Racial Differences in Cardiorespiratory Fitness between Blacks and Whites: A Meta-Analysis

By

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PURPOSE: Cardiorespiratory fitness (CRF) is a major risk factor for cardiovascular disease (CVD), all-cause mortality and CVD mortality. Some researchers have speculated that Blacks have lower levels of CRF when compared to Whites, which may contribute to the health disparities in CVD. However, this racial difference in CRF has not been previously evaluated quantitatively across published clinical trials. The purpose of the present study is to perform a meta-analysis to quantify the CRF differences between Black and White Adults. We hypothesized that the analysis would find that Blacks' CRF values would significantly lower than the Whites Adults. METHODS: A systematic literature search was performed for studies that compared CRF values between Black and White Adults. Articles were included if: (1) CRF was assessed by an exercise test (submaximal or maximal); (2) CRF was assessed in Blacks and Whites; (3) examined adults only; and (4) published in a peer review journal. Studies were excluded if: (1) the study population was children or adolescents (2) the sample size had less than 15 participants per group and, (3) health conditions were not cardiovascular in nature or type two diabetes (e.g. neurological). The meta-analysis was performed using the R Studio Software (Boston, MA). RESULTS: Twenty-three studies (77,776 subjects; 17,314 Blacks; 60,462 Whites) were eligible out of the 47 studies identified. The first analysis (N=23) comparing CRF levels between Blacks and Whites from epidemiological and clinical studies quantifying fitness in maximal METs from exercise testing had a difference of 0.93 between the means. The second analysis comparing CRF levels between Blacks and Whites from studies only utilizing maximal oxygen consumption had a difference of 3.27 between the means. DISCUSSION: The present meta-analysis supports previous literature indicating that Blacks have a lower CRF levels when compared to Whites in many published clinical trials. The following results supports that exercise interventions should be specifically designed for Blacks to help combat the racial differences found in CRF and future researchers should investigate the potential mechanisms that may be contributing to lower CRF in Blacks.

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List of Abbreviations

Cardiovascular Disease (CVD)

Centers for Disease Control (CDC)

Cardiorespiratory Fitness (CRF)

National Health and Nutrition Examination Survey (NHANES)

Cardiovascular (CV)

Aerobics Centers Longitudinal Study (ACLS)

Veterans Exercise Testing Study (VETS)

Health, Risk Factors, Exercise Training, and Genetics (HERITAGE)

Coronary Heart Disease (CHD)

Respiratory Exchange Ratio (RER)

Chapter I: Introduction

Cardiovascular disease (CVD) is the leading cause of death in the United States and represents an important health disparity [1]. According to the Centers for Disease Control (CDC) Health Disparities and Inequality report, the premature mortality rates among Blacks continues to be higher than their White counterparts [1]. As of 2009, the Blacks CVD mortality rates were seven times greater compares to Whites [1]. One of the four foundations of health that helps drives the entire *Healthy People of 2020* initiative is the reduction of health disparities. An objective of the *Healthy People of 2020* is to reduce the amount of premature CVD mortality rates thus attempting to address the health disparity affecting Blacks has important public health implications [1].

Recent evidence has emerged that Blacks have lower levels of cardiorespiratory fitness (CRF) compared to Whites [1, 2]. This is clinically important since low CRF is an independent risk factor for CVD, all-cause mortality, and CVD mortality [2, 3]. Moreover, CRF represents a major risk factor for CVD specifically in Blacks. This racial health disparity in CRF between Blacks and Whites has been observed across various populations including men and women with diabetes [4], premenopausal women [5], young and middle aged adults [6]. Additionally, these racial differences in CRF have been shown across different measurement techniques for evaluating CRF levels including the current gold standard of maximal oxygen consumption. Proposed etiologies for the lower CRF values observed in Blacks include lower physical activity levels [7], resting metabolic rate [8], hemoglobin levels, and muscle oxidative capacity [9] compared to Whites. Narrowing the CRF gap between Blacks and Whites is of great public health concern. Helping the Black community increase their CRF would decrease their risk for CVD, CVD risk factors and CVD mortality, thus improving their overall health and well-being. However, the existing literature that assesses CRF differences between Blacks and White Adults has limitations that make it difficult to generalize the literature as a whole. Due to the differences between the studies such as the measurement techniques, study populations, and disease states it is difficult to estimate the magnitude of the racial differences and how clinical relevant they are. At the present time, there has not been a meta-analysis conducted to provide an objective measure that summarizes the abundance of literature on this health disparity.

The purpose of this present study is to perform a meta-analysis to quantify the CRF differences between Blacks and Whites Adults. To our knowledge, there is an overwhelming amount of research establishing the racial differences in CRF. However, there has not been a meta-analysis done to estimate the magnitude of these differences. The published research that examines racial differences in CRF has several limitations that can be addressed with a meta-analysis. The meta-analysis could help evaluate if CRF will be different after the stratification of age and obesity status in the participants of the literature. The results of this meta-analysis could provide data to define the magnitude of CRF between Blacks and Whites. This could be beneficial to society as a whole by identifying the quantitative relationship between Blacks and low CRF values and to establish if the differences are within the range of clinical significance. We hypothesize that the meta-analysis will provide clinically significant differences in CRF with Blacks having lower fitness levels.

Delimitations

This meta-analysis is restricted to studies that include adults and will include most clinical conditions. It will also only examine data between Blacks and Whites and no other racial groups.

Limitations

The limitations of the meta-analysis are that it will not include studies that look at children or the elderly population.

Chapter II: Review of Literature

Risk of CVD in Blacks and Whites

Cardiovascular disease (CVD) is a major health concern as it represents the leading cause of death in the United States [10]. Currently, racial health disparities are present for CVD as Blacks have a higher prevalence compared to their White counterparts in both men (White: 36.6%, Black: 44.9%) and women (White: 32.4%, Black: 48.9%). Additionally, Blacks have a greater prevalence of several important CVD risk factors; such as hypertension, obesity, stroke and type 2 diabetes [2, 10]. The aforementioned health disparities in CVD prevalence and risk factors results in a higher CVD mortality rate in Blacks compared to Whites. According to data from the Centers for Disease Control in 2009, CVD mortality rates per 100,000 were seven times greater in Blacks than Whites for men and women. Black adults had higher mortality rates at all ages when age-specific death rates for CVD were compared to White adults [2]. The Black population is in a great need for prevention strategies to reduce the existing health disparities in CVD and CVD risk factors between Blacks and Whites.

CRF as a CVD Risk Factor in the General Population

CRF is an independent risk factor for all-cause and CVD mortality [11], and is a well-established risk factor in the general population. Thus, lower levels of CRF are associated with disproportional levels of health risks and as a result, are a strong predictor for premature morbidity [12].

Blair et al. [11] evaluated the relationship between CRF and all-cause mortality in Aerobics Center Longitudinal Study (ACLS). 13, 334 participants were assigned to CRF categories based on their sex, age, and the maximal time they spent completing a treadmill test.

This study defined low CRF as the first quintile, which also had the highest relative risk for mortality [11]. The lowest CRF quintile was associated with a 3.4 fold and 4.7 fold increases in all-cause mortality in men and women respectively after adjusting for age [11]. Blair et al. [3] in another study from the ACLS dataset investigated the influence of CRF and other factors on CVD and all-cause mortality in men and women. Low CRF was classified as the least fit 20% of participants in each group based on age and sex [3]. After adjusting for age, examination year, and other confounding factors, the men and women who were classified in the low CRF group had a 1.5 fold and 2.2 fold increases in all-cause mortality. Additionally, there was also 1.7 fold (men) and 2.4 fold (women) increased risk for CVD mortality risk [3]. Importantly, these observations were independent of other traditional CVD risk factors as smoking status, systolic blood pressure, cholesterol, family history, BMI, fasting glucose, chronic illness, and abnormal electrocardiographs [4].

Kokkinos et al [13] also examined the relationship between exercise capacity and all-cause mortality in a population of White and Black men (N=5314), (Blacks: n= 2090, Whites: n= 3224) from the Veterans Exercise Testing Study (VETS). Participants within the lowest 20th percentile of CRF (achieved 4 or less METs) had a 56% greater risk of morality compared to the participants who achieved more than 9 METs [13]. Additionally, it was observed that as CRF was increased the mortality risk ratios progressively decreased. In this cohort, the authors observed a 1 MET increase in CRF was associated with a 12% reduction in mortality in the fully adjusted model [13].

Kodama et al. [14] performed a meta-analysis composed of 33 studies evaluating on CRF and CV/all-cause mortality. Overall, the meta-analysis included 102,980 participants and 6,910 cases for all-cause mortality and 84,323 participants with 4,485 cases in CVD/CHD[14], and a mean follow-up of 1.1 to 26 years. The authors observed that a 1 MET increase in maximal aerobic capacity was associated with a 13% reduction all-cause mortality and a 15% decrease in CHD/CVD mortality risk [14]. This meta-analysis demonstrated that small increments or decrements in CRF can have a significant impact on all-cause and CVD mortality risk in individuals.

Relationship between CRF and mortality outcomes specifically in Blacks

Although, the relationship between CRF and CVD has been well established in the general population, few studies have evaluated this relationship specifically in the Black population. However, the existing evidence does suggest that CRF is also an important risk factor for CVD and mortality specifically in Blacks [3, 12] . Kokkinos et al [15] also noted that mortality risk was decreased with increased CRF in male veterans (Blacks = 6,749, Whites = 8,911). In this study the participants completed the Bruce Treadmill protocol. Low CRF was defined as achieving less than 5 METs [15]. Kokkinos et al [15] observed that the mortality in the Black participants was 11% higher than the White participants. Within this cohort, the exercise capacity of the participants was the strongest predictor of CVD [15]. Blacks who were in the low CRF category had a 74% greater risk for all-cause mortality compared to those in the high CRF category. [15]. Similarly, Whites who were in the low CRF category had a 66% greater risk for all-cause mortality compared to those in the high CRF category [15]

Racial health disparity has also been observed in participants with type 2 diabetes. Kokkinos et al. [4] observed exercise capacity and mortality risk in Black (n=1,703) and White (n=1,445) men with type 2 diabetes, who were recruited from the Veterans Affairs Medical Center. The Bruce protocol was used to perform exercise testing and based on the MET level achieved [4]. The lowest tertile for CRF was defined as achieving 5 or less METs, in which was the lowest 33% of the cohort [4]. Approximately, 42.2% of the individuals were in the low fit category and of that amount about 46.4% of those individuals were Blacks [4]. The adjusted hazard ratios (age, CVD, risk factors, CV medications, insulin and oral glycemic agents, resting diastolic blood pressure and METs) revealed that Blacks had a 23% higher risk for all-cause mortality when compared to their White counterparts [4]. For each 1 MET increase in CRF, Blacks lowered their mortality risk by 14% and Whites lowered their mortality risk by 19% [4].

Carenethon et al [16] examined women (Blacks: n= 1,035, Whites: n= 1,119) and men (Blacks: n=806; Whites: n= 1,026) who developed diabetes during the 20-year study who also experienced a larger decline in their CRF levels. CRF was assessed using the Balke treadmill protocol. Within this study, 823 Blacks women who were not obese at the baseline visit developed diabetes within the 20 years. These women not only developed diabetes, but their CRF decreased also [16]. The decrease in CRF was inversely associated with developing diabetes over the 20-year study, which increased their chances of developing CVD. The adjusted hazard ratios for developing the CVD risk factor was 50% higher in women and double in men per 19% decrement in treadmill duration from baseline to posttests [16]. However, this association between diabetes development and decreased CRF was not found in all of the participants. This was only found significant in the Black women. [16]. Although anyone can increase their mortality risk by having a low CRF, recent studies suggest that Blacks are more at risk for CVD mortality and low CRF values.

CRF and risk in Blacks

According to the American Heart Association 2013 statistic report, Black adults are more likely to be inactive than White adults, 41.1% compared to 27.7% [10]. CRF has also been observed to be lower in Blacks compared to Whites in a variety of studies [17-20], which has the potential to influence CVD risk between Blacks and Whites. Importantly, racial differences in CRF have been observed in studies utilizing estimates of CRF such as submaximal exercise tests, maximal metabolic equivalents from exercise tests, to the gold standard method of maximal oxygen consumption. For the present review, we have limited our discussion to studies, which have quantified CRF level using a submaximal testing or maximal METs/oxygen consumption from a maximal exercise test. This review also will focus only on studies that were conducted in adult study populations and will exclude children or adolescents.

Low CRF in Blacks

CRF levels between Blacks and Whites (submaximal estimation)

The National Health and Nutrition Examination Survey (NHANES) data does not measure CRF using maximal metabolic equivalents or maximal oxygen consumption. The NHANES data estimates CRF from submaximal testing [21]. Error rates are higher for submaximal testing because CRF is not being measured directly, but is derived from estimation. [21, 22]. Despite this limitation, the data sample is designed to representative of the US population, which is the only study to do this that looks at the CRF differences in Blacks and Whites [21].

Duncan et al [23] observed that approximately 33% of the Black women from the NHANES (examination years 1999-2002) were categorized as having a low CRF compared to only 13.5% of White women and 18.9% of Mexican-American women having a low CRF [23]. A lower estimated CRF was also observed in Blacks (33.1 mL $\cdot kg^{-1}$ $\cdot min^{-}$) compared to Whites (36.4 mL $\cdot kg^{-1}$ $\cdot min^{-1}$) [23]. When CRF was stratified by race and sex, Black women had lower CRF among all of the race groups, while there was no difference observed between the different racial groups for men within the study [23]. The authors concluded that Blacks had the lowest CRF compared to the major ethnic groups in the United States [23].

In the examination years, 1999-2004 of NHANES, Ceaser et al [21] observed that non-Hispanic blacks were twice as likely to have a low CRF when compared to their counterparts, non-Hispanic white adults [21]. Blacks still had a lower CRF after adjustments were made for education level, smoking status, physical activity volume, marital status, and sex [21].

In NHANES examination years 1999-2004, Wang et al [24] observed differences in CRF between Blacks and Whites at in all age groups (e.g. 20-29, 30-39 and 40-49 years) [24]. Wang et al [24] also examines these differences in CRF and its association with BMI. The average CRF for the Black and White men were 42.7 mL $\cdot kg^{-1}$ $\cdot min^{-1}$ and 42.7 mL $\cdot kg^{-1}$ $\cdot min^{-1}$ [24]. Among the men, the only age group to experience a lower CRF mean in Blacks was in the 30-39 age group [24]. The average CRF for the Black and White women were 32.9 mL $\cdot kg^{-1}$ $\cdot min^{-1}$ and 35.9 mL $\cdot kg^{-1}$ $\cdot min^{-1}$ [24]. Unlike the men, the women experienced a lower CRF mean in Blacks in all age groups except for the 20-29 group [24]. The racial disparity was more distinct among people who were overweight or obese compared to people with normal weight [24]. However, regardless of race or gender, individuals who were overweight or obese had a significantly lower CRF than individuals who were at a normal weight [24].

CRF levels between Blacks and Whites (maximal METs)

The following studies used METs, as the CRF measure. Although this is not considered the gold standard of quantifying CRF levels, it is still an acceptable measure for CRF opposed to estimating CRF from submaximal test because it is a maximal test [22]. Several epidemiological studies have used maximal METs as a CRF measure and generally these studies see a difference in METs with Blacks [5, 18, 20].

Howard et al [36], using data from the Cooper Center Longitudinal Study (Blacks: n = 589; Whites: n = 33,105), observed socioeconomic status in the participants as well as their CRF. CRF was quantified using a modified Balke treadmill protocol [36]. CRF levels were lower in Blacks when compared to Whites in both men (10.9 METs vs 11.7 METs) and women (8.8 METs vs 9.8 METs) [36]. After socioeconomic status was adjusted for, the racial CRF disparity was still present, with Blacks having a lower CRF level [36]. Quintile 1 represented low CRF and Blacks had a higher prevalence of being in this quintile [36]. There was 25.2% of the Black men in quintile 1 compared to only 11.5% of the White men [36]. Similarly, there was 18.2% of Black women in quintile while only 7.6% of the White women were in quintile 1 [36]. The fully adjusted relative risk of low CRF in Black men and women were 2.06 and 1.34. Although this study supports other literature that Blacks tend to have lower CRF values when compared to Whites, one limitation was that the cohort was mostly composed of White males and the Blacks participants, both for men and women, were under-represented.

LaMonte et al [26] examined CRF and c-reactive protein in middle-age obese women of the Cross-Cultural Activity Participation Survey (Black women: n= 44; White women: n= 46). The Black women were slightly older than the White women, 56.5 ± 10.1 vs. 54.3 ± 10.1 [26].

Low CRF was defined as being in the first tertile. This study also observed lower mean maximal MET levels in Blacks when compared to the White women (p-value < 0.05) There were 13 Black women within the first tertile compared to 16 White women in this tertile [26]. In addition, the Black women mean MET level was 7.2 compared to the 10.0 of the White women (p-value < 0.05) [26]. The Black women in the cohort highest level of CRF was generally lower than the lowest CRF levels of the White women [26].

Brown et al. [27] studied CRF in healthy adults who had a high risk for CVD (Blacks: n= 498; Whites: n= 556). The participants had a family history of premature coronary artery disease, which was defined as having coronary artery disease before the age of 60. This study also observed a significant lower mean CRF in the participants (Blacks: 6.3 METs; Whites: 7.3 METs) [27]. Additionally, in a multiple linear regression model that included age, sex, ethnicity, BMI, physical activity, smoking and other independent factors, it was observed that Black race was a significant predictor of CRF (p-value < 0.0001) [27]. A limitation of this study is that the Blacks were slightly older than the Whites, which was compensated for with age being adjusted in the analysis.

<u>CRF levels in Blacks and Whites (maximal oxygen consumption)</u>

The following studies used maximal oxygen consumption to assess CRF, which is considered the gold standard technique for assessing CRF [22]. This procedure allows for oxygen (O_2) and carbon dioxide (CO_2) consumption and production to be continuously monitored throughout the test through indirect calorimetry [22]. Specific criteria have been developed to distinguish an acceptable test. This includes the respiratory quotient being greater than or equal to 1.1, oxygen consumption levels out with an increase in exercise intensity and/or if the maximum heart rate reaches within 10 beats/min of the age predicted heart rate [22].

Zeno et al [6] observed CRF in healthy Blacks (n= 91) and Whites (n=51). Tertiles were formed based on CRF, sex and age, which included fair/low, average and good/high [6]. About 57.1% of the Blacks were classified as low/fair CRF compared to the 31.4% of the Whites who were classified in the same group [6]. CRF was lower in both Black and White men (42.0 mL $\cdot kg^{-1} \cdot min^{-1}$ vs. 46.5 mL $\cdot kg^{-1} \cdot min^{-1}$) and women (32.2 mL $\cdot kg^{-1} \cdot min^{-1}$ vs 38.0 mL $\cdot kg^{-1} \cdot min^{-1}$) [6]. Limitations of this study are that participants had to meet inclusion criteria, which might limit the results to be generalized and also the sample [6]. The participants within this study were healthy young adults and middle- aged adults. Some of the inclusion criteria required the participants to not on any hypertension or high glucose medications, free of other known major diseases (CVD), and fasting blood glucose less than 126 mg/dL [24]. The results of this study can only be generalized for healthy individuals up to about 45 years old.

Arena et al. [17] examined aerobic CRF in healthy Black (n= 33) and White (n= 33) participants. There were 215 White participants within the study, which made the Black participants disproportionally represented. A sub-analysis was performed that matched the participants' age and sex with 33 participants from each race group. A modified Balke treadmill test was conducted to assess CRF in the participants [17]. A lower CRF mean was observed in Blacks with age and sex matched. Blacks had a mean CRF of 27.9 mL $\cdot kg^{-1} \cdot min^{-1}$ compared to the Whites mean CRF of 38.3 mL $\cdot kg^{-1} \cdot min^{-1}$ [17].

Skinner et al. [28] in the Health, Risk Factors, Exercise Training and Genetics (HERITAGE) study also researched this CRF disparity in healthy participants. The HERITAGE study evaluated the participants' CRF before and after a 20 week exercise training intervention [28]. The HERITAGE study was unique with their methods as the study evaluated CRF level twice at baseline to ensure accuracy. The CRF was lower in the Black men and women than in White men and women [29]. The initial CRF of the Black men and women were 33.3 mL $\cdot kg^{-1}$ $\cdot min^{-1}$ and 24.7 mL $\cdot kg^{-1}$ $\cdot min^{-1}$ [28]. While the initial CRF of the White men and women were 37.3 mL $\cdot kg^{-1}$ $\cdot min^{-1}$ and 29.8 mL $\cdot kg^{-1}$ $\cdot min^{-1}$ [28]. Blacks continuously produce lower CRF levels when compared to Whites.

Conversely, Carpenter et al. [30] did not report significant differences between Blacks and Whites. This study examined older men and women who were older than 55 years old. To our knowledge, this is the only study that has not found significant racial differences. The Black (n= 37) and White (n= 52) women had the same CRF value (1.4 L/min) [30]. The Black men (n= 28) had a lower CRF than the White men (n= 47) but it was not significant, p value <0.001, (1.9 L/min vs. 2.1 L/min) [30]. Possible limitations of this study could be that there were more White participants than Black participants. Also, the White men were slightly older than the rest of the participants aging about 70 years to 64 years [30].

Potential Causes of CRF

Although there is are great deal of studies that have observed Blacks experiencing lower CRF values and greater risk for CVD mortality than Whites, there is not a clear reason to be causing this health disparity. Some potential causes for the lower CRF values include low physical activity levels, low hemoglobin levels, low muscle oxidative capacity, and low resting metabolic rates.

The lower levels of physical activity Blacks have been shown to possess could potentially cause the lower CRF levels. There has been a strong association between CVD and physical activity levels [7]. According to the American Heart Association, 22.9% of Blacks engage in regular physical activity compared to the 33.9% of Whites who engage in physical activity [10]. Irwin et al [31] examined age-adjusted physical activity and CRF in Black, Native American, and White women with metabolic syndrome, who were enrolled in the Cross-Cultural Activity Participation Study. The Black women were found to engage in less moderate and vigorous physical activity than the White women (79 and 2 minutes/day vs. 110 and 6 minutes/day) [31]. In addition to the Black women having lower levels of physical activity, the CRF of the Black women was 25% lower than the White women (7.3 METs vs. 9.7 METs) [31]. Low levels of physical activity could be a potential contributor to the low CRF levels in Blacks because this may lead to a lower oxidative capacity of the muscle tissue. Individuals who are aerobically trained are characterized by the expansion in mitochondrial oxidation capacity [32]. [32].

Potential physiological causes for a lower CRF in Blacks include hemoglobin levels and muscle oxidative capacity. Hunter et al. [9] observed these factors and CRF in Black (n=43) and White (n=46) women. CRF was quantified using the modified Bruce protocol, magnetic resonance imaging (MIRs) of the calf muscle were analyzed over several days, and blood samples were obtained to analyze hemoglobin levels. Black women had lower CRF (1.84 L/min vs. 2.16 L/min) both in the unadjusted and adjusted models for body weight, fat free mass or leg lean tissue [9]. Muscle oxidative capacity was quantified using the ADP time constant, in which low values are associated with high aerobic capacity [9]. The White women had lower values (21.3 s) than the Black (24.3 s) women, (p-value = .02) resulting in the Black women having lower muscle oxidative capacity in their calf muscles [9]. Similarly, the Black women had lower hemoglobin levels (11.8 $g \cdot dL^{-1}$) than the White women (12.9 $g \cdot dL^{-1}$) [9]. Within this cohort the Black consistently had lower functioning values. It was concluded after correlations were performed that race, hemoglobin levels, muscle oxidative capacity were all significantly related to CRF values, whether it was adjusted or unadjusted [9]. These factors could potentially be contributing to Blacks having low CRF values.

One other potential physiological cause is the resting metabolic rate of Blacks. Shook et al. [8] observed the relationship between low CRF and the resting metabolic rate of Black (n=38) and White women (n=141). The Black women had a lower resting metabolic rate compared to the White women after it was expressed relative to body mass, 4.28 compared to 4.47 mL/kg of fat free mass/min [8]. Additionally, the Black women also had a lower CRF when it was expressed in absolute and relative terms, 2.05 L/m vs. 2.30 L/m and 26.2 mL/kg/min vs. 35.3 mL/kg/min [8]. The CRF values were added into the model with the adjusted resting metabolic rates to investigate the relationship between CRF and resting metabolic rates; the model adjusted for race, age, skeletal muscle, residual mass, fat mass, bone mass and cardiorespiratory CRF [8]. After adding CRF values into the model, there was a 25% difference between the Black and White women resting metabolic rate [8]. The participants' lower CRF values could have potentially be in part by their lower resting metabolic rates.

Another potential cause for low CRF values is the different fiber types that are present within the muscle tissue. Tanner et al [33] examined the association of muscle fiber types with obesity and weight loss in Black and White women. There are two major fiber types which are type I and type II fibers [33]. Type I fibers (slow twitch) are more oxidative and vascularized, while type II fibers (fast twitch) are more glycotic by nature [33]. The obese Black women possessed more type II fibers than the obese White women [33]. Blacks' skeletal muscle still contained more type II fibers than White without taking into account adiposity. Having more type II fibers than type I fibers contributes to lower oxidative enzyme activity and fat oxidation [34].

Summary

A review paper by Swift et al. [5] provided a detailed discussion of low CRF in Blacks. Swift et al examined the many studies that addresses the relationship between CRF and mortality in Blacks and a few amount of epidemiology studies that compare CRF in Blacks to Whites [5]. This review paper demonstrated that regardless of how CRF is quantified (estimated METs, VO_2 max, estimated CRF) Blacks had lower CRF than Whites [5]. Swift et al. also mentioned several limitations that previous studies investigating racial differences in CRF have exhibited. One limitation in some studies was that often CRF was not the primary outcome measure, which limited the amount of statistic adjustments for confounding factors. Another limitation was that some studies did not correct CRF for lean mass but for body weight [5]. Correcting for lean mass could be more appropriate when comparing CRF levels as adjusting for body weight includes fat mass and other components, which do not contribute to oxygen uptake during exercise [5]. One last limitation that was discussed in the review paper was that several studies recruited their participants through convenient samples. Participants were found within the a hospital database or even referred to exercise testing, which may not be representative of both races in the United States [5]. Although there is a great amount of evidence supporting Blacks having lower cardiovascular CRF, it has not been quantified with using meta-analysis approach. This study could potentially generate more interest from researchers to conduct interventions specifically for the Black community. When compared to their White counterparts, Blacks have higher CVD risk factors, CVD mortality and lower fitness levels. This study will allow researchers to quantitatively explore the differences in CRF between the races, which will show them the need for exercise interventions within the Black community. A meta-analysis would be able to address some of the various limitations of the previous literature. Additionally, stratification for age, sex, race, and different body masses index could be performed. It is important to establish CRF as a health disparity and to be able to quantify the difference not only between Blacks and Whites, but between several studies that includes several different populations.

Chapter III: Methods

The purpose of this present study was to perform a meta-analysis to quantify the CRF differences between Blacks and Whites. It was hypothesized that the analyses would find significant differences between the Black and White adults, with the Blacks having lower CRF levels.

Data Sources and Study Selection

The review of the literature and meta-analysis was conducted according to the checklist of the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA). A systematic literature search was performed for peer-reviewed articles using academic search engines (Pubmed, Web of Science, Google Scholar, ProQuest,), which compared CRF values in Blacks and Whites. The search terms used included CRF, mortality, race, Blacks, Whites, African Americans, Caucasian, fitness, CVD, health disparity, VO2 max, and oxygen consumption. The bibliography of all identified articles was subsequently reviewed for additional relevant studies. The amount of studies that are found using this criterion has been defined, in addition with the amount of studies that have met the inclusion/exclusion criteria, using the PRISMA Flow Diagram.

Inclusion and Exclusion

All identified studies was included only if they met the following inclusion criterion. Articles were included if (1) CRF was assessed by an exercise test (submaximal or maximal) (2) CRF was assessed in Blacks and Whites, (3) examined adults only, and (4) Published in a peer review journal. This inclusion criterion was used to ensure CRF was measured using acceptable methods, the studies included the racial groups in interest and to examine similar age ranges.

Studies were excluded if (1) children or adolescents were examined (2) sample size had less than 15 participants per group (3) health conditions that were not cardiovascular in nature or type two diabetes (e.g. neurological). Excluding children and adolescents would allow the analysis to examine similar participant ages within the studies. Children and adolescents are still developing their cardiovascular system. Additionally, this meta-analysis was to help generalize information for adults. Preexisting diseases were excluded to help reduce its potential bias on fitness. The Prisma 2009 Flow Diagram, shown on the following page, was used to illustrate how many articles was included, excluded and used in the analysis.

Statistical Analysis

The meta-analysis was performed using a statistical program, R Studio, MA, Boston. The primary purpose of this analysis was to evaluate the magnitude in CRF between Blacks and Whites. The different modalities used for assessing CRF will also be adjusted for while performing the meta-analysis.

Chapter IV: Results

Study Characteristics

The PRISMA statement for the present study is shown in Figure 1. Of the 47 studies identified through the initial database search (e.g. Pubmed, Web of Science, Google Scholar), 22 studies were excluded because they did not compare CRF between Blacks and Whites. Two more articles were further examined and excluded from the analyses because the CRF values were quantified in L/min and we were unable to convert the values to ml/kg/min [30, 35] (In order to convert CRF values from ml/kg/min to L/min, the weight of the participants are needed and these values were not included in these studies.). There were 23 studies that met the full criteria to be included in the main analysis, which compared CRF between Blacks and Whites with studies that quantified fitness using maximal METs. The studies in this analysis were comprised of a total of 77,776 subjects (17,314 Blacks; 60,462 Whites). The secondary analysis compared CRF levels between Blacks and Whites using maximal oxygen consumption as the criteria for CRF. Twelve of the 23 studies were used in this analysis. Three studies were excluded because they used submaximal testing to assess CRF and not maximal testing [21, 23, 24]; and nine [4, 8, 15, 18, 20, 26, 27, 36, 37] were excluded because they quantified CRF only in METs (oxygen consumption levels were not collected during exercise testing).

In Figure 2, the forest plot comparing CRF levels between Blacks and Whites quantified in METs is shown. The difference in MET levels in the model was 0.93 (95% CI 0.75-1.1). There were four studies that were position more to the right of the forest plot [17,19,8,6]. Their positioning implies a more pronounced difference in fitness between Blacks and Whites. These four studies all investigated fairly healthy populations. In Figure 3, a forest plot comparing fitness levels of Blacks and Whites quantified using VO_2 max values. The difference in VO_2 values for this analysis was 3.27 (95% CI, 1.63-2.29). This forest plot had two articles that were more positioned to the right [17,8]. These two articles also investigated fairly healthy populations. The summary effect indicates that Whites had higher fitness levels than Blacks when fitness was both measured as METs and maximal oxygen consumption.

Chapter V: Discussion

The primary findings of this meta-analysis suggest that Blacks tend to have a lower fitness level compared to Whites based on the available data from published clinical trials. This finding was consistent whether CRF was quantified: 1) Using maximal METs, which has clinical significance and has been associated with CVD and mortality risk; or 2) Maximal oxygen consumption which is the gold standard method for evaluating fitness in exercise physiology settings [22]. This meta-analysis is the first to our knowledge that quantitatively evaluates racial differences in CRF between Blacks and Whites across many clinical trials and supports previous review papers that have speculated that racial difference in CRF may exist [4, 5, 9]. This could add to the literature that fitness may represent a health disparity risk factor [5, 25] and further support the rationale for physical activity interventions in Black populations.

The public health relevance of the present paper is that CRF is an independent risk factor for cardiovascular disease in the general population [3, 11, 30] and specifically for Blacks [13, 38]. The difference of means in CRF observed between Blacks and Whites in the present study was about 0.93 METs. Kodama et al. [29] reported that one MET was associated with a 13% reduction in all-cause mortality and a 15% reduction in CVD risk. Therefore, the racial differences in CRF noted in the present study are associated with a 12.1% increased risk for all-cause mortality and a 13.9% increased risk for CVD mortality. This may suggest that lower levels of CRF in Blacks compared to Whites could contribute to racial health disparities in CVD. There is a need for more epidemiology studies to investigate the overall contribution of CRF to racial cardiovascular health disparities between Black and Whites. Additionally, different physical activity programs should be examined to see which strategy best improves CRF specifically in Blacks.

The present results support arguments in a review papers by Swift et al [5] and others [34, 38] that have speculated that Blacks have lower CRF levels than Whites. Potential physiological mechanisms explaining the racial differences in CRF include reduced hemoglobin levels, higher amounts of type II fibers and low mitochondrial function in Blacks compared to Whites. Hemoglobin is a protein found in red blood cells that transport oxygen the working musculature [9]. Therefore, lower levels of hemoglobin can potentially hinder oxygen transport during aerobic exercise [9]. Several studies have shown that Blacks have lower levels of hemoglobin compared to Whites, which could contribute to racial differences in CRF [9, 40]. Pivarnik et al. [40] investigated hemoglobin levels in Black and White adolescent girls. Statistically significant differences were reported in CRF values, with the Blacks adolescents having lower values (31.8 $mL \cdot kg^{-1} \cdot min^{-1}$ vs. 38.5 $mL \cdot kg^{-1} \cdot min^{-1}$) [40]. In addition to racial differences in CRF, there were also racial differences observed in hemoglobin. The Black adolescent girls had lower hemoglobin levels when compared to the White adolescent girls (13.0 g/dl vs 13.8 g/dl) [40]. These racial differences in hemoglobin have not only been observed in adolescents but have also been reported in adults. Hunter et al. [9] investigated hemoglobin levels and CRF in premenopausal Black and White women. It was reported that the Black women not only had a lower CRF than the White women (33.6 $mL \cdot kg^{-1} \cdot min^{-1}$ vs. 29.3 $mL \cdot kg^{-1} \cdot min^{-1}$), but also lower hemoglobin levels (12.9 g/dl vs. 11.8 g/dl) [9]. After adjusting for the hemoglobin levels within the women, the racial differences in CRF persisted, with the Black women having lower CRF values [9]. The authors suggested that the reduced hemoglobin levels were related to the reduced VO2 max values among their Black participants, but this did not fully explain racial differences in CRF. Swift et al. [25] also investigated racial differences in the response to fitness with exercise training in postmenopausal women. At baseline, the Black women had a lower CRF when compared to the White women (15.1 mL· kg^{-1} · min^{-1} vs. 15.7 mL· kg^{-1} · min^{-1}) [25]. The Black postmenopausal women also had lower hemoglobin levels than the White women (12.6 g/dl vs. 13.2 g/dl)[25]. However, after adjusting for the lower hemoglobin levels, the racial differences in CRF still persisted. Thus, racial differences in hemoglobin may be a contributing factor, but likely does not fully account for racial differences in CRF between Whites and Blacks.

Another potential contributing factor to lower CRF levels in Blacks may be due to the mitochondrial density/fiber type distribution of the muscle tissue. Blacks have been shown to have a higher percentage of type II muscle fibers [33], which tend to be more glycolytic [33] compared to type II fibers, which are more oxidative. Having a greater percentage of type II fibers (compared to type I) may hinder their ability to sustain aerobic activities, possibly contributing to the lower CRF levels. Tanner et al. [33] observed that Black participants had higher amounts of type II fibers present in their skeletal muscle compared to White participants (23.4% vs. 16.3%) [33]. The authors also investigated the relationship between obesity levels and muscle fiber types. The obese women possessed more type II fibers when compared to the lean women (25.1% vs. 14.4%) [33]. It was also observed that the obese Black women had higher amounts of type II fibers when compared to the obese White women (31% vs. 19.2%) [33]. However, there was no significant difference found in the relative percentage of type II fibers between the lean Black and White women (15% vs. 13.8%) [33]. Similar findings were also reported by Ama et al. [41] who investigated skeletal characteristics in sedentary Black and White males. The Black males had more type IIa fibers (48.6% vs. 41.9%) and IIb fibers (19.7%

vs. 17.1%) than the White males [41]. Conversely the White males had more type I muscle fibers when compared to the Black males (40.9% vs. 32.6%) [40]. Hunter et al. [9] finding racial differences in CRF and hemoglobin levels, they also found differences in the muscle oxidative capacity between the women. Low ADP time constants are associated with high muscle oxidative capacities [9]. It was reported that Black women had an ADP time constant of 24.3 s compared to the White women who had 21.3 s [9]. The Black women had a lower aerobic capacity, which could be contributing to their lower levels of CRF that was observed.

Potential behavioral and environmental factors that may represent contributing factors to the lower CRF levels in Blacks include low physical activity levels compared to Caucasians and neighborhood demographics. The American Heart Association has indicated that only about 22.9% of Blacks engage in regular physical activity compared to the 33.9% of Whites [7]. Similarly, Haskell et al. [42] reported that 41.8% of Blacks met the Centers of Disease Control/ACSM recommended physical activity guidelines compared to the 51.1% of the Whites [42]. Higher levels of physical activity have been associated with higher CRF levels [7,10] and exercise training tends to show an increase in CRF levels [28,45]. Although lower levels of physical activity have been observed in Blacks compared to Whites, this is not supported in all studies. [21,43].

Another potential environmental factor potentially affecting CRF is the availability of physical activity facilities in neighborhoods with higher proportions of minorities. Powell et al. [44] investigated this phenomenon throughout the United States. It was observed that neighborhoods with higher proportions of Black residents and other minorities were significantly less likely to have physical activity-related facilities, in addition to lower socioeconomic neighborhoods [44]. Predominantly White communities were 5 times more likely to have at least one physical fitness facility or public golf course, 7 times more likely to have at least once dance studio and 58% more likely to have at least once membership sports/recreation club [44]. Having limited access to different physical activity-related facilities could create a potential barrier for Blacks to engage in regular physical activity. Griffin et al. [46] conducted focus groups with Black residents living in low-income communities and observed similar findings. It was reported that poor neighborhood environmental infrastructure, lack of walking paths and lack of sidewalks within predominantly Black communities were barriers to engaging in regular physical activity [46]. Another environmental barrier observed were safety issues within the communities such as stray dogs, gang activity, lack of lightening, and mugging [46]. These environmental factors could be deterring Blacks from engaging in regular physical activity resulting in their lower CRF values.

There are limitations to consider in the present study. There are a variety of populations included in this meta-analysis (diabetics, premenopausal women, healthy adults, high risk for CVD), however subgroup analyses did not appear to show differential effects based on these demographic factors. Although, Blacks and Whites were compared from the various studies, it cannot be fully confirmed that selection biases may not be affecting the enrollment of Whites and Blacks in the studies. For example, some studies recruited through convenient sampling participants referred to exercise testing and or utilized data within hospital databases [15, 37]. In addition, the majority of the articles available for this meta-analysis were from the middle-age adult population. Therefore, our results may not be generalizable to children, adolescents, the elderly or Blacks not living in the United States. Lastly, CRF was not always the primary measure of the studies used in the analysis. CRF was a secondary measurement, which could limit the amount of statistical adjustments made that would potentially account for confounding factors (i.e. potential racial differences in age, disease status or other factors influencing CRF). Despite these limitations, a strength of the present study is that the studies assessed CRF using maximal METs, which has clinical significance and maximal VO2 testing, the gold standard of exercise testing [22].

In this present study, there was approximately one MET difference between the means in CRF for Blacks and Whites. This finding supports the previous literature speculating that racial differences in CRF may exist between Blacks and Whites [5, 9, 15, 28, 34]. The differences we observed in the present study maybe within a clinically significant range, which may suggest that CRF could represent a health disparity risk factor. Future research should investigate racial CRF differences between Blacks and Whites in populations not represented in the present meta-analysis including children, adolescents, and elderly. In addition, the potential physiological, molecular mechanisms and sociological explanation between the racial differences in CRF should also be explored further. Lastly, methods of increasing physical activity participation in Blacks and evaluating how to maximize the CRF response in Blacks through exercise interventions may facilitate how to reduce this disparity in racial disparity in CRF.

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Tables and Figures

Table 1: PRISMA 2009 Flow Diagram

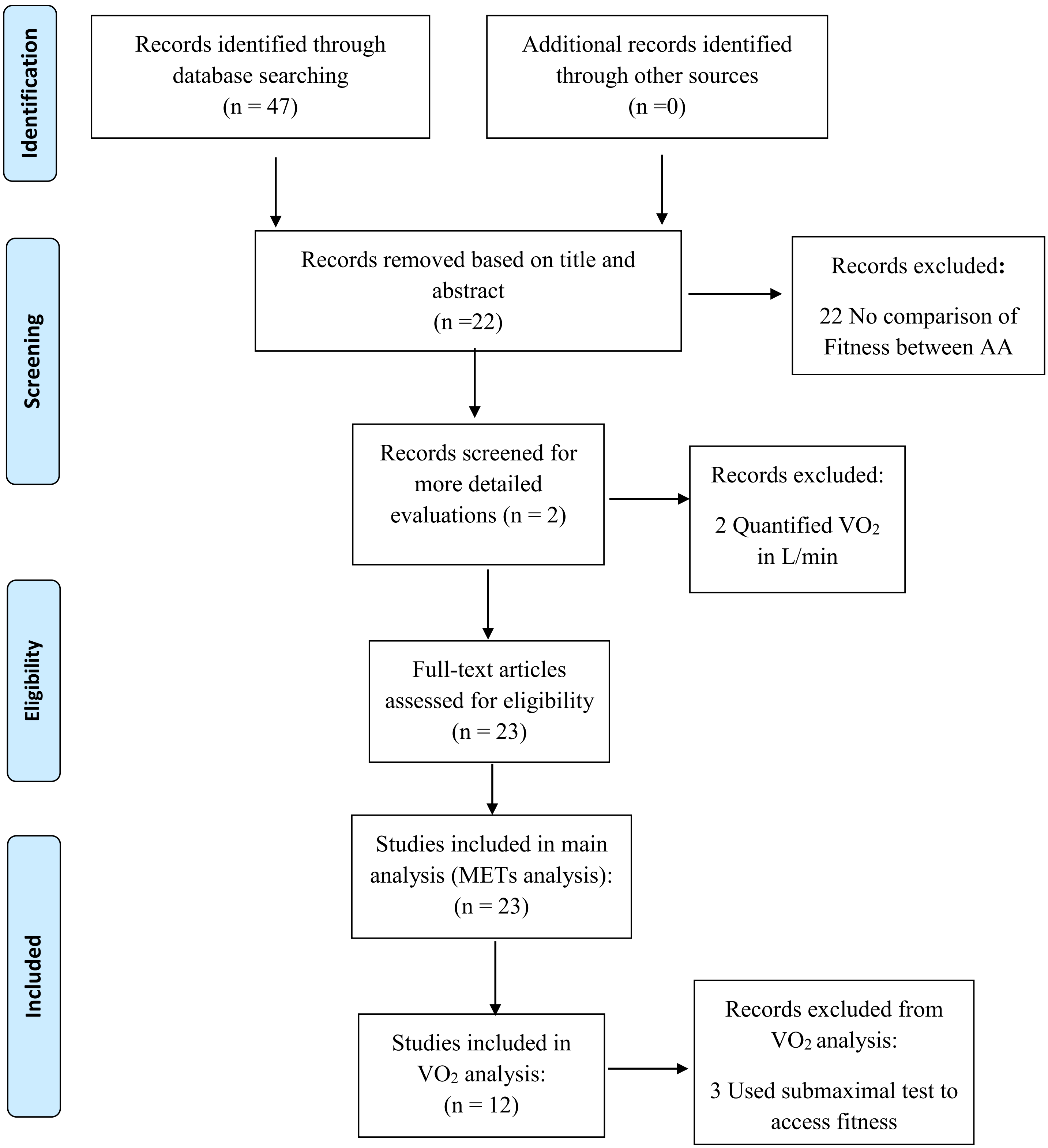

Figure 1. Forest Plot of CRF in METs

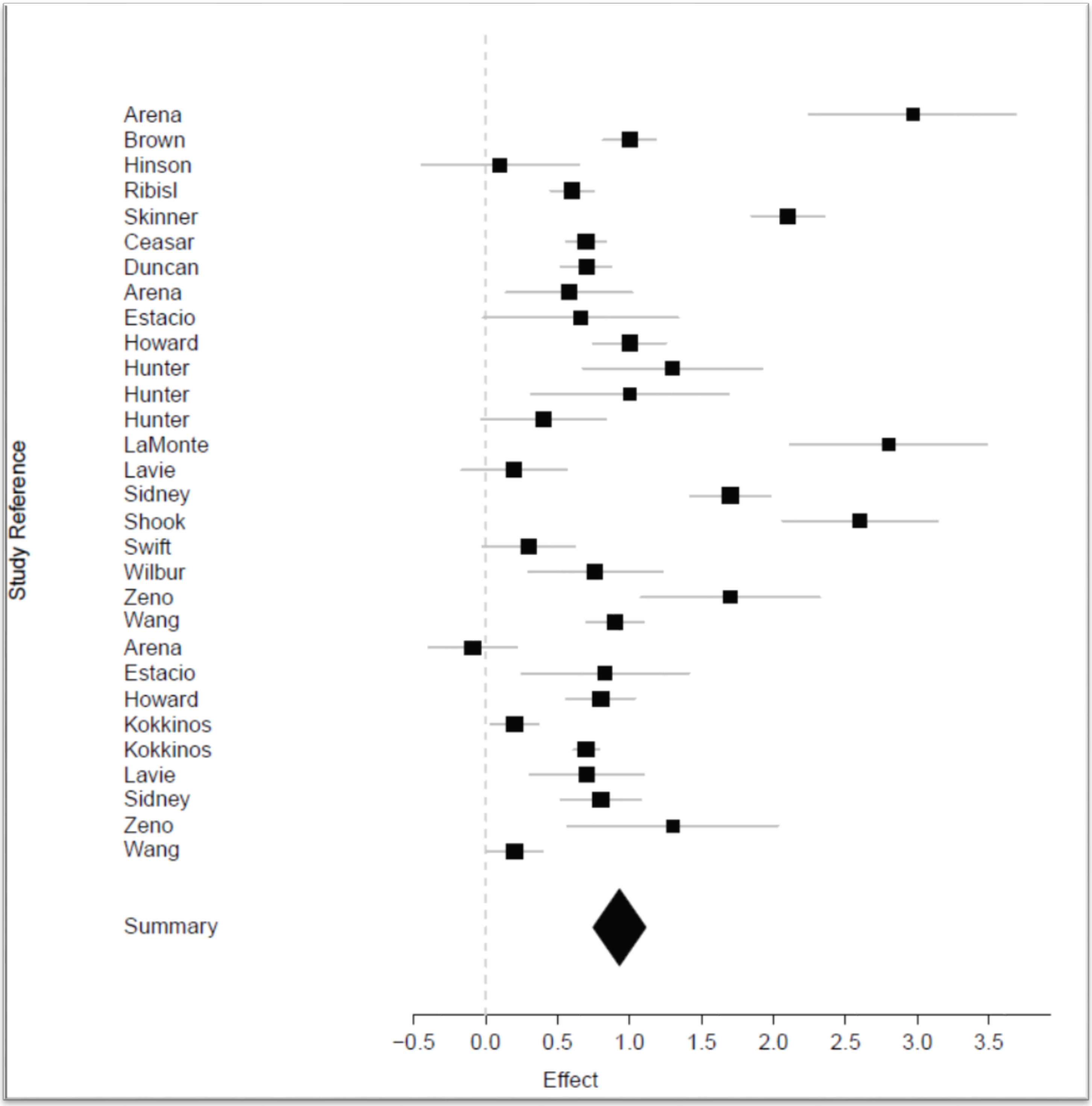

Figure 2: Forest Plot of CRF in VO2