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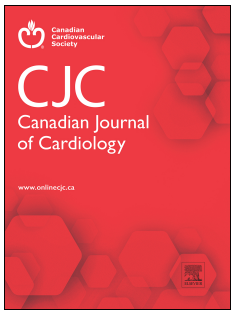

Are the cardiovascular benefits and potential risks of physical activity and exercise dependent on race, ethnicity or sex?

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Are the cardiovascular benefits and potential risks of physical activity and exercise dependent on race, ethnicity or sex?

Short Title: Impact of race, ethnicity, and sex on the cardiovascular effects of exercise

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ABSTRACT

Physical activity (PA) is established as a cornerstone of cardiovascular health, however, disparities in participation exist across sociocultural groups, which in turn impacts cardiovascular outcomes. Evidence suggests that while the positive cardiovascular effects of exercise are consistent across populations, notable differences in the magnitude of these benefits exist for racial and ethnic minorities and female sex. Females derive greater protection from PA compared to males, with reduced rates of sudden cardiac death (SCD). This review examines the complex interplay of race/ethnicity and sex on the cardiovascular benefits associated with PA and exercise, cardiovascular adaptations to exercise, and risks of SCD and "excessive" volume of exercise. Understanding these factors is crucial for developing targeted interventions to promote cardiovascular health and offset disparities.

Key words: race, ethnicity, sex, female, exercise, MACE, cardiovascular adaptation, sudden cardiac death

INTRODUCTION

The impact of physical activity (PA) on cardiovascular health is well established, with known cardioprotective effects, including risk modulation by improving blood pressure (BP) control, lipid profile, and insulin sensitivity.[1–3] This is reinforced by the fact that inactivity poses a threat to well-being, particularly in individuals with chronic, long-term health conditions.[4] Distinguishing PA from exercise is required to understand the impact of various modalities on the cardiovascular system. Physical activity is defined as energy expenditure resulting from bodily movements produced by skeletal muscles, broadly incorporating activities relating to functional activities of daily living, household chores, one's occupation, recreational and competitive sport, and other incidental activities.[5] Comparatively, exercise refers to planned, structured and repetitive activity, precisely prescribed using the FITT principles (frequency, intensity, time, type) with the goal of maintaining or enhancing specific components of an individual's physical fitness or sporting performance.[5] Exercise is generally classified based on the predominant energy system and metabolic pathway involved, namely aerobic (endurance) or anaerobic, or based on muscle contraction type in the case of resistance training (static/isometric or dynamic/isotonic).[6]

Exercise provides irrefutable benefits to an individual's health and well-being via established physiological effects and adaptations, in proportion to the volume, intensity, and modality which is undertaken. Exercise specifically plays a key role in the primary and secondary prevention of cardiovascular disease (CVD), including tailored prescription for treatment of specific conditions, in addition to reducing the burden of cardiovascular risk factors (RF) and associated metabolic conditions, as outlined in international guidelines.[2,6–9] Despite the extensive benefits, exercise is not without risk, such as sudden cardiac death (SCD) in individuals with and without established cardiac conditions, as well as in the context of excessive volume and intensity in the long-term.[6,10,11] Understanding factors which influence both the benefits and risks of exercise is imperative, particularly in the era of precision medicine.

The social determinants of health (SDOH) as defined by the World Health Organization (WHO), encompass nonmedical elements pertaining to economic, social, environmental, and psychological factors that impact an individual's state of

wellness or disease.[12–18] This incorporates any social situation or circumstance within which people are born, grow up, live (including exercise participation), learn, work, play, worship, and age.[12–18] Such social constructs are not only of importance on a sociocultural level, but are also highly individualised and dynamic, thus limiting generalisability. Understanding the impact of social processes via established frameworks, such as stigmatisation, discrimination, and marginalization, is important in identifying vulnerable populations with specific needs who are prone to facing the extremes of disparities resulting from complex relationships between SDOH and specific outcomes of interest.[17,18] Race, ethnicity, and sex are amongst the SDOH which are more commonly encountered in the literature, including their impact on cardiovascular health.[12–18] They too are linked to associated SDOH, such as income and education, which must also be considered. This article will focus on addressing the question of whether race, ethnicity, and sex influence both the positive and negative cardiovascular effects of PA and exercise.

THE SOCIOCULTURAL INFLUENCE OF SOCIAL DETERMINANTS OF HEALTH ON EXERCISE

Distinguishing Race, Ethnicity and Sex in Biomedicine

In biomedical research a social constructivist approach can be taken to describe race/ethnicity, traditionally referring to ancestry and physical characteristics, compared to modern conceptualisation integrating self-identification and social affiliation which are borne of sociopolitical processes.[12,19,20] One important limitation identified in the literature is the absence of providing a definition of each term and inconsistent application across numerous studies, reflecting the dynamic nature of the terms and fluidity of the boundary separating them.[20,21] Research in the PA and exercise realm has used the terms race/ethnicity interchangeably, utilising ethnicity to refer to specific racial groups, or combining the terms to encompass both racial groups and relevant ethnic groups as a collective SDOH.[22–24]

Race describes a group of people typified by shared physical traits based on geographic origin. This has been well demonstrated across numerous studies, which utilise the key racial categories, such as those outlined by the Canadian Cardiovascular Society definition of ethnic groups, which include Aboriginal/Indigenous, black, East-Southeast Asian, South Asian, Hispanic, Middle

Eastern, white, and mixed.[25] Ethnicity is a broader construct which is group-defined from a social perspective, incorporating cultural tradition, history, values, religion, and shared genetic heritage.[20,21] Contrary to these definitions, a recent review implored that race itself be recognized as a sociopolitical construct which represents an important SDOH which must be recognized to overcome potential harm to implicated individuals, and shift towards race-conscious practice.[26] The authors share the same sentiment highlighted; therefore, this review will focus on distinguishing race from ethnicity using the aforementioned definitions, other than where studies have used the terms interchangeably or whereby specific cultural aspects pertaining to ethnicity influence the discourse. An important limitation is that not all racial and ethnic groups are equally represented in most studies, nor have all groups been studied in detail. The increasing racial, and thus ethnic, diversity for a given population reinforces the importance of understanding specific needs of respective groups and the insight population-based studies continue to provide. Accurate description of racial and ethnic groups is also important, which in part is limited by historical terminology utilized in previous studies. Nonetheless, terms applied in specific articles have been reported on in the same manner to best understand the population examined.

Sex is distinct from gender, defined on the basis of one's biologic make up as determined by chromosomal and phenotypic traits, compared to an individual's social and behavioural expression of their sex.[12,16] Similarly to race/ethnicity, sex and gender are often used interchangeably in some aspects of biomedical research, which is often incorrectly conceptualised as a binary factor (i.e. female or male) rather than incorporating the spectrum of gender identities and expressions that exist.[27] Although contemporary gender differences pose unique challenges from a social perspective, for example the gender role of primary caregiver predominantly taken up by women and associated stressors, this review will focus on the biological differences between females and males. Gender is referred to for this same distinction solely for common concepts that have been previously defined as such in the literature. Since the majority of work in this sphere has been undertaken in males, a greater emphasis has been placed on distinguishing unique differences in females.

Disparities related to Participation in Exercise and Physical Activity

Disparities in exposure to PA and exercise across sociocultural groups, each with different contributing factors, is likely to negatively affect cardiovascular outcomes. On a population level, participation in exercise as per national PA guidelines has been documented to be as low as approximately 24% in Australia[28] and the United States (U.S.)[29–32], compared to almost 50% in Canada[33] and the 63% in the United Kingdom (U.K.).[34] A consistent trend amongst all the populations evaluated, is that females were found to have lower rates of participation compared to males, with an all-inclusive group named “other gender” noted to have the lowest overall participation in the U.K.[34] Of the reports focussing on differences based on race/ethnicity, individuals from ethnic minorities were found to be less active than their white counterparts; noting again that females from ethnic minorities were less active than males.[30,34]

Disparities Associated with Exercise and the Primary Prevention of Cardiovascular Disease

Participation in PA and exercise is greatly influenced by factors linked to broader SDOH of interest, which in turn impact cardiovascular outcomes (Figure 1). These incorporate aspects of one’s lived experience, including everyday discrimination in the form of racism and sexism, neighbourhood, environment perception, health literacy, social needs, stigma, and implicit bias.[13,16–18,35,36]

Racial and Ethnic Factors

Despite their increased cardiovascular risk and higher body mass index (BMI), indicating a greater need to prioritise PA, racial/ethnic minorities are less likely to engage in healthy lifestyle behaviours.[37] Ali et al.[1] outlined the epidemic of physical inactivity in this cohort is influenced by cultural, socio-ecological, and sociocultural drivers. The review identified important barriers, including cultural expectations, areas of deprivation being unsuitable environments for PA, and poor engagement with health professionals.[1] Morris et al.[37] identified education, BMI and weight perception to be important factors associated with engaging in PA across white, black and Hispanic participants, whereas the impact of income was variable. Additional barriers identified include reduced availability of appropriate commercial facilities in low-income neighbourhoods, perception of safety, financial hardship,

income, perception of social class, immigration status, lack of time, lack of familiarity, unease in taking the first step, language, racism, and sex.[22,37–39]

Sex-Specific Factors

Cardiovascular outcomes in females are influenced by unique SDOH, including race/ethnicity, racism and discrimination, rurality, postal code, education, social support, communication barriers, cultural norms, and sexual orientation.[40,41] Cardiovascular RF unique to females also need to be considered, such as pregnancy-related factors including gestational hypertension, gestational diabetes, and preeclampsia.[40] The concept of a “gender gap”, referring specifically to reduced levels of engagement with PA based on female sex, is well established.[29] This has been shown to occur across the life span, with male participation exceeding that of females from the early years throughout adulthood.[23,29,42,43] Recent epidemiological data presented reinforces this issue persists. Additional distinct barriers to account for this include race, income, safe exercise locations, increased stress and reduced time associated with working multiple jobs and childcare responsibilities in individuals with low incomes.[22,40]

CARDIOVASCULAR BENEFITS OF EXERCISE

The positive effects of exercise on cardiovascular health and outcomes are dose-dependent, with higher volumes proffering greater benefits.[6,11,44,45] International guidelines outline the minimum requirements to achieve cardiovascular health benefits, including both primary and secondary prevention.[2,6–9,32] Recommendations include aerobic exercise of moderate intensity for 150 minutes/week, or vigorous intensity for 75 minutes/week.[2,6–9,32] METs (metabolic equivalent of task), a measurement of energy expenditure based on oxygen consumption, is used to grade exercise intensity. For example, slow walking is a mild intensity activity equivalent to <3 METs, compared to running at >9 kilometers/hour which is a vigorous activity equivalent to $\geq$6 METs.[6,32] The addition of at least two days of resistance training propagates these benefits due to skeletal muscle adaptations leading to metabolic benefits, which improve one’s cardiovascular risk profile.[6,7,29,32]

These guidelines summarize a generalised approach, which do not reflect specific needs based on race/ethnicity, or sex; thus, limiting our understanding of how these

SDOH impact benefits on cardiovascular health. A significant proportion of the literature evaluating effects of exercise on the cardiovascular system, specifically focusing on cardiovascular outcomes including mortality and major adverse cardiovascular events (MACE), incorporate PA levels in their findings. This in turn enables a range of activity levels to be distinguished from sedentary status. As such, this article will include the impact of PA on cardiovascular outcomes. Much of the research focussed on cardiovascular adaptations to exercise is based on cross-sectional comparisons, as demonstrated by a recent meta-analysis.[46] Data on longitudinal outcomes would enable further insight in further insights, thus, the studies presented need to be interpreted in the context of this limitation.

Cardiovascular Outcomes

Influence of Race/Ethnicity on All-Cause Mortality and Cardiovascular Outcomes

Cardiovascular disease and risk profiles vary according to race/ethnicity within a given population. Although not all groups are represented in each study, important disparities have been identified. A Canadian study evaluating 371,154 individuals from three cross-sectional cycles, which adjusted for sociodemographic characteristics, demonstrated individuals from the most apparent minorities had lower levels of PA engagement and would also benefit from prioritising detection and control of diabetes mellitus and hypertension.[47]

The MESA study (Multi-Ethnic Study of Atherosclerosis) recruited 6,814 black, white, Hispanic, and Chinese adults in the U.S. and followed them for approximately 15 years.[48] All-cause mortality was 34% higher for black participants and 21% lower for Chinese participants compared to white participants, whilst there was no difference for Hispanic participants.[48] After adjusting for socioeconomic status, the excess mortality risk for black compared with white participants reduced to 16%.
After further adjusting for additional RF and immigration history, Hispanic participants had a lower mortality risk than white participants, and black and Chinese participants had similar risk to white participants. Cardiovascular mortality shared similar trends, however, adjusting for sex and age resulted in even greater risk (72%) for black compared to white participants.[48]

Physical activity remains a key behavioural strategy for reducing cardiovascular risk in diverse and underserved racial and ethnic groups, despite disparities in participation.[49] Mathieu et al.[50] looked at the impact of PA participation and health perceptions on cardiovascular mortality in 3,018 African American, Hispanic, and white adults recruited as part of the Dallas Heart Study. African American and Hispanic participants were less likely to be active, despite accounting for income, education, sex, BMI and other cardiovascular RF; however, beliefs surrounding the benefits of PA was not a contributing factor.[50] The authors proposed other factors established in the literature may be accountable, including the safety and quality of surrounding facilities, perceptions towards gender roles and exercise, and different peer support requirements.[50]

Disparities relating to race have also been demonstrated by rates of initiation, adherence and completion of cardiac rehabilitation (CR). These disparities are also likely to influence disparities in cardiovascular mortality. Despite findings from a recent review indicating both sexes elicit a similar physiological response to CR,[51] women have been shown to face greater barriers to participation in a cohort comprising of 16 countries from all six WHO regions, despite similarities between sexes.[52] A study involving 822 patients, composed of 52% non-white minority individuals, consecutively referred to CR, showed that non-white individuals were 78% less likely to initiate CR than white participants. Reductions in mortality were demonstrated for individuals who participated.[53]

Bell et al.[54] examined the effect of PA on CVD in 3,707 African Americans and 10,018 Caucasians, recruited as part of the ARIC study (Atherosclerosis Risk in Communities), who were followed up for 21 years. An inverse relationship was demonstrated for CVD, heart failure, and coronary artery disease (CAD) in both races, and with stroke in African Americans, following adjustment for confounders.[54] Hazard ratio patterns correlated to PA levels for race, indicating regular PA reduces the risk of CVD in both African Americans and Caucasians.[54]

Vásquez et al.[55] studied the association between varying levels of PA and all-cause and cardiovascular mortality across different races/ethnicities in older adults. The study analysed 2,520 females and 2,398 males recruited as part of the National

Health and Nutrition Examination Survey III aged 60 years or older, categorising individuals as inactive (no PA), active (3-6 METs ≥5 times/week or <6 METs ≥3 times/week), or insufficiently active (not meeting either criterion). Overall, any level of PA was associated with a lower all-cause mortality across all racial/ethnic groups. Inactive non-Hispanic blacks and Mexican Americans had a reduced risk of all-cause mortality versus non-Hispanic whites, whilst insufficiently active Mexican Americans were found to have lower all-cause mortality versus non-Hispanic whites.[55]

Influence of Sex on All-Cause Mortality and Cardiovascular Outcomes

Data on sex differences in cardiovascular RF and outcomes associated with exercise are limited. Sex is often a confounder which is accounted for as part of study design. Some studies have selectively evaluated findings in a particular sex amongst a mixed cohort or have only recruited a single sex. This makes it difficult to draw generalised conclusions applicable at a population level. Physical activity has been previously shown to have similar favourable effects on traditional cardiovascular RF, with no substantiative differences identified between females and males.[45] Sex-specific differences pertaining to PA and cardiovascular outcomes have been explored independently in most instances, with a focus placed on all-cause and cardiovascular mortality, dose-response, and minimum PA required to achieve these benefits.

One study of males which utilised two medical examinations, comprising of a maximal exercise test and health evaluation with a mean interval of 4.9 years, demonstrated men who maintained or improved their fitness between assessments had reduced all-cause and cardiovascular mortality versus unfit participants.[56] Mortality risk decreased by 7.9%/minute increase in exercise time between initial and repeat evaluations.[56] Exercise capacity achieved during a maximal exercise test was also shown to be a more significant predictor of mortality in men compared to other established cardiovascular RF.[57] Survival increased by 12% for every 1-MET increase in exercise capacity.[57]

Kokkinoss et al.[58] studied the association between cardiorespiratory fitness and mortality in a cohort of 750,302 U.S. veterans aged 30-95 years, basing their analysis on sex, age and race. Males and females were shown to have the lowest

risk in individuals achieving 14.0 METs during a standardised exercise treadmill test, with no further benefit demonstrated at the extremes of fitness.[58] Comparatively, individuals with the lowest fitness levels were shown to have a fourfold greater risk of mortality compared to extremely fit individuals, however, a 50% reduction in risk could be achieved by the majority of individuals with moderate fitness relative to their age category.[58]

Similarly, PA has been shown to act as an independent predictor of all-cause mortality using the Framingham Risk Score-adjusted mortality risk measurement in asymptomatic females, leading to a 17% reduction in mortality for every 1-MET increase in exercise capacity.[59] Gulati et al.[60], showed predicted exercise capacity, as determined using the Bruce protocol treadmill exercise stress test, should be readjusted with lowered values for asymptomatic and symptomatic females compared to males with reference to both all-cause and cardiovascular mortality. This study used exercise stress test data to determine a sex-specific nomogram in females across different age groups, demonstrating predicted exercise capacity of 85% or greater, as determined by the “predicted MET” formula, halved the risk of death.[60]

Dose-response was explored by a prospective study involving 97,230 women aged 27-44 years at its inception, who were followed up over 20 years.[61] Of the parameters evaluated, including frequency, type, and volume, total volume of exercise equating to $\geq$30 MET-hours/week had a significantly reduced risk of CAD compared to those who were the least active, completing less than 1 MET-hour/week.[61]

Similarities between sexes has been shown in a Taiwanese cohort aiming to establish the minimum amount of exercise required to reduce all-cause mortality, evaluating results from a self-administered questionnaire for individuals at risk of developing CVD.[62] It was demonstrated that a 14% risk reduction could be achieved with either 15 minutes/day or 90 minutes/week of moderate-intensity exercise in both females and males.[62] Sattelmair et al.[63] performed a meta-analysis, comprising 33 studies, investigating the dose-response relationship between PA and the risk of CAD. Individuals who participated in 150 minutes/week of moderate-intensity PA

achieved a 14% risk reduction compared to sedentary individuals, which increased to 20% for those who completing 300 minutes/week at the same intensity.[63] A significant sex interaction was identified, whereby this risk was two-fold lower in females.[63]

Ji et al.[29] recently conducted a prospective study of 412,413 adults in the U.S., of whom 55% were female with a mean age of 44 years, involving survey data on leisure-time PA. Sex-specific multivariable-adjusted associations were undertaken for measurements of PA with both cardiovascular and all-cause mortality reported between 1997-2019).[29] Race/ethnicity were classified in the cohort characteristics, with no significant difference identified between females and males based on this specific SDOH.[29] There were 11,670 cardiovascular deaths amongst the 39,935 deaths observed during follow-up. Regular PA compared with inactivity resulted in a 24% versus 15% lower all-cause mortality in females compared to males, respectively.[29]

Maximal survival benefit was reached at 300 minutes/week of moderate-to-vigorous exercise in males, whereas females not only achieved a similar benefit at less than half this volume (i.e. 140 minutes/week) but these positive effects continued up to a maximum survival benefit achieved at 300 minutes/week. Similar sex-specific findings were observed for cardiovascular death, which was consistent across all measurements of aerobic activity and strength training. An age-interaction was identified, with benefits being more pronounced for middle-aged females between 40-59 years, compared to older females whereby benefits were mitigated.[29] These provocative results indicate that females stand to benefit more than males for a given exercise prescription, across multiple measures of PA.[29] The authors have suggested that overcoming the “gender gap” may be achieved by shifting a focus on the engagement of females with exercise, opposed to matching exercise volume with males.[29]

The protection PA provides in relation to MACE has been shown to be reasonably well-balanced between the sexes, with some sex-specific findings identified. Fransson et al.[64] studied the effect of aerobic exercise and PA and acute myocardial infarction, demonstrating a greater degree of protection in females with reduced

relative risk shown for the most versus least PA and frequency of three times/week versus seldom.[64] Manson et al.[65] prospectively investigated the role of walking versus vigorous exercise in 73,743 postmenopausal women aged 50-79 years as part of the Women's Health Initiative study. Significant reductions in coronary events and a composite of total cardiovascular events were identified with increasing levels of PA, independent of intensity, which was similar according to race, age, and BMI.[65]

The inverse relationship between PA and stroke risk is similar for females and males. A Norwegian cohort of 34,868 females and 32,872 males were followed for 16 years, documenting cause-specific mortality relative to PA.[66] The *p* trend for total activity and stroke mortality was <0.001 for females and 0.009 for males, with a significant relative risk reduction in both sexes for high levels of PA versus inactive (i.e. "never active") status, namely an RR of 1.45 (95% CI 1.14-1.83) for inactive females (vs. 1.00 reference for highly active females) and an RR of 1.35 (95% CI 1.05-1.74) for inactive males (vs. 1.00 reference for highly active females). A Japanese study which recruited 42,242 females and 31,023 males, who were followed up over a mean of 9.7 years, showed walking and sports participation were inversely related to cardiovascular mortality, all stroke, and ischemic stroke mortality.[67]

A U.S. cohort partaking in the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study did not demonstrate a significant relationship between PA and total or ischemic stroke in both sexes in the younger age group of 45-64 years compared to the 65-74 years group, however, the study did show a strong association between PA and stroke for white women.[68] Sex-specific findings were also demonstrated in the Nurses' Health Study, which analysed PA levels using METs in hours/week in 72,488 female nurses aged 40-65 years.[69] During 8 years of follow-up, increasing PA levels lead to a strong inverse association with the risk of total stroke, with a considerable reduction in in total stroke and ischemic stroke seen even with lower levels of PA, such as moderate-intensity brisk walking, in a dose-dependent manner.

Cardiovascular Adaptation

Race/Ethnicity and Cardiovascular Adaptations to Exercise

Regular exercise can result in significant electrical and structural cardiovascular changes, as identified on the 12-lead electrocardiogram (ECG) and various imaging modalities. While many studies on cardiac remodelling in athletes focus on adult, male, white athletes participating in common sports, evidence suggests sporting discipline, age, sex, race/ethnicity are important determinants of cardiovascular adaptations to exercise.[23,24,70] Growing interest and subsequent experience through preparticipation screening of an increasingly diverse population of athletes over the last three decades has significantly enhanced our understanding in this area. Table 1 summarizes electrical and structural adaptations observed across the racial/ethnic cohorts evaluated in the literature. Figure 2 shows examples of anterior T wave inversion (TWI) on the 12-lead ECG, as influenced by race/ethnicity, sex, one's chosen sport, and age. African and Afro-Caribbean (black) athletes represent the most distinct paradigm of cardiovascular adaptation, as they frequently demonstrate repolarisation anomalies and left ventricular hypertrophy (LVH) compared to white athletes, making the differentiation between athlete's heart and cardiac conditions implicated in exercise-related sudden cardiac death (SCD) more challenging.[23,24,70,71] These distinct adaptations observed in this population are labelled "black athlete's heart" in the Sports Cardiology literature, thus, have been referred to as such in this section of the review. The discourse in recent work by Krishnan et al.[26] is an important one striving for equity and offsetting structural racism within the subspecialty, which has the protentional to drive a change in nomenclature of this phenotypic variation observed in "athlete's heart".

Electrical Remodelling in Black Athletes

Repolarisation changes are more common in black versus white athletes.[23,24,70,71] Papadakis et al.[72] reported on a cohort of 2,842 individuals who underwent cardiac screening, comprised of 904 black athletes, 1819 white athletes and 119 black controls. Ethnicity was determined through self-reported questionnaires. The authors identified TWI in 22.8% of black athletes compared to 3.7% in white athletes and 10.1% of black controls. A significant proportion of TWIs in athletes (55%) were isolated to contiguous anterior leads (V1-V4) and were associated with J point elevation and convex ST segment elevation. This pattern was not associated with disease on short-term follow-up. In contrast, lateral TWI (I, aVL, V5, V6) which was present in 4.1% of black and 0.3% of white athletes, was associated with a diagnosis

of hypertrophic cardiomyopathy (HCM) in a small number of athletes (n=3) during subsequent follow-up, and was also the predominant TWI pattern in a cohort of 52 black patients with HCM. Although the authors reported that the pattern of TWI in V1-V4 with associated J point elevation and convex ST segment elevation represented an ethnic variant of athlete's heart, "black athlete's heart", subsequent studies revealed that the same pattern can be present in athletes of other ethnicities and highly prevalent in endurance and adolescent athletes. [24,73–77] A study by Riding et al.[78] further highlighted the challenges of using skin colour to attribute a particular characteristic, as they demonstrated significant variation in the prevalence of TWI in black athletes of different geographical origins ranging from 0-8.5%.

Other ECG changes identified include an increased prevalence of early repolarisation in the inferior leads, which can be associated with an increased risk of SCD, RV hypertrophy, and atrial enlargement.[24,72,79,80] Although these ECG changes have been observed to have a greater prevalence in this cohort, the literature indicates these findings are not exclusive to black athletes. Thus, in time the focus of interpretation may shift towards understanding the broader spectrum of ECG findings specific to athletic adaptation relevant to individuals rather than considering them to be purely specific to racial/ethnic groups.

Structural Remodelling in Black Athletes

Left ventricular (LV) and right ventricular (RV) cavity volumes are similar with those of white athletes.[23,24,81,82] Increased LV wall thickness (LVWT) is the most prominent adaptation in black athletes, with 12.4% of male black athletes found to have an LVWT measuring between 13-16 mm versus 1.6% of white athletes.[81–83] Basavarajaiah et al.[81] evaluated echocardiogram data from 300 national black male athletes to delineate LV remodelling from HCM, with findings compared to 150 black and white sedentary individuals and 300 highly trained white athletes. Black athletes had greater LVWT versus white athletes (11.3±1.6 mm vs. 10±1.5 mm; $p<0.001$), of whom 18% of black athletes had LVWT >12 mm versus 4% of white athletes, and 3% of black athletes had an LVWT $\geq$15 mm.[81] Consequently, black athletes exhibit higher relative wall thickness and more frequent rates of concentric remodelling compared with white athletes.[84] This further highlights the challenges a physician

may face when assessing athletes of black ethnicity and the potential to falsely attribute disease or conversely offer false reassurance.

Rawlins et al.[83] studied 240 nationally ranked black adolescent female athletes, who were shown to have greater LVWT compared to white female athletes (9.2±1.2 mm vs. 8.6±1.2 mm, p<0.001). Amongst these individuals, 3% of black athletes were found to have an LVWT >11 mm (up to 13 mm) compared with none of the white athletes.[83] Sheikh et al.[76] demonstrated similar adaptations in a group of adolescent black athletes, consisting of 245 males and 84 females, of whom 7% were identified to have an LVWT between 13-15 mm compared to 0.6% of white athletes. Di Paolo et al.[77] evaluated 154 soccer players participating in the 2009 under 17 African Championship, comparing them to 62 Italian players, finding LVWT was 5% greater in the African versus Caucasian cohorts; of whom 4 Africans had an LVWT exceeding 13 mm.

LV trabeculations are more prevalent in black athletes compared to white athletes (28.8% vs. 16.3%, p=0.002) and controls, posing a diagnostic challenge in relation to distinguishing this adaptation from a cardiomyopathy phenotype.[85]

Sex and Cardiovascular Adaptations to Exercise

Female athletes typically exhibit less pronounced adaptations compared to males, however, the quantitative changes compared to sedentary females are proportionate to similar comparisons made between athletic and sedentary males.[71] These sex-specific differences (Figure 3) have been described to occur from early adolescence, with remodelling beyond pediatric reference values for both sexes seen more frequently for males from the mid-adolescent years.[86]

Despite similarities in cardiac physiological adaptation in both sexes, females have less lean body mass, a different hormonal profile, a lower sympathetic adrenergic response to exercise, peak systolic BP, stroke volume and peak oxygen consumption; and are anthropometrically smaller.[87,88] Underrepresentation of female participants in research has limited our understanding of why these sex differences in adaptations and outcomes exist, in addition to whether the differences seen later

in life result from biological mechanisms or reduced access to sports across the lifespan in females.[89,90]

Electrical Remodelling in Female Athletes

ECG abnormalities have consistently been identified at a higher prevalence in males.[71,73,87,89–97] Despite this, unique observations pertaining to ECG findings in females have been made. These include: lower resting heart rate, longer PR interval, higher voltage R and T waves, shorter QRS intervals, lower QRS voltages which are less likely to meet LVH and RV hypertrophy criteria, reduced early repolarisation, more frequent prevalence of incomplete RBBB, anterior TWI, and greater QTc prolongation.[71,73,87,89–97] Considerations explaining some of these findings include differences in cardiac mass, chest size, breast tissue, electrical conductance with respect to anterior TWI, and hormonal factors resulting in QT prolongation.[71,73,87,89–97] Sporting discipline was not shown to impact ECG changes in females in a recent review.[98]

Structural Remodelling in Female Athletes

Left ventricular end-diastolic volume (LVEDD >54 mm and LVWT are greater in female athletes versus controls, with LVWT consistently shown to not exceed 11 mm, and reduced structural remodelling compared to males.[71,83,87,90,98–100] When indexed to body surface area, a dilated LV cavity (LVEDD $\geq$31 mm/m^2) is more prevalent in female athletes.[82,98,107] Female athletes tend to adapt with eccentric hypertrophy more frequently than males in the setting of dynamic sport, therefore concentric remodelling should raise suspicion of cardiac pathology rather than physiology.[99]

Changes to cavity dimension in females has been shown to involve both ventricles, understanding the RV is more sensitive to volume loading.[87,98] Although overall RV dimensions are larger in males, similarly to the LV, indexed volumes are generally higher in female athletes.[87,101,102]

CARDIOVASCULAR RISKS OF EXERCISE

Sudden Cardiac Death

From an epidemiological perspective, SCD in young athletic populations is dependent upon multiple factors, including age, sex, race/ethnicity, and sporting

discipline.[6,10,11,103–105] SCD has recently been highlighted as an important racial disparity in Sports Cardiology.[26,106] National Collegiate Athletic Association (NCCA) data from the U.S. has provided important insights, demonstrating a strong link between race/ethnicity and SCD. Black athletes have consistently been shown to experience a threefold higher incidence of SCD, with reduced rates of survival post cardiac arrest despite a similar incidence of inherited cardiac conditions, versus white athletes.[6,10,11,26,103–105,107–112]

Petek et al.[105] recently conducted a retrospective analysis of 143 SCD cases amongst 1,102 total deaths in NCAA athletes between 2002-2022, identifying a higher incidence of SCD in black (1:26,704 athlete-years) compared to white (1:74,581 athlete-years) athletes. Peterson et al.[107] undertook a prospective analysis from 2014-2018 via the National Center for Catastrophic Sports Injury Research, utilising data from High School Associations and the NCAA, which specifically showed African American male Division I NCCA basketballers had the highest incidence of death (1:2,087 athlete-years). Harmon et al.[108] reviewed deaths identified from an NCAA database between 2003-2013, similarly identifying black athletes (1:21,491 athlete-years) were at higher risk of SCD than white athletes (1:68,354 athlete-years). These more recent studies follow the same trend identified in earlier work showing a disproportionately higher risk of SCD in black athletes, quoted to be fivefold greater, inclusive of specified causes in some instances, including HCM and congenital coronary anomalies.[109–111]

Finocchiaro et al.[103] investigated the aetiology of SCD in a U.K. cohort of 7,880 cases referred to their national cardiac pathology centre for detailed autopsy by cardiac experts between 1994-2022, of whom 848 (11%) were athletes, with clinical data provided by the referring coroner. A total of 758 athletes were white (89%), 51 were black (6%) and 39 were Asian (5%), with death occurring during exercise in 737 (87%) cases.[111] Cause of death in descending order of prevalence was sudden arrhythmic death syndrome (SADS) in 385 (45%) cases, myocardial diseases CAD in 58 (7%) cases, and coronary artery anomalies in 29 (3%) cases.[103] Arrhythmogenic cardiomyopathy (ACM) was a more prevalent cause of death in black (25%) versus white (14%) (p=0.03) and Asian athletes (8%) (p=0.04).

Moreover, the death was attributed to CAD more commonly in Asian (15%) versus white (7%) (p=0.03) and black athletes (2%) (p=0.02).

A sex-based disparity for SCD has consistently been demonstrated, whereby males exhibit a higher incidence.[10,88,105,107–111,113,114] Finocchiaro et al.[113] reported on data from a large U.K. registry which included 748 cases of SCD in individuals who participated in more than 3 hours of PA/week. Females constituted 13% (n=98) of all SCD cases, amongst whom 41 (42%) were competitive athletes and 57 (58%) were recreational athletes.[113] Overall, a greater proportion of deaths was identified in males, noting a significantly lower incidence of death during intense exertion in females (58% vs. 83%, p<0.001).[113] SADS accounted for 57% of all deaths in females compared to 43% in males, as determined by a structurally normal heart on autopsy.[113] Deaths due to myocardial disease, including HCM, myocarditis and idiopathic LVH, were less common in females.[113] These findings showed consistency over time when compared to an earlier study undertaken by the same group.[115]

Corrado et al.[114] undertook a prospective study over 21 years which identified 300 cases of SCD in 1,386,600 adolescents and young adults, amongst whom 112,790 were competitive athletes. The incidence of SCD amongst athletes was 2.6/100,000 person years in males compared to 1.1/100,000 person years in females.[114] Maron et al.[109] identified 11% of deaths occurred in females in their evaluation of 1,049 cases of SCD in young athletes, equating to a male-to-female SCD risk ratio of approximately 10:1. A greater proportion of SCD in males has been identified by studies, which quoted rates of 81%[108], 83%[105,107] and 90%[111]. With regard to aetiology, a female predominance has been demonstrated for mitral valve prolapse (MVP), in addition to the aforementioned relationship established for SADS.[92,115,116] Basso et al.[116] identified 43 cases amongst 650 young adults included in a cardiac pathology registry who had MVP listed as the cause of SCD, of whom 61% were female. The authors concluded that MVP is both an understated cause of SCD and the leading structural cardiovascular cause in females.[116]

Factors contributing to racial and sex-based differences in SCD are summarized in Figure 4. Postulated explanations behind these include differences in cardiac

adaptation to exercise, such as increased hypertrophy and associated myocardial fibrosis, which may act as substrate risk of life-threatening arrhythmias; hormonal differences, for instance the protective effects etsrogen which can also introduce the risk of arrhythmias via QT prolongation; differences in atherosclerotic CAD, genetic polymorphisms, and inflammatory response; and psychological factors, which can influence the intensity of training and engagement with competitive performance.[99,104,113,117] Social and environmental factors, including low socioeconomic status, income and education, have also been implicated on a population level.[118–121] Zhao et al.[121] highlighted the impact these factors may have, including unhealthy behaviours, poor healthy literacy, and limited access to healthcare.

The Paradox of Excessive Exercise

Athletes routinely exercise at volumes and intensities that far exceed recommendations for cardiovascular health, posing the risk of diminishing cardiovascular benefit and potential harm, as described by a reverse U-shaped relationship. Concerning physiological effects associated with sustained elevations in cardiac pressure and volume loading include LVH, elevated coronary artery calcium (CAC) scores, acute cardiac biomarker release, myocardial fibrosis, and cardiac arrhythmias. [6,11,89,122–124] This typically applies to master/veteran endurance athletes, aged 35 years and older.

Most studies evaluating CAC, myocardial fibrosis, and AF in this cohort have been limited to males.[125] Despite this, female sex may be protective given the reduced prevalence of elevated CAC, atherosclerosis, myocardial fibrosis, and arrhythmias; thought to be mediated via estrogenic mechanisms.[89,92,126–129] Merghani et al.[128] assessed 152 masters athletes, consisting of 70% males, who were shown to have a higher prevalence of atherosclerotic plaques of any luminal irregularity compared to their sedentary counterparts; with predominantly calcific versus mixed morphology.[128] Late gadolinium enhancement was identified on cardiac magnetic resonance imaging in 15 athletes, all of whom were male, with seven demonstrating a pattern indicative of previous myocardial infarction; three of whom possessed a luminal stenosis of 50% or greater in the corresponding coronary artery.[128] No

female athletes were observed to have clinically significant coronary artery stenoses.[128]

CAC scores in female athletes versus sedentary females are known to be similar, suggesting protective hormonal benefits independent of a lifetime of exercise.[92,105,128] Similarly, reduced rates of myocardial fibrosis may be explained by lower peak BP attained during exercise and lower levels of testosterone, which is known to be responsible for myocardial inflammation.[89,92,130] Although some studies have shown female athletes also appear to be protected from developing AF, recent evidence suggests their risk may actually be enhanced as observed in males.[129,131] Mohanty et al.[129] conducted an extensive literature review and meta-analysis which demonstrated reduced rates of AF, a benefit which appeared to be propagated by increasing exercise intensity; with women participating in moderate PA found to have an 8.6% reduced risk of AF versus 28% lower risk in women performing intense exercise.[129] Comparatively, men engaging in vigorous exercise were found to have a significantly increased AF risk.[129] Drca et al. [132]retrospectively evaluated a cohort of 228 high level Swedish female endurance athletes, comparing them to 1,368 controls. National registry data enabled identification of AF in ten athletes (4%) and 23 controls (<2%), with a hazard ratio of 2.56 (95% CI 1.22-5.37), indicating elite female endurance athletes in this study had an increased risk of AF compared to the general population.[132]

Dose-response and cardiovascular outcomes, with respect to harm associated with high volumes of exercise in a general rather than athletic population, was studied by German et al.,[133] who evaluated CAC score to determine cardiovascular risk and cardiovascular outcomes in 6,777 participants recruited as part of the MESA study. Individuals with low cardiovascular risk within the highest quartile of PA had a significant reduction in the hazard ratio for cardiovascular outcomes and all-cause mortality, whereas solely a reduction in all-cause mortality was seen in individuals with high cardiovascular risk within the highest quartile of PA.[132] High levels of PA specifically saw a reduction in all-cause mortality for high risk black and white participants, as well as low-risk and high-risk Hispanic participants, whilst there was no relationship identified for Chinese participants.[132] There was no increased risk

associated with cardiovascular outcomes or all-cause mortality in any racial or ethnic group engaging in the highest levels of PA, independent of CAC score.[132]

CONCLUSION

This review investigates the impact of SDOH, namely race, ethnicity, and sex, on the cardiovascular benefits and risks of PA and exercise. Despite consistent evidence supporting the positive effects of exercise on cardiovascular health, disparities in PA participation exist amongst racial/ethnic minorities and females, influencing cardiovascular outcomes which have been shown to correlate best with PA levels. Notably, females appear to derive greater cardiovascular benefits from exercise compared to males and have reduced rates of SCD. Black race/ethnicity and male sex is consistently linked with increased rates of SCD. While the relationship between race, ethnicity, sex and cardiovascular outcomes is complex and evolving, the need for further research to elucidate the interplay between SDOH and exercise is evident. Addressing these factors is crucial for promoting equitable PA participation and optimising cardiovascular health across diverse populations.

Ethics Statement

This material is the authors' own original work, which has not been previously published elsewhere. The discussion is appropriately placed in the context of prior and existing research. All sources used are properly disclosed and correctly cited. The author takes public responsibility for the content of this review.

Patient Consent

The author confirms that patient consent is not applicable to this article, as it is a review article that is conceptual and therefore does not rely on any original data analysis. No institutional review board approval was sought for the writing of this review.

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TABLES

Table 1. Electrical and structural cardiovascular adaptations in athletes based on race/ethnicity.

AV: atrioventricular, BSA: body surface area, LV: left ventricular, RBBB: right bundle branch block, RV: right ventricular, RVH: right ventricular hypertrophy, RVOT: right ventricular outflow tract, TWI: T wave inversion.

Race and/or Ethnicity	Electrical Remodelling	Structural Remodelling
Caucasian (white)	Sinus bradycardia First degree & Mobitz type 1 second degree AV block ↑ QRS voltage Incomplete RBBB Early repolarisation	↑ LV wall thickness ↑ LV cavity dimensions LV eccentric vs. concentric hypertrophy Atrial dilatation Aortic root dilatation
African/Afro-Caribbean (black)	TWI anterior leads V1-V4 TWI lateral leads Early repolarisation in inferior leads RVH Left atrial enlargement	↑ LV wall thickness ↑ RV & RVOT dimensions LV trabeculation
West Asian (Arabic & Middle Eastern)	↓ Prevalence ECG changes vs. Caucasians ST elevation with upward convexity & TWI in V1-V4	↑ in LV wall thickness ↑ LV cavity dimensions *(↓ BSA)*
East Asian & South Asian	ECG changes more common in Chinese vs. South Asians ↑ Prevalence of convex ST elevation & biphasic or inverted T waves in *(Japanese)*	↑ in LV wall thickness ↑ LV cavity dimensions *(Japanese)*
Mixed Race	↑ TWI ↑ Left axis deviation ↑ LV hypertrophy Atrial dilatation	↑ LV wall thickness
Pacific Islanders	↑ TWI	↑ LV mass ↑ Relative wall thickness

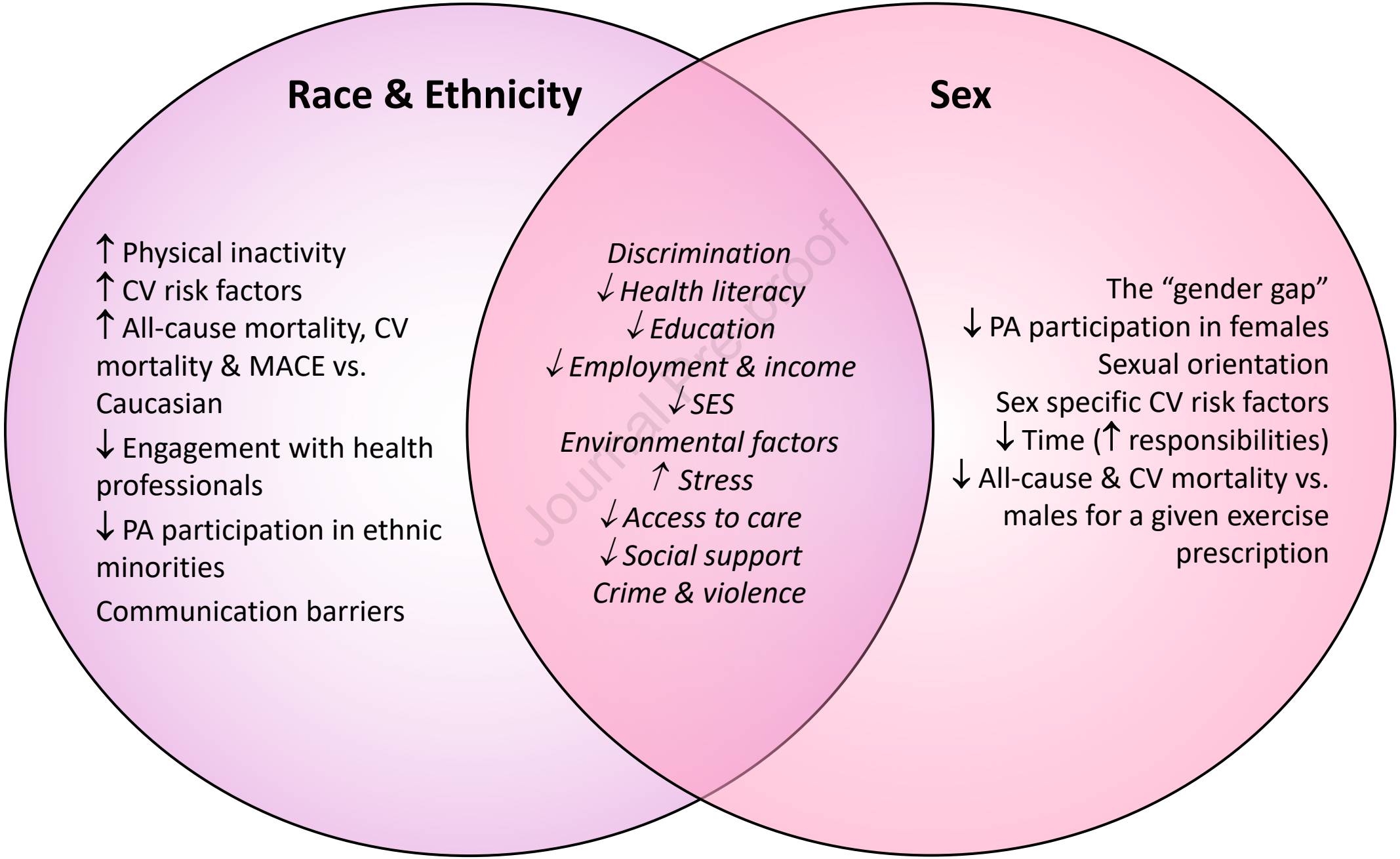
FIGURE LEGENDS

Figure 1. Sociocultural and physiological factors influencing participation and cardiovascular outcomes unique to race/ethnicity and sex; and those factors which are common to both social determinants of health (*italics*). Discrimination encompasses racism and sexism, bias (implicit and explicit), and victimisation. Environmental factors include housing instability, homelessness, postal code, and areas of deprivation limiting suitability and safety for participation in PA. CV risk factors specific to females include pregnancy related considerations (preeclampsia, gestational hypertension, gestational diabetes, preterm delivery, delivery of small for gestation age infant, recurrent spontaneous miscarriage), polycystic ovarian syndrome, early menarche, premature menopause, hormone-based contraception, autoimmune disorders, chronic inflammatory conditions, depression and other mental health comorbidities accompanying increased levels of stress.
CV: cardiovascular, MACE: major adverse cardiovascular events, PA: physical activity, SES: socioeconomic status.

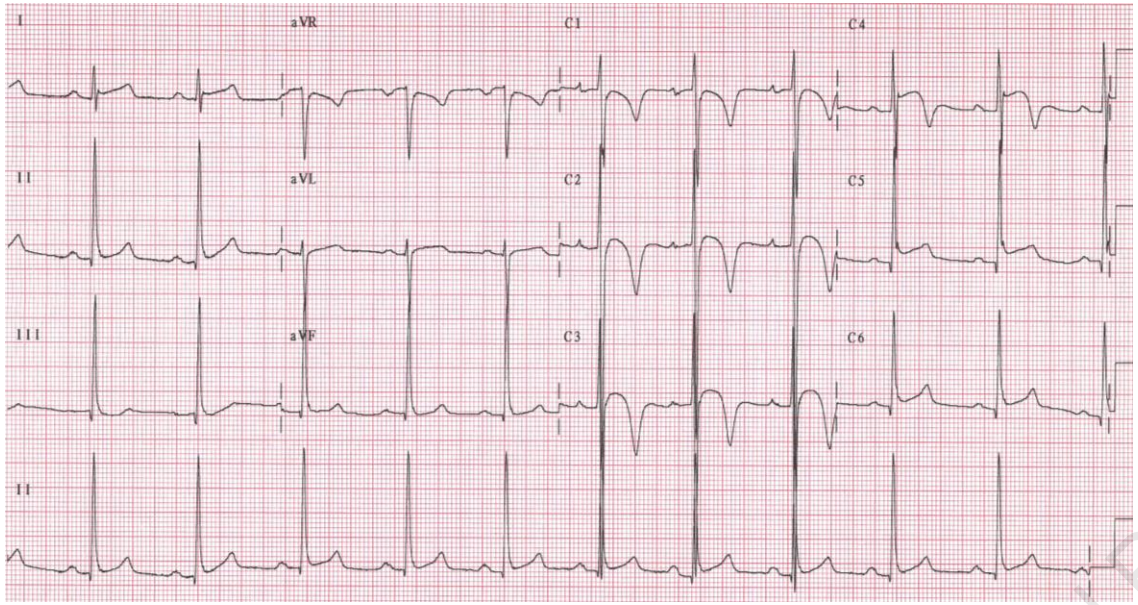
Figure 2. Examples of common causes of anterior T wave inversion encountered during preparticipation screening, including black (A), “juvenile” (B), endurance (C) and white female (D) athletes.

Figure 3. Sex specific exercise-based considerations for females compared to males.
AD: annular disjunction, AF: atrial fibrillation, CAC: coronary artery calcium, CAD: coronary artery disease, CV: cardiovascular, LV: left ventricular, LVH: left ventricular hypertrophy, MVP: mitral valve prolapse, RBBB: right bundle branch block, RVH: right ventricular hypertrophy, SADS: sudden arrhythmic death syndrome SCD: sudden cardiac death, TWI: T wave inversion.

Figure 4. Factors contributing to differences in exercise associated sudden cardiac death based on sex and race.
CAD: coronary artery disease, CV: cardiovascular, SCD: sudden cardiac death.



A



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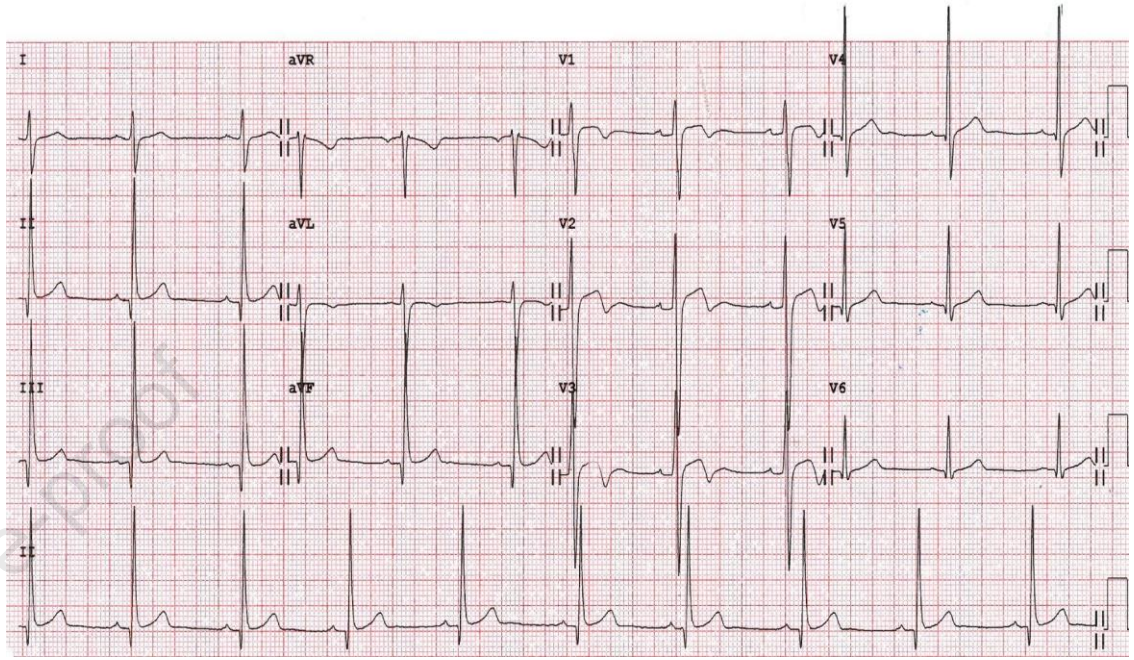

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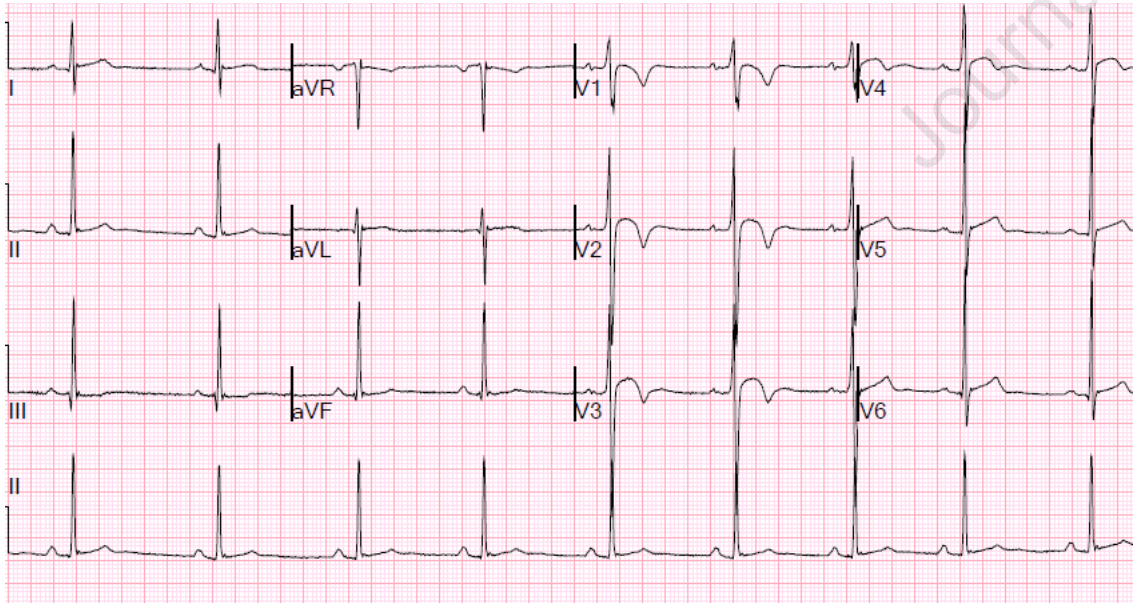

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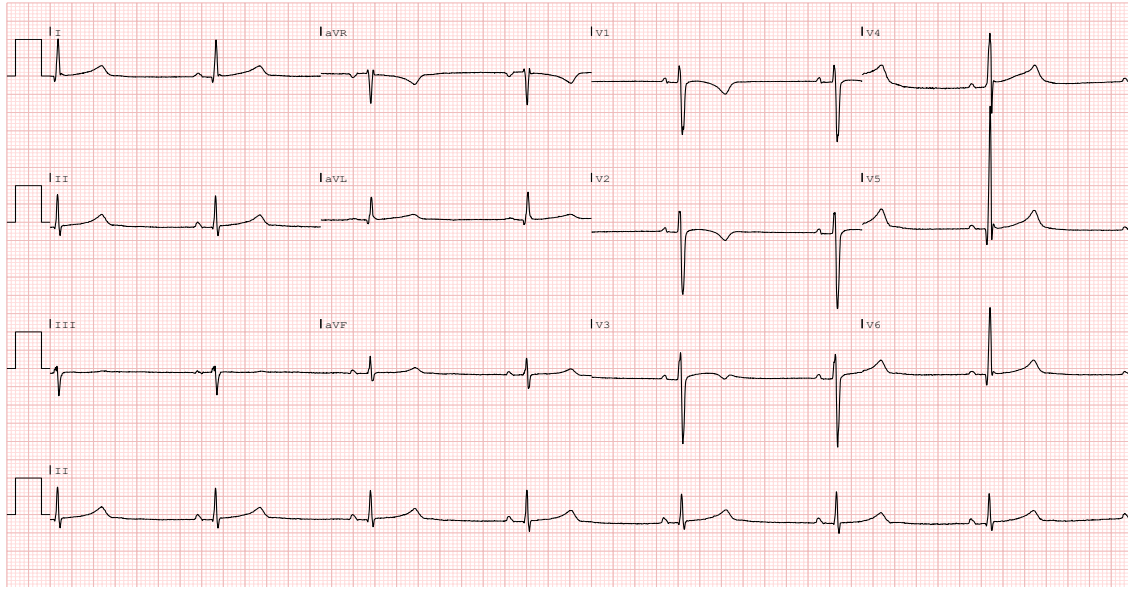

Electrical Remodeling

↓ Resting heart rate
↑ PR interval
↑ Voltage R & T waves
↓ QRS intervals
↓ QRS voltages (↓ LVH & RVH)
↓ Early repolarisation
↑ Incomplete RBBB
↑ Anterior TWI (V1-V3)
↑ QTc prolongation

Structural Remodeling

↓ Absolute ventricular dimensions
↑ Indexed ventricular volumes
↓ LV wall thickness
↑ Eccentric hypertrophy

Effect on CV Outcomes

↓ All-cause & CV mortality for a given exercise prescription

Findings with Long-term Exercise

↓ CAC scores
↓ CAD
↓ Myocardial fibrosis
↓ AF

Factors Associated with SCD

↓ SCD
↑ SADS
↑ MVP, AD & associated arrhythmias