

The impact of objectively-measured physical activity and sedentary behaviour in cardiovascular risk and health-related quality of life in adults: a systematic review

Master's Thesis

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RESUMO

As doenças cardiovasculares, onde se inclui o acidente vascular cerebral e o enfarte agudo do miocárdio, são as doenças não transmissíveis mais fatais em todo o mundo. Desta forma é essencial identificar os fatores de risco das doenças cardiovasculares e promover a sua redução na população. Os fatores de risco mais comuns são a hipercolesterolemia, a hipertensão, os hábitos tabágicos, a diabetes mellitus, a obesidade, a inatividade física e o comportamento sedentário. Estes fatores de risco, para além de estarem relacionados com o aumento do risco cardiovascular (probabilidade de um indivíduo ter um evento/ doença cardiovascular em 10 anos) e com o aumento da prevalência de doenças cardiovasculares, também estão associados a níveis mais baixos de qualidade de vida relacionada com a saúde. No entanto, o aumento da atividade física e a diminuição do comportamento sedentário está associado a uma diminuição dos fatores de risco de doença cardiovascular assim como a um aumento dos níveis de qualidade de vida relacionada com a saúde. Deste modo, realizámos uma revisão sistemática, com o objetivo de averiguar o impacto da atividade física e do comportamento sedentário, avaliados objetivamente, no risco cardiovascular e na qualidade de vida relacionada com a saúde, com especial atenção para o impacto da intensidade da atividade física nesta associação. Concluimos que a atividade física aparenta estar associada a um menor risco cardiovascular e a uma maior qualidade de vida relacionada com a saúde, ao contrário do comportamento sedentário que aparenta estar associado a um maior risco cardiovascular e uma menor qualidade de vida relacionada com a saúde. Verificamos ainda que atividade física de alta intensidade aparenta estar associada a níveis mais altos da componente física da qualidade de vida relacionada com a saúde, enquanto que atividade

física de baixa intensidade aparenta estar associada a níveis mais altos da componente mental da qualidade de vida relacionada com a saúde. No que diz respeito ao risco cardiovascular, aparentemente, pessoas que despendem mais tempo a realizar atividade física, tem um menor risco cardiovascular, mesmo que seja atividade física de baixa intensidade. Será importante continuar a investigar o impacto da atividade física e do comportamento sedentário no risco cardiovascular e na qualidade de vida relacionada com a saúde, assim como a associação de cada componente da atividade física, com o risco cardiovascular e a qualidade de vida relacionada com a saúde.

Palavras chave

Acelerómetro, adultos, fatores de risco cardiovascular, qualidade de vida, sedentarismo.

ABSTRACT

Cardiovascular diseases, including stroke and acute myocardial infarction, are the most fatal non-communicable diseases worldwide. Therefore, it is essential to identify the risk factors for cardiovascular diseases and promote their reduction in the population. The most common risk factors are hypercholesterolemia, hypertension, smoking habits, diabetes mellitus, obesity, physical inactivity and sedentary behaviour. These risk factors are related to increased cardiovascular risk (probability of an individual will have a cardiovascular event/disease in 10 years), to increased prevalence of cardiovascular diseases as well as to lower levels of health-related quality of life. However, increased physical activity and decreased sedentary behaviour are associated with a decrease in cardiovascular disease risk factors as well as an increase in health-related quality of life levels. Thus, we carried out a systematic review, with the objective of investigate the impact of physical activity and sedentary behaviour, objectively evaluated, on cardiovascular risk and health-related quality of life, with special attention to the impact of the intensity of physical activity in this association. We conclude that physical activity appears to be associated with a lower cardiovascular risk and a higher health-related quality of life, unlike sedentary behaviour which appears to be associated with a higher cardiovascular risk and a lower health-related quality of life. We also verified that high-intensity physical activity appears to be associated with higher levels of the physical component of health-related quality of life, while low-intensity physical activity appears to be associated with higher levels of the mental component of health-related quality of life. About the cardiovascular risk, apparently, people who spend more time active have a lower cardiovascular risk, even if it is low-intensity physical activity. It is important to continue to investigate the impact of physical activity and sedentary behaviour on cardiovascular risk and health-related quality

of life, as well as the association of each component of physical activity with cardiovascular risk and health-related quality of life.

Keywords

Accelerometer, adults, cardiovascular risk factors, quality of life, sedentary lifestyle.

LIST OF PUBLICATION

The present thesis is comprised of the following paper:

- Santos, B., Monteiro, D., Silva, F., Flores, G., Duarte- Mendes, P. (Submitted in *Journal of Sport and Health Science*). The impact of objectively-measured physical activity and sedentary behaviour in cardiovascular risk and health-related quality of life in adults: a systematic review

ORAL COMMUNICATIONS

The study of this thesis was presented in the following congresses:

- **The impact of objectively-measured physical activity and sedentary behaviour in cardiovascular risk and health-related quality of life in adults: a systematic review protocol** presented in II Congresso Internacional de Atividade Física (International Congress of Physical Activity) held at School of Education of Polytechnic of Castelo Branco and Sport, Health & Exercise Research Unit, on September 28th- 30th, 2023 (Appendix 1)

- **The impact of objectively-measured physical activity and sedentary behaviour in cardiovascular risk and health-related quality of life in adults: a systematic review** presented in International Congress – CIDESD 2023 held at University of Trás-os-Montes and Alto Douro and Research Centre in Sports Sciences, Health Sciences and Human Development – CIDESD, on October 12th and 13th, 2023 (Appendix 2)

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ABBREVIATIONS

BMI- Body Mass Index

CD- Cannot determine

CHD- Coronary Heart Disease

CVD- Cardiovascular Disease

DBP- Diastolic Blood Pressure

HDL- High Density Lipoproteins

HRQoL- Health-Related Quality of Life

LDL-Low Density Lipoproteins

LIPA- Light intensity physical activity

MET- Metabolic Equivalent Intensity Level

MIN- Minutes

MVPA- Moderate- Vigorous Physical Activity

N- No

NA- Not applicable

NIH- The National Institute of Health

NR- Not reported

RAND- 36- RAND 36-Item Health Survey

PA- Physical activity

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-analysis

PROCAM- Prospective Cardiovascular Münster

SB- Sedentary Behaviour

SBP- Systolic Blood Pressure

SED- Time Spent Sedentary

SF-36- Short-Form Health Survey 36

ST- Sedentary Time

WHOQOL-BREF- World Health Organization Quality of Life – Bref

Y- Yes

INTRODUCTION

This thesis was developed under the scope of the master's degree in Exercise Prescription and Health Promotion, of the School of Education and Social Sciences, Polytechnic of Leiria. This work focuses on the development of a systematic review about the impact of objectively-measured physical activity and sedentary behaviour in cardiovascular risk and health-related quality of life in adults.

Cardiovascular diseases, including stroke and acute myocardial infarction, are the most fatal non-communicable diseases worldwide. Consequently, it is essential to identify the risk factors for these diseases and promote their reduction in the population. The most common risk factors are hypercholesterolemia, hypertension, smoking habits, diabetes mellitus, obesity, physical inactivity and sedentary behaviour.

These risk factors are related to increased cardiovascular risk (probability of an individual will have a cardiovascular event/disease in 10 years), to increased prevalence of cardiovascular diseases as well as to lower levels of health-related quality of life. However, increased physical activity and decreased sedentary behaviour are associated with a decrease in cardiovascular disease risk factors as well as an increase in health-related quality of life levels.

These associations have already been studied but there is currently no systematic review that investigate the impact of objectively-measured physical activity and sedentary behaviour in cardiovascular risk and health-related quality of life in adults without previous cardiovascular disease.

In order to filling this gap in the literature, in the Chapter 1, is presented a systematic review who analyse the association between physical activity and sedentary behaviour (objectively measured) with cardiovascular risk and health-related quality of life in adults without previous cardiovascular disease as well as the impact of the intensity of the physical activity in this association.

CHAPTER 1 - THE IMPACT OF OBJECTIVELY-MEASURED PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR IN CARDIOVASCULAR RISK AND HEALTH-RELATED QUALITY OF LIFE IN ADULTS: A SYSTEMATIC REVIEW

ABSTRACT

Background: Physical activity has been associated with better health outcomes while sedentary behaviour has been considered a risk factor to health. The aim of this systematic review is to analyse the association between physical activity and sedentary behaviour (objectively measured) with cardiovascular risk and health-related quality of life (HRQoL) in adults without previous cardiovascular disease (CVD). Additionally, we intend to analyse the impact of the intensity of the physical activity in this association. Methods: The search was carried in three electronic databases (Web of Science, SCOPUS and PubMed) with access until February 2023 in order to find studies with an observational design. For quality assessment we used The National Institute of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (National Heart Lung & Institute, 2019). Results: Initially we identified 5819 potentially eligible studies but only 5 studies met the inclusion criteria. One of the studies show a positive association between physical activity and HRQoL while the sedentary behaviour was negatively related to the HRQoL. Other study shows an association between high intensity physical activity with better physical component of HRQoL and low intensity physical activity with better mental component of HRQoL. Three studies concluded that higher levels of physical activity are associated with lower levels of cardiovascular risk and higher levels of sedentary behaviour are associated with higher levels of cardiovascular risk. Conclusion: Our findings suggested that people who spend more time being active and spend less time being sedentary appears to have lower cardiovascular risk and higher HRQoL. Further research should be performed to investigate the association of each component of physical activity with cardiovascular risk and HRQoL.

Keywords: quality of life, sedentary time, accelerometry, cardiovascular risk factors, sitting time, adults

PROSPERO registration number: CRD42023401025.

INTRODUCTION

Cardiovascular diseases (CVD) - including coronary heart disease, acute myocardial infarction and stroke - are the most fatal non-communicable diseases globally (European Society of Cardiology, 2021; Visseren et al., 2021). CVD are the cause of 45% and 39% of all the deaths in female and male, respectively, according to the most recent year of available data of the European Society of Cardiology member countries (Timmis et al., 2022). In order to prevent these diseases and minimize the related mortality, it is necessary to identify the risk factors of them and promote its reduction in the population. The most well-known risk factors are hypercholesterolemia, hypertension, smoking habits, diabetes mellitus, high body mass index, physical inactivity, and sedentary behaviour (Alwan et al., 2009; Edwardson et al., 2012; Grundy, 2015; Timmis et al., 2022; Visseren et al., 2021). So as to objectively evaluate the cardiovascular risk, there is some models/algorithm validated that calculated the risk that each individual will have a cardiovascular event/ diseases in 10 years. Examples of this is the SCORE2 (European Society of Cardiology, 2021), the Framingham Risk Model (D'Agostino et al., 2008) and the PROCAM (Assmann et al., 2002). In these three models/ algorithms the risk is calculated based on risk factors like: sex, age, family history of CVD, cigarette smoking, systolic blood pressure, fasting HDL-cholesterol, LDL-cholesterol, total cholesterol, triglycerides and fasting glucose concentration, diabetes mellitus diagnostic. The result is presented in score or a percentage.

Some of risk factors mentioned above (i.e., hypertension, hypercholesterolemia, diabetes mellitus, high body mass index and sedentary behaviours) are also associated to low levels of HRQoL (Martinelli et al., 2008; Mitu et al., 2016; Salinas-Rodríguez et al., 2022) and this association is valid too for individuals with high cardiovascular risk and with this risk factors (Cao et al., 2022). In other hand, ideal cardiovascular health since early adulthood to middle age are associated to higher HRQoL (Pool et al., 2019).

Even in adults with no history of CVD, lower levels of HRQoL are associated with a higher risk of incident CVD (Pinheiro et al., 2019).

Increase physical activity and reduce sedentary behaviour is highly recommended for all but specially for people with high cardiovascular risk since physical inactivity (when an individual not follow the physical activity recommendation (Bull et al., 2020)) and sedentary behaviours (SB) (i.e., any activity, in a position lying down, reclining or sitting, with energy expenditure ≤ 1.5 metabolic equivalents (METs) (Barnes et al., 2012; Tremblay et al., 2017)) are associated with a higher death rate (Ballin et al., 2021; Richardson et al., 2004). At the level of mechanisms, it is known that the absence of regular physical activity and the increased sedentary behaviour promotes visceral fat accumulation and hence an increased metabolic disorder, including metabolic syndrome (Booth et al., 2017; Pedersen, 2017; Rynders et al., 2018). Consequently this represents an increase in risk factors, such as abdominal obesity, hyperglycemia, hypertriglyceridemia, low high-density lipoprotein cholesterol, and insulin resistance (Wildman et al., 2008), which contribute for the development of type 2 diabetes mellitus and CVD (Edwardson et al., 2012; Grundy, 2015). At the same time, people who follow physical activity recommendations have high levels of HRQoL in the physical and mental domains (Vallance et al., 2012). On the other hand, individuals who spend more daily hours in sedentary behaviours have lower levels of HRQoL (Salinas-Rodríguez et al., 2022). For people with cardiovascular risk, this association is also valid (Pucci et al., 2012; Sanchez-Aguadero et al., 2016).

The association between physical activity with cardiovascular risk and HRQoL has been studied for some authors (Hamer et al., 2012; Hamer & Stamatakis, 2009; Salinas-Rodríguez et al., 2022; Sanchez-Aguadero et al., 2016; Vallance et al., 2012) as well as subject of systematic reviews (Oguma & Shinoda-Tagawa, 2004; Pucci et al., 2012). All this authors found a beneficial association between physical activity and cardiovascular risk as well as a beneficial association between physical activity and HRQoL but had some limitations. Oguma and Shinoda-Tagawa (2004) developed a systematic review and meta-analysis about the association between physical activity and cardiovascular risk but in the inclusion criteria of the studies, they do not specify the physical activity assessment instrument and they only include studies that evaluated the CVD- related morbidity and/or mortality, not the cardiovascular risk. Pucci et al. (2012) made a systematic review about the association between physical activity and quality of life but

in the inclusion criteria of the studies, they do not specify the physical activity assessment instrument and they included studies with different population groups (health and with diverse clinical conditions).

According to this and to the best of our knowledge, no systematic review has explored the impact of physical activity and sedentary behaviour (objectively evaluated) in cardiovascular risk and in the HRQoL in adults without previous CVD. Additionally, is unclear the impact of the intensity of the physical activity (objectively evaluated) in the association between physical activity and cardiovascular risk and HRQoL in adults.

Therefore, the aim of this systematic review is to analyse the association between physical activity and sedentary behaviour (objectively measured) with cardiovascular risk and HRQoL in adults without previous CVD. At the same time, we intend to analyse the impact of the intensity of the physical activity in this association. According to this, our hypotheses in study are: a) Adults who are more active have less cardiovascular risk and higher levels of HRQoL; b) Adults who spent more time in sedentary behaviours have higher cardiovascular risk and lower levels of HRQoL; c) The intensity of physical activity influences its benefits in terms of cardiovascular risk and health-related quality of life of the people with cardiovascular risk, proportionally.

MATERIAL AND METHODS

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines (Page et al., 2021). According to the original PRISMA checklist, which describes the four stages (identification, screening, eligibility and final selection) used for researching and selecting the most appropriate articles (Page et al., 2021), was created a graphical flowchart design option. PRISMA presents the PICOS acronym (P - population; I - intervention; C - comparison; O - outcome; S - study design), which facilitated the definition of the research question and makes systematic research more effective.

The protocol of this systematic review was registered in the PROSPERO International Prospective Register of Systematic Reviews with the registration number: CRD42023401025.

SEARCH STRATEGIES

The search was carried out in the following databases: Web of Science, PubMed and SCOPUS, with access until February 2023. In the databases Web of Science and PubMed, the search was made using the following combination of free-text and MeSH terms in “All Fields” and in the database SCOPUS, the search was made using the following combination of free-text and MeSH terms only in “Article Titles, Abstract, Keywords”. The search included studies with an observational design and was limited to studies published in English, Spanish and Portuguese. The grey literature and reference lists of the selected articles were also assessed to identify eligible articles.

The literature search was performed according to the PICO strategy (Methley et al., 2014), and included a combination of free-text and the Key Medical Subject Heading (MeSH terms), as follows: (“cardiovascular risk” OR SCORE2 OR “cardiovascular disease risk factor” OR “CVD risk” OR “cardiometabolic risk factor” OR “clustered cardiometabolic risk” OR “composite score” OR “health related quality of life” OR “quality of life” OR HRQoL) AND (“physical activity levels” OR “moderate physical activity” OR “moderate-to-vigorous physical activity” OR “vigorous physical activity” OR “light physical activity” OR MVPA OR “energy expenditure” OR “sedentary behaviour” OR “sedentary behaviour” OR “sedentary time” OR “sitting time”) AND (acceleromet* OR “objectively measured” OR objective* OR “activity monitor” OR “heart rate monitor” OR pedomet* OR “motion sensor” OR device* OR count* OR armband* OR ActiGraph OR activPAL OR SenseWear OR Actical OR Actiheart) AND (adult* OR “middle aged” OR man OR men OR women OR woman).

ELIGIBILITY CRITERIA AND SELECTION OF STUDIES

Studies included in this review respect the following criteria created with the PICO (Population: Adults, without history of cardiovascular disease; Intervention: Objectively measured physical activity and/or sedentary behaviour assessment; Outcome: Cardiovascular risk and HRQoL): a) Studies that investigated the association between physical activity and/or sedentary behaviour and cardiovascular risk and/or HRQoL in adults; b) Studies that evaluated cardiovascular risk objectively with SCORE2 or other validated scale/algorithm (European Society of Cardiology, 2021) that present the result

in a score/percentage; c) Studies that evaluated HRQoL with WHOQOL- BREF (Whoqol Group, 1994) or other validated questionnaire; d) Studies that evaluated physical activity and sedentary behaviours objectively; e) Studies that include individuals without previous CVD; f) Studies in which the minimum age of participants exceeds 18 years and the maximum age of participants does not exceed 65 years; g) Epidemiological studies of cross-sectional, observational, cohort and population-based designs; h) Peer-reviewed studies published in English, Spanish or Portuguese.

DATA EXTRACTION

Data from search were imported into Endnote X9 (Thomson Reuters EndNote X9), and all duplicates were removed. The process of the selection was performed in phases by two independent reviewers. Initially the studies were selected based on the titles and abstracts. After this, the studies selected were reviewed in their entirety taking into account the specific eligibility criteria. In case of a disagreement over the inclusion of articles, these were resolved through mediation by a third reviewer.

The extraction of data from the selected studies as well as the extraction of the characteristics of these studies (name of the author, year of publication, the country in which it was carried out, the methodological design, characteristics of the sample, main outcomes and the instruments which are used to obtain the main outcomes) was performed independently by the two reviewers involved in the selection of the studies.

QUALITY OF INFORMATION

To evaluate the quality and risk of bias of the studies, was used The National Institute of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (National Heart Lung & Institute, 2019). This checklist includes 14 items and each one was classified as “yes” (Y), “no” (N), “not applicable” (NA), “not reported” (NR) or “cannot determine” (CD). Based on number of items classified with “yes” and the total of items applicable for each study was calculated a total score and a percentage. Based on this percentage, the studies were classified according to quality rating: Poor <50%, Fair 50–75% and Good >75% (Musa et al., 2022).

This assessment would not be intended as a condition for the study to be included in this systematic review, but rather to identify studies in which poor-quality assessment could interfere with outcomes. The quality scoring was performed by two independent reviewers and in case of a disagreement these were resolved by a third reviewer.

RESULTS

DATA SEARCH

The sequence followed for the selection of the studies that were included in this systematic review is shown in Figure 1.

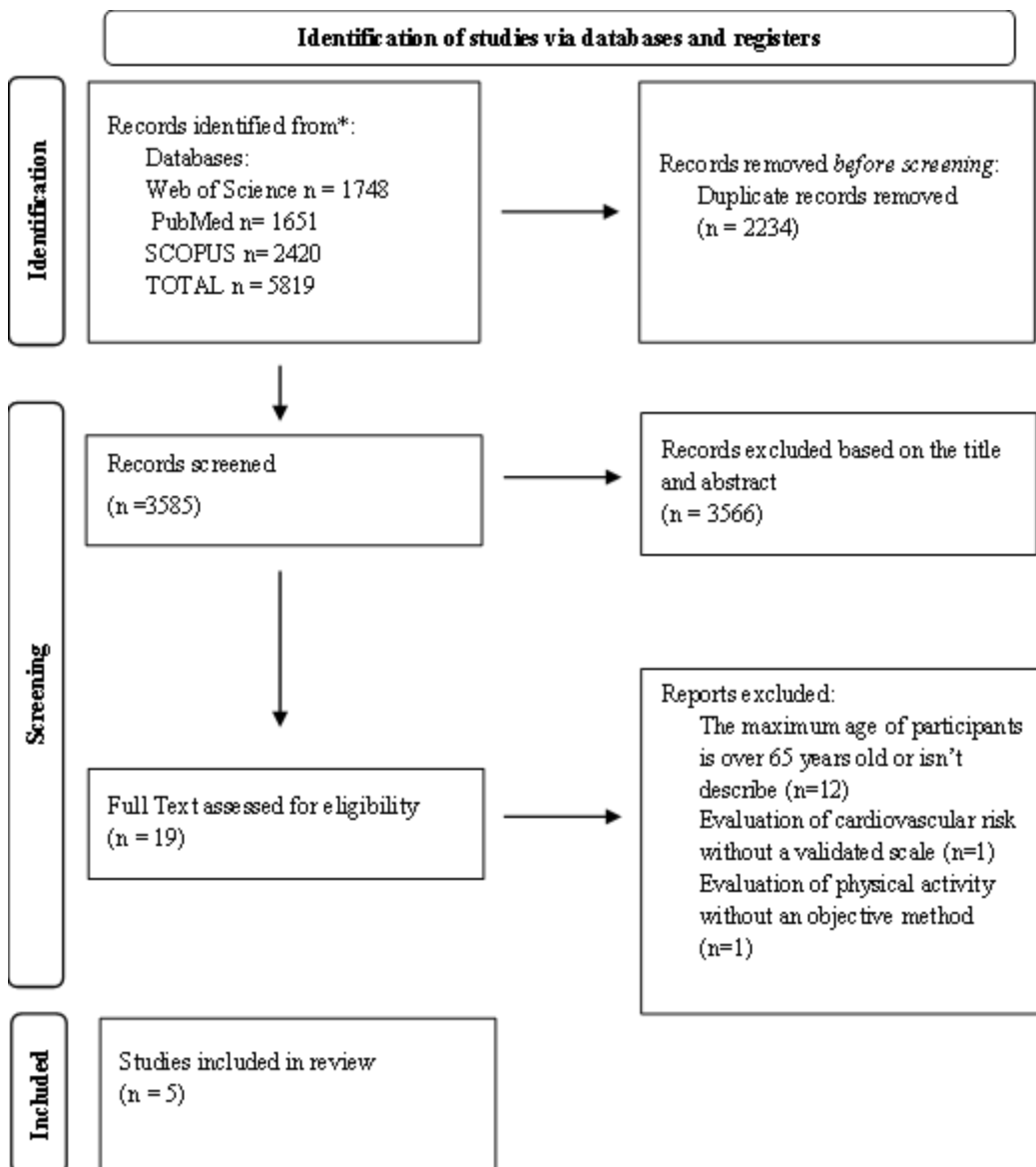


Figure 1: Search strategy and studies selection flow chart

The initial search in the database identified a total of 5819 potentially eligible studies. After excluding studies based on duplicates (n = 2234), titles and abstracts (n = 3566), 19 full-text articles were analysed according to inclusion and exclusion criteria. Most of the studies was exclude because the maximum age of participants was over 65 years old or was not describe. After this phase, 14 studies were excluded, and 5 studies were included in this systematic review.

CHARACTERISTIC OF STUDIES

Details of the five studies included in the systematic review are presented in Table 1.

Table 1: Characteristics of the 5 included studies

Author, Year, Country	Sample Size (n total; n ♂/ n ♀)	Age (years) (mean ± SD; Range)	Study Design	Sedentary Behaviour/ Physical activity Assessment	Health Related Quality of Life (HRQOL) assessment	Cardiovascular Risk assessment	Central outcomes	Main Goals	Main results
1. Marín-Jiménez et al (2020) Spain Fitness League Against MENopause COst (FLAMENCO) project	182 (182 ♀)	52.6 ± 4.5 (45-60 y)	Cross-sectional study	<p>Device: GT3X, Pensacola, FL;</p> <p>Days of wear: 9 days, but the first and the last was excluded from the analyses</p> <p>Minimum wear: N/A</p> <p>Epochs: N/A</p> <p>Cut points: N/A</p> <p>Parameters evaluated: Sedentary time (ST), time in light, moderate, moderate-vigorous (MVPA), and vigorous physical activity (PA), total PA time per day and per week, bouts MVPA (period of 10 or more consecutive minutes (min) of duration in MVPA) and percentage of</p>	Short-Form Health Survey 36 (SF-36) (score)	—————	Weight, Height, body mass index (BMI), ST, PA and health-related quality of life (HRQoL)	To analyse the association of ST and PA with HRQoL in middle-aged women	<p>Lower ST and greater light PA were associated with a better SF-36 emotional role (B: -0.03; 95% confidence interval (CI): -0.07 to -0.00; $p = 0.02$ and B: 0.04, 95% CI: 0.00-0.08; $P = 0.01$, respectively). Higher MVPA was associated with a better SF-36 physical function (B: 0.01, 95% CI: 0.00-0.02; $P = 0.05$) and SF-36 vitality (B: 0.02, 95% CI: 0.00-0.03; $P = 0.01$).</p> <p>Higher vigorous PA was associated with a better SF-36 physical function (B: 0.34,</p>

				participants who met the international PA recommendations of at least 150 min of MVPA per week					95% CI: 0.0-0.66; P =0.03), SF-36 bodily pain (B: 0.63, 95% CI: 0.02-1.25; P = 0.04), and the SF-36 physical component scale (B: 0.20, 95% CI: 0.00-0.39 P = 0.04). Higher total PA was associated with a better SF-36 emotional role (B: 0.03, 95% CI: 0.00-0.07: P = 0.02).
2.Tigbe et al (2017) United Kingdom	111 (96 ♂/ 15 ♀)	39 ± 8 ♂/ 42 ± 9 ♀ (22 to 60y)	Cross-sectional study	Device: ActivPAL monitor; Days of wear: 7 consecutive days; Minimum wear: three 24-hour periods, including a non-work day Epochs: N/A Cut points: N/A Parameters evaluated: time spent stepping, standing and sitting/lying as well as steps, mean stepping rate and number of sit-to-stand transitions per day.	—————	PROCAM (score) Presence of the metabolic syndrome using the following specific	PA, weight, height, waist circumference and CHD risk	To examined the associations between CHD risk and time spent in objectively-measured postures (sitting, lying and standing) and of stepping	Higher 10-year PROCAM risk was significantly (p < 0.05) associated with ST adjusting for age, sex, Scottish Index of Multiple Deprivation, family history of CHD, job type and shift worked.

						criteria			
3. Niemelä et al (2019)	4582	(46-48y)	Cross-sectional	<p>Device: Polar Active, Polar Electro Oy, Kempele</p> <p>Finland;</p> <p>Days of wear: 14 days</p> <p>Minimum wear: 7 consecutive days with enough PA data (wear time \geq 600 min/day), starting from the second measured day;</p> <p>Epochs: N/A</p> <p>Cut points: very light: 1–1.99 MET, light: 2–3.49 MET, moderate: 3.5–4.99 MET, vigorous: 5–7.99 MET, and vigorous+ \geq 8 MET; MVPA was assessed as all activity at least 3.5 METs, while ST was assessed as the duration of very light activity</p> <p>Parameters evaluated: Daily</p>		<p>Framingham risk model</p> <p>(percentage)</p> <p>Height, weight, BMI, body fat percentage and visceral fat area, total cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels, Systolic (SBP) and diastolic blood pressures (DBP), PA, CVD risk,</p>	<p>To</p> <p>identify temporal patterns of continuously measured physical activity</p> <p>beneficial for cardiovascular health in a middle-aged group using cluster analysis and to study how the widely used 10-year CVD risk model is associated with different PA profiles.</p>	<p>Significant differences in CVD risk between clusters were found both in men ($p = 0.028$) and women ($p < 0.001$). The inactive cluster had higher CVD risk compared with the very active cluster in men ($p < 0.05$). In women, the inactive cluster had higher CVD risk compared to moderately active and very active clusters, and the evening active cluster had higher risk compared to the moderately active cluster ($p < 0.05$).</p>	

				averages of time spent in different activity levels; Total daily duration obtained in					
				MVPA and ST bouts (at least 30 min of consecutive					
				MET values between 1 and 2 METs).					
4. Kobayashi Frisk et al (2022) Sweden	812 (48 %♂/ 52% ♀)	57.6±4.4 (50-64y)	Cross-sectional analysis	Device: ActiGraph GT3X and GT3X +, ActiGraph, LCC, Pensacola, FL, USA. Days of wear: 7 consecutive days Minimum wear: at least 600 min per day of wear time for at least 4 days Epochs: N/A Cut points: time spent sedentary (SED): 0–199 cpm, time spent in light intensity physical activity (LIPA): > 199 & < 2690 cpm, and time spend in moderate to vigorous intensity physical activity (MVPA): ≥ 2690 cpm	—————	SCORE2 (score)	Chronotype, Mid-sleep time, Subjective sleep quality, Habitual sleep duration, PA, SED, Estimation of the 10-year risk of first-onset CVD,	To investigate the relationship between chronotype, objectively measured physical activity patterns, and 10-year first-onset CVD risk assessed by the Systematic Coronary Risk Evaluation 2 (SCORE2)	Extreme evening chronotypes exhibited the most sedentary lifestyle and least MVPA (55.3 ± 10.2 and 5.3 ± 2.9% of wear-time, respectively). Extreme evening chronotype was associated with increased SCORE2 risk compared to extreme morning type independent of confounders ($\beta = 0.45$, SE = 0.21, p = 0.031). SED was a significant mediator of the relationship between chronotype and SCORE2.

				<p>Parameters evaluated:</p> <p>Daily percentage of SED and MVPA, total</p> <p>volume of physical activity (mean cpm of wear time), bout of SED (at least 20 min of consecutive cpm values <199 with no allowance for interruption above the threshold), bout of MVPA (10 min consecutive \geq 2690 cpm, with an allowance of up to 2 min below this threshold), percentages of SED and MVPA in the morning (06:00 to 12:00), afternoon (12:00 to 18:00) and evening (18:00 to 00:00)</p>					
5. Kolt et al (2017) Australia	504 (176♂/ 328♀)	50.8 ±13.1 (18-65y)	Cross-sectional	<p>Device: ActiGraph GT3X activity monitor</p> <p>Days of wear: 7 consecutive days</p> <p>Minimum wear: 10 hours of wear time on at least 5 days in the 7day period.</p>	5-item 'general health' subscale of the RAND 36-Item Health	_____	PA, Sedentary behaviour (SB), HRQoL	To examine the association of HRQoL with PA and sedentary behaviour, using both continuous duration (average	The duration measure (average daily minutes) of physical activity was positively related to general HRQoL (path coefficient = 0.294, p<0.05) after adjusting for covariates of age, gender,

WALK 2.0 randomised controlled trial				<p>Epochs- 1 second</p> <p>Cut- points: MVPA - more than 1951 counts/min; Sedentary behaviour - less than 100 counts/min;</p> <p>Parameters evaluated: Daily measures</p> <p>of MVPA, sedentary behaviour, bouts (consecutive 10-min period) of MVPA, bouts of sedentary time and wear time.</p>	Survey (RAND-36) (Score)			daily minutes) and frequency measures (average daily number of bouts ≥ 10 min).	<p>BMI, level of education, and activity monitor wear time. In contrast, the physical activity bouts measure was negatively related to general HRQoL (path coefficient = -0.226, $p < 0.05$) after adjusting for covariates.</p> <p>The duration measure (average daily minutes) of sedentary behaviour was negatively related to general HRQoL (path coefficient = -0.217, $p < 0.05$) after adjusting for covariates of age, gender, BMI, level of education, and activity monitor wear time.</p>
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Four studies were conducted in Europe (Spain, United Kingdom, Sweden and Finland) and one was conducted in Australia. One of the studies included only female participants (Marín-Jiménez et al., 2020), while the other four studies include participants from both sexes (Kobayashi Frisk et al., 2022; Kolt et al., 2017; Niemelä et al., 2019; Tigbe et al., 2017). The studies included a total sample of 6,191 participants. The age of all participants varies between 18 and 65 years. All studies included had a cross-sectional design.

All the studies evaluated the physical activity and sedentary behaviour objectively with different devices (ActivPAL monitor; Polar Active, Polar Electro Oy, Kempele Finland; ActiGraph GT3X and GT3X +, ActiGraph, LCC, Pensacola, FL, USA). Tigbe et al. (2017) analysed the time that the participants spent stepping, standing and sitting/lying as well as steps, mean stepping rate and number of sit-to-stand transitions per day while the others authors (Kobayashi Frisk et al., 2022; Kolt et al., 2017; Marín-Jiménez et al., 2020; Niemelä et al., 2019) analyse the sedentary time (ST), time spent in different intensity's of physical activity (light, moderate, moderate-vigorous (MVPA), and vigorous physical), bout of MVPA and bout of ST although each study has its definition of bouts and cut points. HRQoL was evaluated in two of the included studies (Kolt et al., 2017; Marín-Jiménez et al., 2020). Marín-Jiménez et al. (2020) used the Short-Form Health Survey 36 (SF-36), a questionnaire with 36 items, grouped into eight dimensions: physical functioning, physical role, body pain, general health, vitality, social functioning, emotional role, and mental health. The scores range from 0 to 100 in every dimension, where higher scores indicate better health. These eight dimensions can be summarized into two global concepts: the physical component scale (covered by physical functioning, physical role, bodily pain, and general health) and the mental component scale (vitality, social functioning, emotional role, and mental health) (J. E. Ware, 1993; J. E. J. Ware & Sherbourne, 1992). Kolt et al. (2017) used the 5-item 'general health' subscale of the RAND 36-Item Health Survey (RAND-36), a license-free instrument developed from the original SF-36 Medical Outcomes Study survey. All items are scored on a scale of 0 to 100, with a higher score indicating a more favourable health state (Lins-Kusterer et al., 2022). Kobayashi Frisk et al. (2022), Niemelä et al. (2019) and Tigbe et al. (2017) analysed the association of physical activity with the cardiovascular risk and used three different instruments to evaluate the cardiovascular risk. Kobayashi Frisk et al. (2022) used SCORE2, European risk scoring model which

estimates the 10-year risk of first-onset CVD based on gender, age, smoking status, systolic blood pressure, and non-high-density lipoprotein cholesterol. The result is reported as a percentage. Niemelä et al. (2019) used Framingham risk model, which estimates the absolute risk over 10 years of overall CVD. Variables used in this model included age, HDL cholesterol, total cholesterol, systolic blood pressure (not treated or treated), and prevalence of smoking (yes/no) and diabetes mellitus (yes/no). The result is presented by a percentage. Tigbe et al. (2017) used the PROCAM, a risk calculator that generates 10-year coronary heart disease risk, for men aged 35-65y and women aged 45-65y, based on sex, age, family history of coronary heart disease, cigarette smoking, systolic blood pressure, fasting HDL-cholesterol, LDL-cholesterol, triglycerides and fasting glucose concentration. Additionally, participants were classified as having metabolic syndrome, or not using the following criteria: fasting serum triglycerides ≥ 1.7 mmol/l, glucose ≥ 5.6 mmol/l, HDL- cholesterol ≤ 1.03 mmol/l for men or ≤ 1.30 mmol/l for women, waist circumference ≥ 102 cm for men or ≥ 88 cm for women, and blood pressure $\geq 130/85$ mmHg. In this study only 67 men and 6 women has the adequate age to use the PROCAM, the other participants have the presence or absence of metabolic syndrome as the indicator of the cardiovascular risk.

Marín-Jiménez et al. (2020) conclude that lower ST and greater light physical activity were associated with a better SF-36 emotional role. Higher MVPA was associated with a better SF-36 physical function and SF-36 vitality. Higher vigorous physical activity was associated with a better SF-36 physical function, SF-36 bodily pain and the SF-36 physical component scale. Finally, moderate physical activity was not associated with any SF-36 dimension. In the study of Kolt et al. (2017) the association of physical activity and sedentary behaviour with HRQoL was analysed taking in account the duration and frequency of the physical activity. The authors concluded the duration measure (average daily minutes) of physical activity was positively related to general HRQoL. In contrast, the physical activity bouts (consecutive 10-minute period) measure was negatively related to general HRQoL. At the same time, the duration measure (average daily minutes) of sedentary behaviour was negatively related to general HRQoL. The frequency measure of sedentary behaviour was not significantly associated with general HRQoL.

Kobayashi Frisk et al. (2022) divided the participants in groups based in theirs chronotype (extreme morning; moderate morning; intermediate; moderate evening;

extreme evening). The groups with higher cardiovascular risk are the groups with higher time spent sedentary, with the lower average daily physical activity, with the lower percentage of light intensity physical activity and with lower percentage of MVPA. The group with the best results is the chronotype “extreme morning” and the group with the worst results are the chronotype “extreme evening”. Niemelä et al. (2019) divided the participants in four clusters (inactive, evening active, moderately active and very active) based on the pattern of activity. The ST is higher in “inactive” cluster and lower in the “very active” cluster. In other hand, all the variables related to the physical activity are higher in the “very active” cluster and lower in the “inactive” cluster. Between the clusters “evening active” and “moderately active”, the second one had the healthy results, slightly below to the “very active” cluster results. About the cardiovascular risk, in men the “inactive” cluster have the higher result and the “very active” cluster have the lower result; in women the results are higher in the “evening active” (3.75%) and “inactive”(3.0%) clusters and lower in the “moderately active” (2.99%) and “very active” (3.06%) clusters (Niemelä et al., 2019). Tigbe et al. (2017) concluded that higher cardiovascular risk is significantly associated with ST (in sitting/lying positions) and in other hand cardiovascular risk is significantly and favourably associated with stepping time, additional cardiovascular risk is inversely associated to daily steps count.

According to the results of Kobayashi Frisk et al. (2022) and Niemelä et al. (2019), the clusters with lower cardiovascular risk are the clusters that presented a higher percentage/ time per day of light physical activity, MVPA, vigorous physical activity and very vigorous physical activity, simultaneous. But, in all the clusters the time spent in light physical activity is much higher than the time spent in MVPA. Suggesting that people, who spend more time been active have a lower cardiovascular risk even if it is low intensity physical activity.

The statistic results of each included study are presented in the Table 1.

QUALITY ASSESSMENT

The quality and risk of bias of the studies was evaluated and the results are shown in Table 2.

Table 2: Quality assessment scores of selected studies (The National Institute of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies)

Author	Items of Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies														Total Score
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Marín-Jiménez et al (2020)	Y	Y	Y	Y	Y	N	N	Y	Y	N	Y	N	N	Y	9/12 (75%)
Tigbe et al (2017)	Y	Y	Y	Y	N	N	N	Y	Y	N	N	N	N	Y	7/12 (58.3%)
Niemelä et al (2019)	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	N	N	Y	8/12 (66.7%)
Kobayashi Frisk et al (2022)	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	N	N	Y	8/12 (66.7%)
Kolt et al (2017)	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	N	N	Y	8/12 (66.7%)

All the studies are cross-sectional and because of this the items 6 and 7 were classified with “No” according to the guidance (National Heart Lung & Institute, 2019). Items 12 and 13 were classified with “Not applicable” and wasn’t accounted for the final score. The final percentage varied between 58.3% and 75% what correspond to the quality rating “Fair”.

DISCUSSION

This systematic review aimed to analyse the association between physical activity and sedentary behaviour (objectively measured) with cardiovascular risk and HRQoL in adults without previous CVD as well as the impact of the intensity of the physical activity in this association.

As hypothesized, all the studies show a positive association between physical activity and HRQoL (Kolt et al., 2017; Marín-Jiménez et al., 2020) and between physical activity and cardiovascular risk (Kobayashi Frisk et al., 2022; Niemelä et al., 2019; Tigbe et al., 2017). On the other hand, all the studies show a negative association between sedentary behaviour with HRQoL (Kolt et al., 2017; Marín-Jiménez et al., 2020) and between sedentary behaviour and cardiovascular risk (Kobayashi Frisk et al., 2022; Niemelä et al., 2019; Tigbe et al., 2017).

About the impact of physical activity intensity in the HRQoL, the results of Marín-Jiménez et al. (2020) study induce that higher intensity is associated with physical component of HRQoL and lower intensity is associated with mental component of HRQoL. What is consistent with the results of one study that analyses the association between MVPA with self-reported mental HRQoL, and physical HRQoL in adults and older age (Vásquez et al., 2019). Vásquez et al. (2019) observed no significant linear trend between accelerometer-measured MVPA and mental HRQoL and a significant positive association between MVPA and physical HRQoL, where higher MVPA corresponded with higher scores in physical HRQoL. The results of Kolt et al. (2017) suggest that higher duration of physical activity and sedentary behaviour are associated to higher and lower HRQoL, respectively. About the frequency, the results suggest that for a given level of physical activity duration, being active in fewer bouts was associated with better HRQoL (Kolt et al., 2017). These results are consistent with a

previous study that demonstrated that both non-bouted and bouted MVPA are associated with HRQoL. However, the authors had already founded a low level of engagement in bouted MVPA (Loprinzi & Davis, 2016). Guallar-Castillón et al. (2014) also studied the association of physical activity and sedentary behaviour with HRQoL in adults and older age, using pattern of activity and his results are consistent with the results of the included articles of this systematic review (Kolt et al., 2017; Marín-Jiménez et al., 2020). Guallar-Castillón et al. (2014) concluded that pattern with vigorous physical activity was associated with better physical health, the pattern with light physical activity was associated with better mental health. Additionally, the patterns that included some types of physical activity (vigorous or light) were associated with better HRQL comparing with the pattern which include more sedentary behaviour.

In a general way, it was expected that physical activity, independently of its duration, intensity or frequency, are associated to better HRQoL because physical activity are associated with many health-related outcomes like low mortality (Ekelund et al., 2019), low risk of depression and anxiety (Schuch et al., 2018), improvements in cognition (Physical Activity Guidelines Advisory Committee 2018, 2018), better sleep quality (Yang et al., 2012) and with low risk of many diseases, like cancer, hypertension, type-2 diabetes (Bull et al., 2020).

In the studies of Kobayashi Frisk et al. (2022) and Niemelä et al. (2019) the participants were in groups/ clusters. Both conclude that the participants with more average daily physical activity, with less ST, with more percentage of light intensity physical activity and with more average time in MVPA are the group of participants with lower cardiovascular risk. These results are consistent with other studies that already analysed the association between physical activity and cardiovascular risk and concluded that higher levels of physical activity are associated to lower cardiovascular risk (Biswas et al., 2022; Hawkins et al., 2013). Tigbe et al. (2017) concluded that higher cardiovascular risk is significantly associated with ST (in sitting/lying positions) and in other hand cardiovascular risk is significantly and favourably associated with stepping time, additional cardiovascular risk is inversely associated to daily steps count. These results are similar to the others authors that analyse the daily step counts with cardiovascular risk or cardiovascular mortality, that concluded that an increase in the

number of daily steps represents a decrease in cardiovascular risk or cardiovascular mortality (Hall et al., 2020; Kraus et al., 2019).

As is already known, physical activity is very important in the control of risk factors for numerous diseases, and CVD is not an exception. Physical activity is recommended for World Health Organization (World Health Organization, 2020) and for European Society of Cardiology (Visseren et al., 2021) in order to reduce cardiovascular risk and in order to control the risk factors for CVD like diabetes mellitus (Thomas et al., 2006) high body mass index, hypertension and hypercholesterolemia (Shaw et al., 2006). After this is expected that people more active have less risk factors and a lower cardiovascular risk.

The results of the included studies reinforce the importance of increasing levels of physical activity and reduce levels of ST in the population, in order to reduce cardiovascular risk and consequently death rate for CVD as well as to promote the increase of the levels of HRQoL in the population.

This systematic review has a great methodological value due to eligibility criteria that guaranteed that only studies with adult participants and studies that utilize objective measures to quantify physical activity and sedentary behaviour as validated instruments to measure cardiovascular risk and HRQoL were included but this systematic review has six limitations. The limitations are the fact that the research was carried out using terms only in English, the limited number of studies that use objective instruments to measure the physical activity and validated instruments to measure cardiovascular risk, the limited number of studies that include only adults and not adults and older people, the heterogeneity of the instruments that evaluated the cardiovascular risk and the HRQoL; the heterogeneity of the protocols to collect, process and analyse the data from accelerometers, as well as the use of different devices to evaluate physical activity.

In the future will be interesting to study the mediator paper of the physical activity between HRQoL and cardiovascular risk, as well as the association of each component of physical activity (frequency, intensity, duration and type) with cardiovascular risk and HRQoL, in order to know what represents more benefit to the population and to guide the physical activity recommendation and the exercise prescription.

CONCLUSION

This systematic review reinforces the importance of increasing levels of physical activity and reduce levels of ST in the population, since our findings suggested that people who spend more time being active and spend less time being sedentary, apparently have lower cardiovascular risk and higher HRQoL. About the physical activity intensity, the higher intensity physical activity appears to be associated to higher physical component of HRQoL and lower intensity physical activity appears to be associated to higher mental component of HRQoL. Apparently, cardiovascular risk tends to be lower in people who are more active even if it is low intensity physical activity.

Despite the limitations of this systematic review and the need to continue studying these associations, the results presented reinforce the importance of sharing the benefits of physical activity with population and the importance of promote a behavioural change in population.

GENERAL CONCLUSIONS

This thesis investigates the impact of objectively-measured physical activity and sedentary behaviour in cardiovascular risk and health-related quality of life in adults as well as the impact of physical activity intensity in this association. We did a systematic review about this subject in order to know what has already been investigate and what the current literature tell us about this associations.

According to the results of the included studies in this systematic review, people who spend more time being active and spend less time being sedentary appears to have lower cardiovascular risk and higher HRQoL and that reinforces the importance of increasing levels of physical activity and reduce levels of sedentary time in the population. About the physical activity intensity, the higher intensity physical activity appears to be associated to higher physical component of HRQoL and lower intensity physical activity appears to be associated to higher mental component of HRQoL. Apparently, cardiovascular risk, tends to be lower in people who are more active even if it is low intensity physical activity.

Studies that investigate this association and use objective instruments to measure the physical activity as well as validated instruments to measure cardiovascular risk in adults without previous CVD are limited. Therefore, is important to continue investigate this subject and we think will be interesting to study the mediator paper of the physical activity between HRQoL and cardiovascular risk, as well as the association of each component of physical activity (frequency, intensity, duration and type) with cardiovascular risk and HRQoL,

Despite the limitations of the systematic review and the need to continue studying these associations, the results presented in this work reinforce the importance of sharing the benefits of physical activity with population and the importance of promote a behavioural change in population.

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APPENDICE

APPENDIX 1



APPENDIX 2

