anang J, Fereshtehnejad SM, Pelletier A, Postuma R. Tango for treatment of motor and non-motor manifestations in Parkinson's disease: a randomized control study. Complement Ther Med. 2015;23(2):175-184. https://doi.org/10.1016/j.ctim.2015.01.015

69. Groeneweg-Koolhoven I, Comijs HC, Naarding P, de Waal MW, van der Mast RC. Apathy in older persons with depression: course and predictors: the NESDO Study. J Geriatr Psychiatry Neurol. 2016;29(4):178-186. https://doi.org/10.1177/0891988716632914

70. Gorzkowska A, Cholewa J, Małecki A, Klimkowicz-Mrowiec A, Cholewa J. What determines spontaneous physical activity in patients with Parkinson's disease? J Clin Med. 2020;9(5):1296. https://doi.org/10.3390/jcm9051296

71. Ito D, Tanaka T, Kunieda Y, et al. Factors associated with post-stroke apathy in subacute stroke patients. Psychogeriatrics. 2020;20(5):780-781. https://doi.org/10.1111/psyg.12551

72. Hamre C, Fure B, Helbostad JL, et al. Factors associated with level of physical activity after minor stroke. J Stroke Cerebrovasc Dis. 2021;30(4):105628. https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105628

73. Abrantes AM, Friedman JH, Brown RA, et al. Physical activity and neuropsychiatric symptoms of Parkinson disease. J Geriatr Psychiatry Neurol. 2012;25(3):138-145. https://doi.org/10.1177/0891988712455237

74. Sacheli MA, Murray DK, Vafai N, et al. Habitual exercisers versus sedentary subjects with Parkinson's disease: multimodal PET and fMRI study. Mov Disord. 2018;33(12):1945-1950. https://doi.org/10.1002/mds.27498

75. Miura K, Takashima S, Matsui M, Tanaka K. Low frequency of leisure-time activities correlates with cognitive decline and apathy in patients with Parkinson's disease. Adv Parkinsons Dis. 2014;3:15-21. https://doi.org/10.4236/apd.2014.33004

76. Farholm A, Sørensen M, Halvari H, Hynnekleiv T. Associations between physical activity and motivation, competence, functioning, and apathy in inhabitants with mental illness from a rural municipality: a cross-sectional study. BMC Psychiatry. 2017;17(1):359. https://doi.org/10.1186/s12888-017-1528-3

77. Ringen PA, Faerden A, Antonsen B, et al. Cardiometabolic risk factors, physical activity and psychiatric status in patients in long-term psychiatric inpatient departments. Nord J Psychiatry. 2018;72(4):296-302. https://doi.org/10.1080/08039488.2018.1449012

78. Lemij AA, Liefers GJ, Derks MGM, et al. Physical function and physical activity in older breast cancer survivors: 5-year follow-up from the Climb Every Mountain Study. Oncologist. 2023;28(6):e317-e323. https://doi.org/10.1093/oncolo/oyad027

79. Henstra MJ, Feenstra TC, van der Velde N, et al. Apathy is associated with greater decline in subjective, but not in objective measures of physical functioning in older people without dementia. J Gerontol A Biol Sci Med Sci. 2019a;74(2):254-260. https://doi.org/10.1093/gerona/gly014

80. Henstra M, Giltay E, van der Mast R, van der Velde N, Rhebergen D, Rius Ottenheim N. Does late-life depression counteract the beneficial dffect of physical activity on cognitive decline? Results from the NESDO Study. J Geriatr Psychiatry Neurol. 2022;35(3):450-459. https://doi.org/10.1177/08919887211002658

81. Krell-Roesch J, Syrjanen JA, Bezold J, et al. Mid- and late-life physical activity and neuropsychiatric symptoms in dementia-free older adults: Mayo Clinic Study of Aging. J Neuropsychiatry Clin Neurosci. 2023;35(2):133-140. https://doi.org/10.1176/appi.neuropsych.20220068

82. Henstra MJ, Houbolt CM, Seppala LJ, et al. Age modifies the association between apathy and recurrent falling in Dutch ambulant older persons with a high fall risk: recurrent falling in Dutch outpatients, does apathy play a role? Exp Gerontol. 2018;112:54-62. https://doi.org/10.1016/j.exger.2018.09.002

83. Henstra MJ, Rhebergen D, Stek ML, et al. The association between apathy, decline in physical performance, and falls in older persons. Aging Clin Exp Res. 2019b;31(10):1491-1499. https://doi.org/10.1007/s40520-018-1096-5

84. Hashimoto M, Araki Y, Takashima Y, et al. Hippocampal atrophy and memory dysfunction associated with physical inactivity in community-dwelling elderly subjects: the Sefuri Study. Brain Behav. 2016;7(2):e00620. https://doi.org/10.1002/brb3.620

85. Grool AM, Geerlings MI, Sigurdsson S, et al. Structural MRI correlates of apathy symptoms in older persons without dementia: AGES-Reykjavik Study. Neurology. 2014;82(18):1628-1635. https://doi.org/10.1212/WNL.0000000000000378

86. Talamonti D, Dupuy EG, Boudaa S, et al. Prefrontal hyperactivation during dual-task walking related to apathy symptoms in older individuals. PLoS One.

2022;17(4):e0266553. https://doi.org/10.1371/journal.pone.0266553

87. Starkstein SE, Mayberg HS, Preziosi TJ, Andrezejewski P, Leiguarda R, Robinson RG. Reliability, validity, and clinical correlates of apathy in Parkinson's disease. J Neuropsychiatry Clin Neurosci. 1992;4(2):134-139. https://doi.org/10.1176/jnp.4.2.134

88. Marin RS, Biedrzycki RC, Firinciogullari S. Reliability and validity of the Apathy Evaluation Scale. Psychiatry Res. 1991;38(2):143-162. https://doi.org/10.1016/0165-1781(91)90040-v

89. Craig CL, Marshall AL, Sjöström M, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003;35(8):1381-1395. http://doi.org/10.1249/01.MSS.0000078924.61453.FB

90. Simonsohn U, Simmons JP, Nelson LD. Better P-curves: making P-curve analysis more robust to errors, fraud, and ambitious P-hacking, a reply to Ulrich and Miller (2015). J Exp Psychol Gen. 2015;144(6):1146-1152. http://doi.org/10.1037/xge0000104

91. Bize R, Johnson JA, Plotnikoff RC. Physical activity level and health-related quality of life in the general adult population: a systematic review. Prev Med. 2007;45(6):401-415. https://doi.org/10.1016/j.ypmed.2007.07.017

92. Rejeski WJ, Mihalko SL. Physical activity and quality of life in older adults. J Gerontol A Biol Sci Med Sci. 2001;56 Spec No 2:23-35. https://doi.org/10.1093/gerona/56.suppl_2.23

93. Tierney SM, Woods SP, Weinborn M, Bucks RS. Real-world implications of apathy among older adults: Independent associations with activities of daily living and quality of life. J Clin Exp Neuropsychol. 2018;40(9):895-903. https://doi.org/10.1080/13803395.2018.1444736

94. Clarke DE, Ko JY, Lyketsos C, Rebok GW, Eaton WW. Apathy and cognitive and functional decline in community-dwelling older adults: results from the Baltimore ECA Longitudinal Study. Int Psychogeriatr. 2010;22(5):819-829. https://doi.org/10.1017/S1041610209991402

95. Franco MR, Tong A, Howard K, et al. Older people's perspectives on participation in physical activity: a systematic review and thematic synthesis of qualitative literature. Br J Sports Med. 2015;49(19):1268-1276. https://doi.org/10.1136/bjsports-2014-094015

96. Boisgontier MP. Research integrity requires to be aware of good and questionable research practices. Eur Rehabil J. 2021;2(1):1-3. https://doi.org/10.52057/erj.v2i1.24

97. Lahart IM, Boisgontier MP. (2024). Apathy and Physical Activity: Data and Rmd script for Meta-Analysis. [Data set, Rmd scripts, supplementary material]. Version 1.0; 2024. https://doi.org/10.5281/zenodo.10929857

98. Allen L, O'Connell A, Kiermer V. How can we ensure visibility and diversity in research contributions? How the contributor role taxonomy (CRediT) is helping the shift from authorship to contributorship. Learn Publ. 2019;32(1):71-74. https://doi.org/http://doi.org/10.1002/leap.1210

99. Brand A, Allen L, Altman M, Hlava M, Scott J. Beyond authorship: attribution, contribution, collaboration, and credit. Learn Publ. 2015;28(2):151-155. http://doi.org/10.1087/20150211

100. Boisgontier MP, Iversen MD. Physical inactivity: a behavioral disorder in the physical therapist's scope of practice. Phys Ther. 2020;100(5):743-746. https://doi.org/10.1093/ptj/pzaa011