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Clinical Research

Physical Activity and Sedentary Behaviour Thresholds for Secondary Prevention of Coronary Heart Disease: Morbidity Survival Tree Analysis

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ABSTRACT

Background: There are no diagnosis-specific guidelines for moderate-to-vigorous physical activity (MVPA) and sedentary behaviour (SB) for coronary heart disease (CHD). This study aimed to identify thresholds of MVPA and SB associated with cardiovascular events.

Methods: This cohort study included individuals with CHD. MVPA and SB were self-reported, and health registries identified cardiovascular events in the years 2006-2022. Survival tree analyses identified thresholds of time associated with the risk of cardiovascular events. Thresholds were explored with the use of Cox regression models.

Results: There were 40,156 Australians, mean age 70 years, 62% men. Over a median 8.3 years, 3260 nonfatal cardiac events, 5161 total cardiac events, and 14,383 major adverse cardiovascular events

RÉSUMÉ

Contexte : Il n'existe pas de lignes directrices spécifiques au diagnostic concernant l'activité physique modérée à vigoureuse (APMV) et le comportement sédentaire (CS) pour la maladie coronarienne (MC). Cette étude visait à identifier les seuils d'APMV et de comportement sédentaire associés aux événements cardiovasculaires.

Méthodes : Cette étude de cohorte a inclus des personnes atteintes de MC. L'APMV et le CS étaient autodéclarés et les registres de santé ont identifié les événements cardiovasculaires survenus entre 2006 et 2022. Des analyses avec un type d'arbre de décision appliqué aux données de survie ont permis d'identifier des seuils temporels associés au risque d'événements cardiovasculaires. Les seuils ont été explorés à l'aide de modèles de régression de Cox.

International guidelines emphasise the importance of regular moderate-to-vigorous physical activity (MVPA) in secondary prevention of coronary heart disease (CHD),[1-3] owing to its positive effects on cardiovascular risk factors[4] as well as its direct association with the risk of cardiovascular disease (CVD) events and mortality.[5-7] In addition, the importance of sedentary behaviour has been discussed in the recent decade.[8] Sedentary behaviour is defined as "any waking behaviour characterised by an energy expenditure $\leq$ 1.5 metabolic equivalents (METs) while in a sitting or reclining posture."[9] There are no diagnosis-specific guidelines for time in MVPA or sedentary behaviour among individuals with CHD. Therefore, international public health guidelines of 150-300 minutes of weekly MVPA are used. The guidelines further emphasise limiting time in prolonged sedentary behaviour, with no specific threshold.[10] Nonetheless, a large study in the general adult population has found an increased risk of all-cause mortality among individuals with self-reported sedentary behaviour $\geq$ 7 h/d.[11]

Few studies have explored the association between achieving $\geq$ 150 min/wk of MVPA and the risk of cardiovascular events among individuals with CHD. A study among 30,644 individuals found a 25% lower risk of cardiovascular events in the first year after myocardial infarction among individuals self-reporting $\geq$ 150 min/wk compared with individuals self-reporting < 30 min/wk.[5] Furthermore, studies indicate that the reduction in risk of a cardiovascular event[5,6] or mortality[12] is greatest for the first minutes of MVPA. This is similar to a large meta-analysis's conclusion that the optimal daily step count to prevent cardiovascular mortality is 7126,

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(MACE) occurred. Thresholds for MVPA were 122 min/wk for nonfatal cardiac events and 94 min/wk for total cardiac events and MACE. Meeting MVPA thresholds was associated with an 18% lower risk for nonfatal cardiac events, 29% lower risk of total cardiac events, and 23% lower risk of MACE than not reaching the thresholds. Thresholds for SB were 4 and 10 h/d, respectively, for risk of total cardiac events and MACE. SB below thresholds was associated with a 14% lower risk of total cardiac events and an 18% lower risk of MACE. There were sex-specific thresholds for MVPA and SB.

Conclusions: To lower cardiovascular event risk, identified MVPA thresholds were lower (94-122 min/wk) than the public health guidelines (150 min/wk) in individuals with CHD. The SB thresholds associated with a lower risk of total cardiac events and MACE varied from 4 to 10 h/d.

Résultats : L'étude comprenait 40 156 Australiens, d'un âge moyen de 70 ans, dont 62 % d'hommes. Sur une période médiane de 8,3 ans, 3 260 événements cardiaques non mortels, 5 161 événements cardiaques totaux et 14 383 événements cardiovasculaires indésirables majeurs (ECIM) sont survenus. Les seuils pour l'APMV étaient de 122 min/semaine pour les événements cardiaques non mortels et de 94 min/semaine pour les événements cardiaques totaux et les ECIM. L'atteinte des seuils d'APMV était associée à un risque 18 % plus faible d'événements cardiaques non mortels, 29 % plus faible d'événements cardiaques totaux et 23 % plus faible d'ECIM que si les seuils n'étaient pas atteints. Les seuils pour le CS étaient de 4 et 10 h/j pour le risque d'événements cardiaques totaux et d'ECIM, respectivement. Un CS inférieur aux seuils était associé à un risque d'événements cardiaques totaux inférieur de 14 % et à un risque d'ECIM inférieur de 18 %. Il existait des seuils spécifiques au sexe pour l'APMV et le CS.

Conclusions : Pour réduire le risque d'événements cardiovasculaires, les seuils d'APMV identifiés étaient inférieurs (94-122 min/semaine) aux recommandations de santé publique (150 min/semaine) chez les individus atteints de MC. Les seuils de CS associés à un risque réduit d'événements cardiaques totaux et d'ECIM variaient de 4 à 10 heures/jour.

which is lower than the general recommendation of 10,000 steps per day.[13] Interestingly, a large study by Jeong et al.[14] compared the benefits of reaching the public health guidelines between individuals with and without CVD. They concluded that individuals with CVD may benefit from MVPA to a greater extent than individuals without CVD. Individuals with CVD reduced their risk for all-cause mortality by 14% for every increase of 500 MET-min/wk of MVPA. In contrast, the risk was reduced by 7% for every 500 MET-min/wk of MVPA among individuals without CVD.[14] This suggests that the benefit of MVPA is greater for individuals with CVD compared with the general adult population. In addition, little is known about sex-specific differences in MVPA benefits among individuals with CHD. A recent publication in the general population found that women seem to have greater benefits than men for risk of all-cause mortality (24% vs 15% lower risk) with reaching the public health guidelines.[15] Similar results can be seen for cardiovascular mortality,[15] emphasising the need to explore potential sex differences among individuals with CHD to guide clinical recommendations.

To our knowledge, no previous studies have explored the association between time in sedentary behaviour with the risk of cardiovascular events among individuals with CHD. Two studies among patients with CHD found an increased risk of all-cause mortality among individuals reporting a higher level of sedentary behaviour. Ku et al. found a 62% higher risk of all-cause mortality among individuals reporting $\geq$ 4 h/d compared with $<$ 4 h/d. Meanwhile, a Swedish study found a 43% lower risk of all-cause mortality among individuals reporting $\leq$ 6 h/d compared with $\geq$ 10 h/d. A 42% lower risk of total hospital readmissions was found among individuals reporting $\leq$ 6 h/d of sedentary behaviour compared with the reference group.[16]

The absence of diagnosis-specific guidelines for individuals with CHD emphasises the need to develop guidelines for MVPA and sedentary behaviour to decrease the risk of cardiovascular events. The present study aimed to identify significant thresholds of time in MVPA and sedentary behaviour associated with a lower risk of nonfatal cardiac events, total cardiac events, and major adverse events (MACE) among men and women with CHD.

Methods

The study is based on the Australian 45 and Up study cohort, among individuals 45 years of age and older randomly sampled from the general population in New South Wales, Australia.[17] Data were collected in waves: first (2006 to 2009), Social, Economic and Environmental Factors (SEEF) (2010), second (2012-2016), and third (2018-2020). To be included in this study, individuals had to self-report CHD. This was assessed by the following questions: being treated for a "heart attack or angina" or "other heart disease" in the last month, or "ever told heart disease as diagnosed by a doctor," or "having a coronary artery bypass graft operation." An individual's baseline was defined as the date they first stated in a questionnaire that they had been diagnosed with CHD. Individuals were followed until they had their first CVD event or death, or to the end date of the study (December 31, 2022), whichever occurred first.

Exposures

Minutes of MVPA in the past week were measured using the Active Australia Survey.[18] The Active Australia Survey has a moderate to strong (r = 0.30-0.52) correlation to accelerometer-assessed MVPA among patients with CHD.[19] The survey combines questions about walking and moderate- and vigorous-intensity physical activity (Supplemental Table S1). Total MVPA was obtained by multiplying the time in vigorous-intensity physical activity by 2 (to account for a higher intensity) and then adding time in walking and moderate-intensity physical activity.[18] If the individual answered at least 1 physical activity question, any missing data for the other physical activity questions were assigned a value

of 0 minutes. The maximum time in MVPA was set to 1680 min/wk.

Sedentary time was assessed by "hours in each 24-hour day they spent: sitting, watching TV/using a computer," in the first and SEEF waves (Supplemental Table S1). In waves 2 and 3, individuals answered questions about how much time they spent in the past 7 days on a usual weekday and weekend day: sitting, watching TV, using a computer at home, other leisure activities, transport, or work. For individuals answering at least 1 sedentary behaviour question, missing data were recorded as 0 minutes. The average daily time spent in total sedentary behaviour in waves 2 and 3 was calculated by: (weekday total sedentary behaviour $\times$ 5 + weekend total sedentary behaviour $\times$ 2)/7. The maximum time for sedentary behaviour was set at 16 h/d.

Outcomes

To identify the first CVD event, the data set was linked with the Admitted Patient Data Collection (APDC) New South Wales,[20] and the New South Wales Register of Births, Deaths & Marriages—Death Registrations, and the Australian Bureau of Statistics Mortality Data.[21] Cardiovascular events occurring within 90 days were excluded, because they could be related to the previous event. International Classification of Diseases, 10th Revision, codes were used to identify 3 outcomes (Supplemental Table S2): 1) nonfatal cardiac events, ie, acute myocardial infarction, ST-segment elevation myocardial infarction, and non−ST-segment elevation myocardial infarction (APDC registry), 2) total cardiac events, ie, nonfatal coronary heart events and cardiac death (APDC and mortality registries), and 3) MACE, ie, nonfatal cardiac events, stroke, heart failure (APDC registry) and cardiovascular death (mortality registry).[22]

Covariates

Covariates were self-reported in the participants baseline questionnaire, including cardiovascular risk factors,[2] and physical activity and sedentary behaviour correlates,[23] and a directed acyclic graph was used for mapping assumptions[24] (Supplemental Fig. S1). Included covariates were, age, sex (male or female), body mass index (BMI, kg/m^2), education level (less than high school, high school, or tertiary education), type 2 diabetes, smoking status (current or not current), and family history of heart disease.

Statistical analyses

Individuals needed full data on exposures, covariates, and outcome variables to be included in the analyses. Baseline differences between included vs excluded individuals, men vs women, and MACE vs non-MACE in the cohort were analysed with the use of unpaired t tests, Mann-Whitney U tests, and χ^2 tests. P values < 0.05 were considered to be statistically significant. Survival trees were used to identify optimal thresholds for the time in MVPA and sedentary behaviour associated with cardiovascular events, (minimum split = 20; complexity parameter = 0.001; and maximum depth = 1). This approach split the data into distinct subgroups based on cardiovascular outcomes. Those settings were applied to ensure the identification of a first split of a significant threshold value per the aim of the study. Survival regression trees were completed for the total cohort, and for men and women separately to explore differences in sex. The newly developed thresholds were then explored by using unadjusted and adjusted Cox regression models with a 95% confidence interval (CI). If the CI did not include 1, the Cox regression models were considered to be statistically significant. Cox regressions were adjusted for age, sex, education level, BMI, type 2 diabetes, smoking status, and family history of heart disease. Adjusted Cox regression models for MVPA were adjusted for sedentary behaviour, and vice versa. Sensitivity analyses were performed in the fully adjusted Cox regression analyses: 1) excluding individuals with follow-up time shorter than 2 years to reduce the risk of reverse causality, 2) stratified by being included in wave 1 vs the other waves to assess if the risk of a long history of preexisting heart disease may affect the association, and 3) stratified by reaching the MVPA thresholds or not to explore if the level of MVPA modified the results of sedentary behaviour.

In addition, hazard ratios (HRs) with 95% CIs for MVPA and sedentary behaviour were examined, categorised according to public health physical activity guidelines as $\geq$ 150 vs $<$ 150 min/wk of MVPA and suggested public health sedentary guidelines as $\geq$ 7 vs $<$ 7 h/d. This analysis determined if the association aligned with the newly identified thresholds. Then, receiver operating characteristic (ROC) curves were calculated with the developed thresholds of time in MVPA and sedentary behaviour as predictors and cardiovascular events (yes or no) as outcome variables. For the ROC analyses, data are presented as the area under the ROC curve (AUC). Sensitivity and specificity analyses were used to identify the proportion of true positive and true negative cardiovascular events. Statistical analyses were performed in R (R Studio version 2023.03.1) using the packages rpart, rpart.plot, survival, and proc.

Results

Among 49,828 individuals with CHD, 40,156 met the inclusion criteria and were included in the study cohort (Supplemental Fig. S2). There were baseline differences between individuals included and excluded in the study cohort. Included individuals were more likely to be men and younger, fewer were diagnosed with diabetes or were current smokers, and they had a higher level of MVPA (Supplemental Table S3). Individuals in the study cohort had a median follow-up time of 8.3 years (interquartile range [IQR] 10 years); 3260 nonfatal cardiac events, 5161 total cardiac events, and 14,383 MACE occurred. The individuals included had a mean age of 70 $\pm$ 10 years, 38% were women. Further baseline characteristics for the study cohort are presented in Table 1. Men had a higher level of education and more frequently diagnosed with diabetes, fewer had a family history of heart disease, and they spent more time in both MVPA and sedentary behaviour compared with women. Furthermore, men had a higher percentage of cardiovascular events than women (Table 1). In addition, there were small but statistically significant baseline differences among individuals with vs without a cardiovascular event. Individuals with cardiovascular events were more often male, older, and with diabetes (Supplemental Table S4).

Thresholds for moderate-to-vigorous physical activity and sedentary behaviour

In the survival tree analyses the threshold for MVPA was 122 min/wk for nonfatal cardiac events (Fig. 1), and 94 min/wk for the risk of total cardiac events (Fig. 2) and MACE (Fig. 3) for the complete cohort. Women had lower MVPA thresholds for all outcomes (Figs. 1-3). In adjusted Cox regression models, individuals reaching the developed thresholds had an 18% lower risk for nonfatal cardiac events, 29% lower risk of total cardiac events, and 23% lower risk of MACE, compared with individuals not reaching the threshold in the total cohort (Table 2). The significantly lower risk among individuals remained in sensitivity analyses (individuals with $\geq$ 2 years of follow-up and included in wave 1 or the other waves) when reaching the identified thresholds (Supplemental Table S5). HRs associated with the public health guidelines ($\geq$ 150 min/wk) were similar to the developed thresholds in the complete study cohort (Supplemental Table S6). Women achieving the sex-specific threshold of MVPA had a significantly lower risk (26%-33%) of CVD events compared with women who did not achieve the threshold (Table 3). The lower risk was more pronounced than the difference observed for men (18%-29% lower risk) achieving and not achieving their sex-specific threshold (Table 3).

For sedentary behaviour, the survival regression tree could not identify a significant threshold for nonfatal cardiac events (Fig. 1). For total cardiac events the identified threshold of sedentary behaviour was 4 h/d (Fig. 2) and 10 h/d for MACE (Fig. 3). The significantly lower risk remained in individuals with $\geq$ 2 years of follow-up and among individuals included in the first wave. It was not maintained among individuals included in the other waves (Supplemental Table S5). Stratified analyses among individuals reaching and not reaching the MVPA thresholds found a significantly lower risk of total cardiac events and MACE among individuals below the sedentary behaviour thresholds compared with those above the thresholds. However, the differences in risk among individuals with sedentary behaviour below and above the thresholds were more pronounced in the group not reaching the MVPA thresholds than among individuals reaching the MVPA thresholds (Supplemental Table S7). There were sex differences in sedentary behaviour thresholds associated with total cardiac events, with men having a threshold of $<$ 3 h/d and women a threshold of 8 h/d (Fig. 2). For MACE, the threshold for women was 9 h/d, and no threshold was identified for men (Fig. 3). In adjusted Cox regression analyses, individuals with sedentary time below the developed thresholds had a 14% lower risk of total cardiac events and an 18% lower risk of MACE compared with individuals above the thresholds (Table 2). The lower risks of total cardiac events and MACE for the developed thresholds in the complete study cohort were similar to the risk associated with the threshold of 7 h/d (Supplemental Table S6). Among women, sedentary time below the sex-specific threshold had a lower (26%-34%) risk of total cardiac events and MACE compared with women above the thresholds. The lower risk among women was more pronounced than the risk difference observed among men for total cardiac events based on sex-specific sedentary behaviour thresholds (13% lower risk) (Table 3).

ROC analysis further validated the adequacy of the newly developed and public health threshold to predict cardiovascular events. The model's ability to discriminate between high- and low-risk groups with the developed threshold was found to be poor, with AUCs of 0.514 to 0.541 and low sensitivity and specificity (Tables 2 and 3). This was slightly lower than the predictive accuracy (0.517 to 0.582), sensitivity, and specificity of the current public health thresholds (Supplemental Table S6).

Discussion

This cohort study of individuals with CHD indicates a significantly lower risk of cardiovascular events when reaching 94-122 min/wk of MVPA that is similar to the risk reduction achieved by meeting the public health physical activity recommendations of 150 min/wk. Importantly, women seem to gain more from lower levels of MVPA to receive health benefits. Thresholds of time in sedentary behaviour with the risk of cardiovascular events varied based on the cardiovascular event assessed. A lower risk associated with total cardiac events and MACE was set to 4 and 10 h/d, respectively, and no threshold was found by the survival tree model for nonfatal cardiac events. Men seemed more vulnerable to time in sedentary behaviour, with a lower threshold of time in sedentary behaviour associated with a higher risk of total cardiac events. The identified thresholds for MVPA and sedentary behaviour exhibit associations (HRs) and predictive capacities regarding cardiovascular event risks similar to current public health guidelines, indicating that the greatest health benefits are achieved before reaching the public health guidelines, although exceeding those lower identified thresholds may lead to further health benefits.

Thresholds for time in MVPA have not previously been identified among individuals with CHD for risk of cardiovascular events. In the present study, individuals with CHD reaching the newly identified thresholds had an 18%-29% lower risk of cardiovascular events in the adjusted Cox regression models. This is a larger percentage decrease in risk than that reported in a meta-analysis of achieving $\geq$ 150 minutes of MVPA a week and 14% lower risk of nonfatal and fatal CHD events for primary prevention.[25] This indicates that individuals with CHD might receive greater benefits from MVPA than the general population without CHD. Similar patterns have been seen for risk of all-cause mortality: Jeong et al. concluded that the slope of the association between MVPA with all-cause and cardiovascular mortality was steeper for individuals with CVD than for individuals without CVD. The risk of all-cause mortality was 14% lower among individuals with CVD achieving the public health guidelines ($\geq$ 150 min/wk) compared with 7% among individuals without CVD.[14] Why this is the case is not yet known. However, individuals with CVD tend to have worse cardiovascular risk factor profiles (ie, diabetes, higher blood pressure, lipid levels, and waist circumference) compared with individuals without CVD,[26] and these risk factors can be improved by greater levels of MVPA.[4] Our study found lower MVPA thresholds for total cardiac events (including fatal events) and MACE compared with the models for nonfatal cardiac events. This is in line with previous studies among individuals with CHD

Table 1. Baseline characteristics of the study cohort and cardiovascular events during follow-up

Characteristic	Total (n = 40,156)	Women (n = 15,278)	Men (n = 24,878)
Age, y	70.25 ± 10.25	70.0 ± 10.8*	70.4 ± 9.9
Tertiary education	8682 (21.6)	2781 (18.2)*	5901 (23.7)
Type 2 diabetes	6535 (16.3)	2187 (14.3)*	4348 (17.5)
BMI, kg/m^2	27.24 (4.71)	27.20 (5.47)	27.26 (4.18)
Family history of heart disease	25,070 (62.4)	10,269 (67.2)*	14,801 (59.5)
Current smoker	1784 (4.4)	665 (4.4)	1119 (4.5)
MVPA, min/wk,	390 (140-840)	380 (120-840)*	390 (150-840)
Sedentary behaviour total, h/d	5 (3-7)	4 (3-6)*	5 (3-7)
Follow-up time, d	3043 (1354-5022)	3098 (1383-5022)	3009 (1339-5021)
Nonfatal cardiac events	3260 (8)	959 (6)*	2301 (9.2)
Total cardiac events	5161 (13)	1502 (10)*	3659 (15)
Major adverse cardiovascular events	14,383 (36)	5506 (33)*	9317 (38)

Values are mean ± SD, n (%) or median (interquartile range).
BMI, body mass index; MVPA, moderate-to-vigorous intensity physical activity.
* $P < 0.05$ compared with men.

showing a lower risk of cardiovascular mortality compared with studies including nonfatal cardiac events with similar thresholds of MVPA.[5,6] The present study focuses on the first split associated with a lower risk of cardiovascular events. Interestingly, Jeong et al. found a curvilinear association between the volume of leisure physical activity and the risk of a cardiovascular event.[14] Emphasising the need for future studies to explore upper potential thresholds of time in MVPA associated with an increased risk of cardiovascular events.

Remarkably, the newly identified sex-specific MVPA thresholds were lower for women than for men for all cardiovascular events. To our knowledge, sex differences in associations between MVPA and cardiovascular events among individuals with CHD have not previously been explored. However, in the adult general population, women seem to gain more health benefits from MVPA in smaller amounts compared with men in primary prevention of CHD,[25] cardiovascular,[15] and all-cause mortality.[15] Ji et al. found that among 412,314 US adults, men reached their maximal survival effect for all-cause mortality (19% lower risk) at 300 min/wk, and women had similar benefit at 140 min/wk.[15] The reason women benefit to a greater extent in our study and in primary prevention is not fully known. The greater benefits for women with CHD may motivate women to do MVPA.

Currently, there are no time-based sedentary behaviour guidelines for the adult population or individuals with CHD

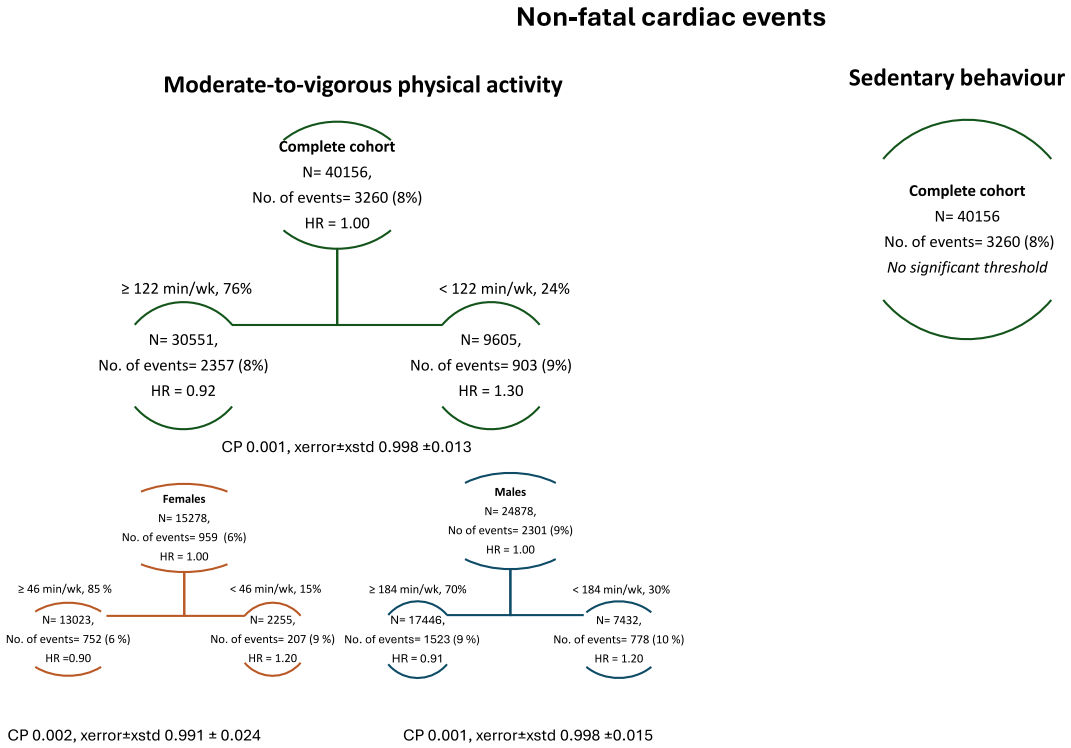

Figure 1. Survival trees with threshold (first split) for time in moderate-to-vigorous physical activity and sedentary behaviour with nonfatal cardiac events among individuals (complete study cohort, women, and men) with cardiac disease. The hazard ratio (HR) is compared with the parent node. CP, complexity parameter.

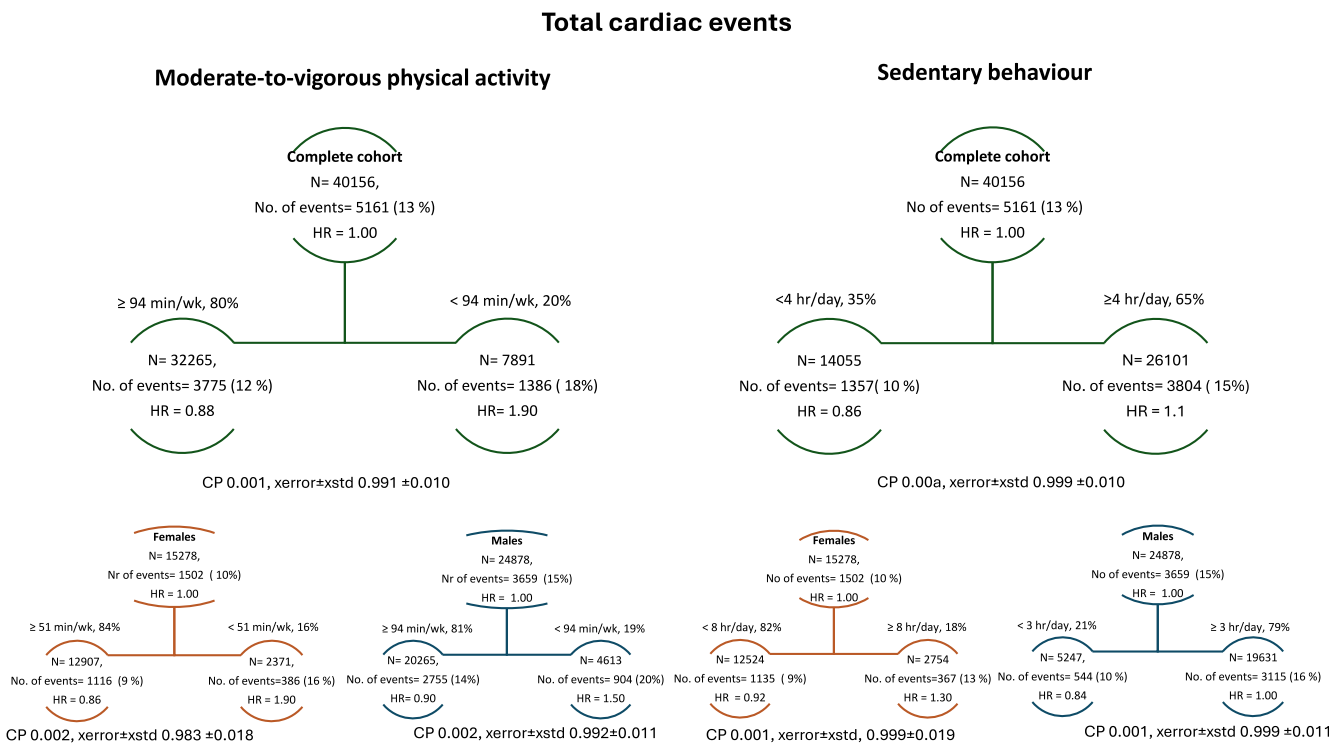

Figure 2. Survival trees with threshold (first split) for time in moderate-to-vigorous physical activity and sedentary behaviour with total cardiac events among individuals (complete study cohort, women, and men) with cardiac disease. The hazard ratio (HR) is compared with the parent node. CP, complexity parameter.

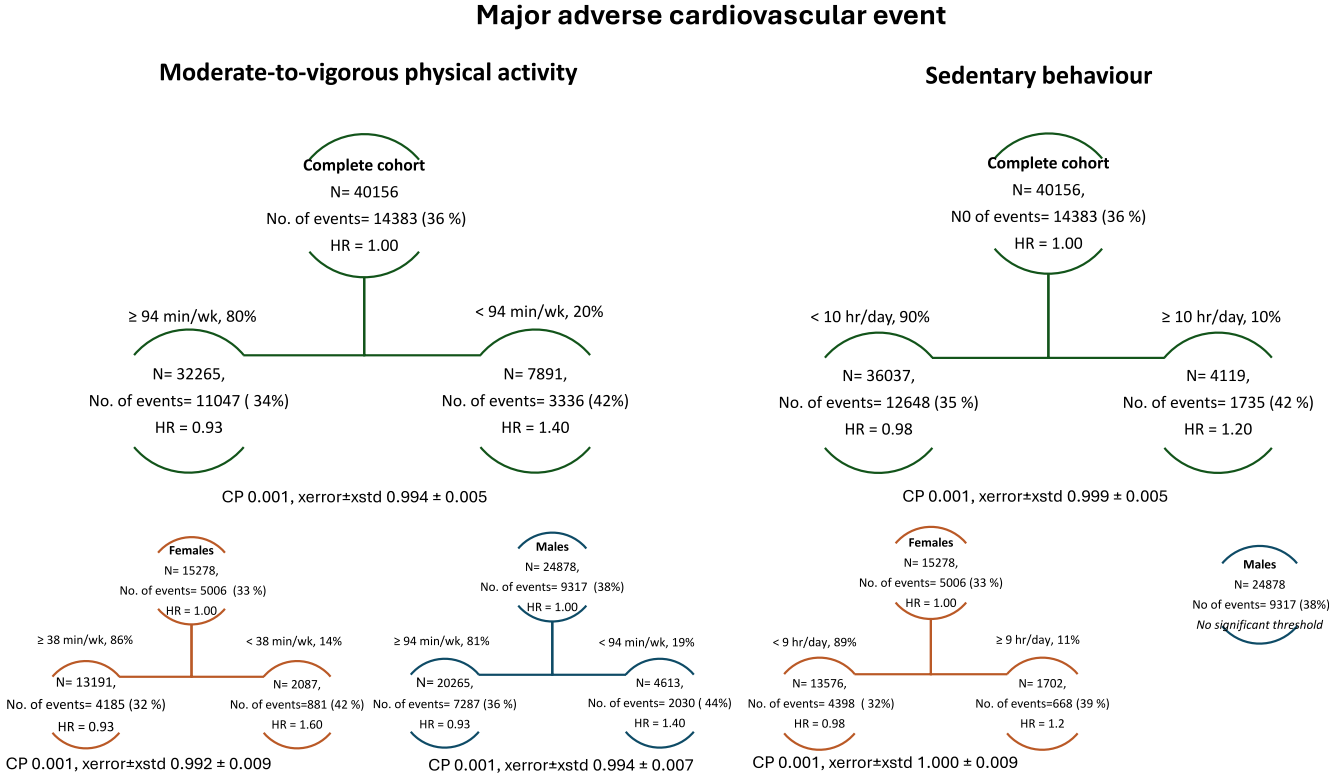

Figure 3. Survival trees with threshold (first split) for time in moderate-to-vigorous physical activity and sedentary behaviour with major adverse events among individuals (complete study cohort, women, and men) with cardiac disease. The hazard ratio (HR) is compared with the parent node. CP, complexity parameter.

Table 2. Number of events and hazard ratios (HRs) for nonfatal cardiac events, total cardiac events, and major adverse cardiovascular events (MACE) by moderate-to-vigorous physical activity and sedentary behaviour thresholds among individuals (n = 40,156) with cardiac disease

	n	No. of events	Unadjusted model, HR (95% CI)	Adjusted model, HR (95% CI)*	AUC[d]	Sensitivity†	Specificity†
Moderate-to-vigorous physical activity‡							
Nonfatal cardiac events							
< 122 min/wk	9605	903	1.000 (ref)	1.000 (ref)			
≥ 122 min/wk	30551	2357	0.712 (0.660-0.769)	0.823 (0.760-0.890)	0.518	0.436	0.401
Total cardiac events							
< 94 min/wk	7891	1386	1.000 ref	1.000 ref			
≥ 94 min/wk	32265	3775	0.562 (0.528-0.598)	0.712 (0.668-0.759)	0.541	0.269	0.186
MACE							
< 94 min/wk	7891	3336	1.000 ref	1.000 ref			
≥94 min/wk	32265	11047	0.68 (0.654-0.706)	0.772 (0.742-0.803)	0.528	0.574	0.505
Sedentary behaviour§							
Nonfatal cardiac events			NA	NA	NA	NA	NA
Total cardiac events							
< 4 h/d	14055	1357	1.000 ref	1.000 ref			
≥ 4 h/d	26101	3804	0.840 (0.795-0.887)	0.858 (0.781-0.908)	0.534	0.574	0.505
MACE							
< 10 h/d	4119	1735	1.000 ref	1.000 ref			
≥ 10 h/d	36037	12648	0.828 (0.787-0.870)	0.822 (0.781-0.865)	0.514	0.120	0.092

AUC, area under the receiver operating characteristic curve; CI, confidence interval.
*Adjusting for sex, age, BMI, smoking, education, family history of heart disease, and type 2 diabetes.
†Based on unadjusted model.
‡Further adjusting for moderate-to-vigorous physical activity.
§Further adjusting for sedentary time.

to decrease the risk of cardiovascular events. Two meta-analyses in the general population found a lower risk of all-cause mortality at < 4 and < 7 h/d.[11,27] Our results found thresholds for lower risk of total cardiac event and MACE at 4 and 10 h/d, respectively. Although women may be able to spend more time in sedentary behaviour than men before they are at a higher risk of total cardiac events, studies in the general population have concluded that a higher level of MVPA modifies the risk of a high level of sedentary behaviour for CVD morbidity.[28] In the present study, the risk for total cardiac events and MACE were lower among individuals with sedentary behaviour below the thresholds, independently from the level of MVPA. However, the difference in risk among individuals with sedentary behaviour above and below the thresholds was greater among individuals with a low level of MVPA. Indicating that a higher level of MVPA to some extent modifies the risk of sedentary behaviour.

We did not identify thresholds for sedentary behaviour for nonfatal cardiac events in the complete cohort or for MACE among men. Thus, thresholds for the time in sedentary behaviour need to be further explored.

Strengths and limitations

Strengths of this prospective cohort study include the use of a large sample, with 40,156 individuals with CHD, thus enabling sex-specific stratified analyses and adjustment for numerous potential confounders. Another strength is the linkage to public health registries to identify cardiovascular events and dates of events. For inclusion in the study cohort, individuals needed complete data on covariates and exposure and outcome variables, increasing internal validity. However, there were differences in baseline characteristics between included and excluded individuals, with excluded individuals being older, women, current smokers, those reporting diabetes, and those with lower levels of MVPA to a greater extent. This contributes to a potentially lower external validity for this population with a risk of collider stratification bias, a common limitation in observation studies among older individuals with chronic disease.[29] This study used survival regression trees to identify thresholds linking time in MVPA and sedentary behaviour to the risk of cardiovascular events. The use of survival trees is a strength in that they can handle censored data, making them suitable for analyses where not all events have appeared by the end of the study period.[30]

A limitation is that the study cohort is based on individuals self-reporting heart disease, with a risk of misinterpretation and misclassification and no information on date of the first CHD event or self-reported medication. However, previous studies have shown that a self-reported history of CVD is a valid measure of diagnosed disease.[31,32] Barr et al. validated self-reported CVD compared with Australian hospital morbidity data, finding that self-reported cardiovascular events were highly accurate, with only 0.2% of cases being unreported despite hospital records.[31] Another limitation is that MVPA and sedentary behaviour were self-reported, with an increased risk of recall and social desirability bias.[33] However, a study has shown that the Active Australia Survey is valid for assessing time in MVPA compared with accelerometers.[19] In addition, the public health guidelines are based on self-reported time in MVPA,[10] making it possible to make equal comparisons. The Cox regression models were adjusted for several confounders affecting MVPA, sedentary behaviour, and CVD, but not all, eg, diet, which also may be of importance for CVD. Blood pressure and cholesterol levels were considered to be mediators in the pathway between MVPA or sedentary behaviour and CVD and therefore not adjusted for in the Cox regression models.

Table 3. Number of events and hazard ratios (HRs) for nonfatal cardiac events, total cardiac events, and major adverse cardiovascular events (MACE) by moderate-to-vigorous physical activity and sedentary behaviour thresholds among men and women with cardiac disease

	n	No. of events	Unadjusted model, HR (95% CI)	Adjusted model, HR (95% CI)*	AUC[d]	Senstitivity†	Specificity†
Men							
Moderate-to-vigorous physical activity‡							
Nonfatal cardiac events							
< 184 min/wk	7432	778	1.00	1.00	0.522	0.338	0.294
≥ 184 min/wk	17446	1523	0.742 (0.680-0.809)	0.824 (0.754-0.900)			
Total cardiac events							
< 94 min/wk	4613	904	1.00	1.00	0.536	0.247	0.175
≥ 94 min/wk	20265	2755	0.581 (0.539-0.627)	0.715 (0.662-0.772)			
MACE							
< 94 min/wk	4613	2030	1.00	1.00			
≥ 94 min/wk	20265	7287	0.682 (0.649-0.716)	0.761 (0.724-0.800)	0.526	0.218	0.166
Sedentary time[c]							
Nonfatal cardiac events	na			na			
Total cardiac events							
≥ 3 h/d	19631	3115	1.00	1.00	0.529	0.755	0.696
< 3 h/d	5247	544	0.870 (0.807-0.938)	0.867 (0.804-0.936)			
MACE	NA			NA			
Women							
Moderate-to-vigorous physical activity[b]							
Nonfatal cardiac events							
< 46 min/wk	2255	207	1.00	1.00	0.536	0.216	0.143
≥ 46 min/wk	13023	752	0.519 (0.323-0.434)	0.715 (0.528-0.721)			
Total cardiac events							
< 51 min/wk	2371	386	1.00	1.00	0.556	0.257	0.144
≥ 51 min/wk	12907	1116	0.439 (0.391-0.493)	0.674 (0.597-0.761)			
MACE§							
< 38 min/wk	2087	881	1.00	1.00	0.528	0.174	0.118
38 min/wk	13191	4185	0.599 (0.557-0.644)	0.737 (0.683-0.794)			
Sedentary time§							
Nonfatal cardiac events			NA	NA			
Total cardiac events							
≥ 8 h/d	2754	367	1.00	1.00	0.524	0.524	0.114
< 8 h/d	12524	1135	0.665 (0.580-0.763)	0.745 (0.648-0.857)			
MACE							
≥ 9 h/d	1702	668	1.00	1.00	0.515	0.132	0.101
< 9 h/d	13576	4398	0.665 (0.580-0.763)	0.811 (0.748-0.880)			

AUC, area under the receiver operating characteristic curve; CI, confidence interval.

*Adjusting for sex, age, BMI, smoking, education, family history of heart disease, and type 2 diabetes.

†Based on unadjusted model.

‡Further adjusting for moderate-to-vigorous physical activity.

§Further adjusting for sedentary time.

The accuracy of the newly developed thresholds to predict cardiovascular events was low, but similar to the public health thresholds; this could be due in part to the low prevalence of cardiovascular events and the presence of important risk factors such as age and sex.[34,35] However, the lower risk among individuals achieving the developed thresholds remained in adjusted Cox regression models compared with individuals who did not reach the thresholds.

Conclusion

Individuals with CHD seem to have a significantly lower risk of cardiovascular events at 94-120 minutes of MVPA per week. This indicates that great health benefits occur before reaching the public health physical activity guidelines, although exceeding the identified lower thresholds might lead to further health benefits. For sedentary behaviour, the threshold varied from 4 to 10 h/d for total cardiac events and MACE. Importantly, women seem to gain proportionally more from MVPA than men in lowering risk of cardiovascular events. In addition, for the risk of total cardiac events, women were less vulnerable to time in sedentary behaviour, with higher thresholds than men.

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Data Availability

The data sets used and analysed during this study are not available from the authors, because they are third party data not owned or collected by the authors. The data are available from the data custodians for approved research projects. Data access enquiries can be made to the Sax Institute (https://

www.saxinstitute.org.au/solutions/45-and-up-study/use-the-45-and-up-study/apply-for-access/).

Ethics Statement

The NSW Population and Health Services Research Ethics Committee approved this study (2022/ETH00559), and the study was carried out in accordance with the Declaration of Helsinki.

Patient Consent

The authors confirm that patient consent forms have been obtained for this article.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2024.11.025.