Evaluation of Pre-Participation Screening and Cardiovascular Risk Assessment in Masters Athletes in British Columbia

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Abstract

**Background:** Middle-aged individuals (≥35 years) are exercising more and living longer. Vigorous exercise can transiently increase the risk of sudden cardiac death (SCD) in those with underlying cardiovascular disease (CVD). Pre-participation screening (PPS) can detect CVD. The optimal screening method in Masters athletes is unclear. Suggested methods include cardiovascular history questionnaire, physical examination, cardiovascular risk scores, resting electrocardiogram (ECG), exercise treadmill test (ETT), and imaging techniques.

**Purpose:** To evaluate the prevalence of CVD and risk factors and the effectiveness of different screening methods for detecting cardiovascular risk in Masters athletes to prevent SCD in sport. To determine the prevalence of atrial fibrillation (AF) in Masters athletes, and its association with volume of activity.

**Methods:** This is a prospective observational study that evaluated Masters athletes from a variety of sports. The initial screen consisted of a physical examination, a resting ECG, Framingham Risk Score (FRS), an American Heart Association (AHA) questionnaire, and a physical activity and lifestyle questionnaire. If the initial screen was abnormal, the participant went on for further evaluations according to criteria defined *a priori*. CVD was confirmed by follow-up examinations and a positive predictive value (PPV) determined the effectiveness of the screening tools.

**Results:** A total of 297 athletes (67% male, mean age 54 ± 8.8, range 35-81 years) were included. The prevalence of CVD was 12% and 9% had a high FRS. CAD was the most frequent diagnosis (9%). Three (1%) athletes were diagnosed with AF. A high cardiovascular risk score was the most effective tool in detecting CAD (56% PPV), and the AHA questionnaire produced the greatest number of false-positives (82%). There was a greater prevalence of AF and valvular heart disease in those with greater volumes of physical activity.

**Conclusion:** Physically fit, asymptomatic Masters athletes are not immune to cardiovascular risk factors and have significant CVD. Systematic screening amongst Masters athletes may be reasonable; however, more research is needed to refine the current PPS methods to better suit the Masters athlete population.
Preface

I, Barbara Morrison, completed the writing and conception of this thesis. Qualified physicians, student volunteers, and colleagues assisted in the collection of data and data entry. I was responsible for data analysis. My committee members, including Drs. Warburton, Taunton, and Isserow provided support for conception and implementation of this research. This research investigation was obtained with approval from the UBC Clinical Research Ethics Board (Certificate H15-00009).

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List of Abbreviations
ABP = ambulatory blood pressure
AF = atrial fibrillation
AHA = American Heart Association
AI = aortic insufficiency
AR = aortic regurgitation
AS = aortic stenosis
AV = aortic valve
ARVC = arrhythmogenic right ventricular cardiomyopathy
BAV = bicuspid aortic valve
CAA = coronary artery anomaly
CABG = coronary artery bypass graft
CACS = coronary artery calcium score
CAD = coronary artery disease
CHD = congenital heart disease
CMR = cardiac magnetic resonance imaging
CTA = coronary computed tomography angiography
CVD = cardiovascular disease
HCM = hypertrophic cardiomyopathy
EACPR = European Association of Cardiopulmonary Rehabilitation
ECG = electrocardiogram
ECHO = echocardiogram
ESC = European Society of Cardiology
ETT = exercise treadmill test
FRS = Framingham Risk Score
H = Holter
HCM = hypertrophic cardiomyopathy
LAD = left anterior descending artery
LBBB = left bundle branch block
LGE = late gadolinium enhancement
LV = left ventricle
LVH = left ventricular hypertrophy
METS = metabolic equivalents
MET-hr/wk = metabolic equivalent task hours per week
MR = mitral valve regurgitation
MVP = mitral valve prolapse
MIBI = myocardial perfusion imaging
MI = myocardial infarction
MVPA = moderate-to-vigorous physical activity
PPS = pre-participation screening
PPV = positive predictive value
PVC = premature ventricular contraction
RBBB = right bundle branch block
RV = right ventricle
RCA = right coronary artery
SCD = sudden cardiac death
SVT = supraventricular tachycardia
WPW = Wolff-Parkinson-White syndrome
YCA = young competitive athlete
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Most importantly, a sincere thank you to all the participants. Without your participation and interest in this area of research, this project would not have been possible.
Chapter 1: Introduction and Rationale

This chapter provides background and rationale for the thesis investigation. Aims and hypothesis will be highlighted.

The news of a seemingly healthy and fit athlete having a sudden cardiac arrest in sport is shocking and tragic. Routine physical activity is associated with improved health, well-being, and a reduction in adverse cardiovascular events and all-cause mortality. Conversely, physical inactivity is known to be a risk factor for the development of cardiovascular disease (CVD) and premature mortality\(^1\). Hippocrates, (400 BC) was one of the first to describe that physical activity, performed in moderate amounts, is good for health. Since then many physical activity experts, through modern epidemiological methods, have tried to quantify physical activity and link it with health outcomes. Two modern instrumental pioneers, Morris, who described how sedentary bus drivers had increased coronary artery disease (CAD) in comparison to the more physically active conductors,\(^2\) and Paffenburger who later added that moderately vigorous sport activity (> 4.5 METS) resulted in a substantial reduction in mortality from all causes (23%), and from CAD (41%) as compared to less vigorous activity\(^3\). Similarly, Blair et al. observed that in those that were unfit and became more fit, lowered their age-adjusted risk of all-cause mortality by 44% (RR 0.56; 95% CI, 0.41 to 0.75), and age-adjusted risk of CVD mortality by 52% (RR 0.48; 95% CI, 0.31 to 0.74)\(^4\). More recently, in an extensive review of the literature, Warburton et al. showed that regular physical activity can reduce the risk of 25 chronic conditions and premature mortality\(^1\). Although the most benefit seems to occur when a physically inactive individual becomes physically active, the mortality benefits are apparent at the other end of the spectrum. Clarke et al. compared 15,714 Olympic athletes from nine countries who won medals in the Olympic games between 1896 and 2010 to the general population and found that Olympic medalists lived, on average, 2.8 years longer\(^5\). Based on more than five decades of epidemiological studies, it is now widely accepted that physical inactivity and lack of cardiorespiratory fitness are independent risk factors for CVD\(^6\).

Many are involved in athletic endeavours for reasons beyond the potential for health benefits such as improved self-image, competition, camaraderie, and stress reduction. As such, there has been a growing interest in recreational and competitive athletics in those greater than 35 years
(i.e. Masters athletes). Maron et al. describes the over 35-year-old athlete as a Masters athlete and includes conditioned, experienced, competitive athletes who continue to compete after their formal careers end but also include “walk up” competitors (sometimes referred to as weekend warriors) with only sporadic training regimes\(^7\). It also includes those who resume competition after long periods of physical inactivity. Competitive Masters athletes are individuals who participate in organized team or individual sport that requires systematic training and regular competition against others, and places a high premium on athletic performance, excellence and achievement, such as at the provincial, national, international and/or Olympic level. An underlying characteristic of competitive sport is a strong appetite for individuals to exert themselves to their limits, and improve performance\(^8\). Leisure athletes are individuals who participate in a variety of informal recreational sports within a range of exercise levels from moderate to vigorous, on either a regular or inconsistent basis, which do not require systematic training or the pursuit of excellence\(^8\). A clear definition of the term is still missing, as such, Araujo recently suggested, the definition of “athlete” needs a more concrete definition so that data obtained from scientific experiments by different researchers can be compared. They proposed that in order to be considered an athlete four criteria must be met: 1) to be training in sports aiming to improve his/her performance or results; 2) to be actively participating in sport competitions; 3) to be formally registered in a local, regional, or national sport federation as a competitor; and 4) to have sport training and competition as his/her primary focus of interest, almost always devoting several hours, if not most of their days to sport activities, exceeding the time allocated to other professional or leisure activities\(^9\).

“How do the physical activities that are supposed to make us live longer increase our risk for a potentially fatal cardiovascular event?” This has become known as the “exercise paradox” where the risk for a potentially life threatening event (such as myocardial infarction, aortic dissection, arrhythmias, sudden cardiac arrest and/or sudden cardiac death [SCD]) during vigorous exercise is transiently increased\(^{10-12}\). SCD is defined as death that occurs unexpectedly; generally \(\leq 1\) hr from the onset of symptoms\(^{13}\). In a recent national prospective survey conducted in France (2005-2010) 90% of sports-related deaths (age 46 ± 15 years) in the general population occurred during recreational sport, and 50 (6%) occurred in young competitive athletes (< 35
years). The majority of sports-related deaths and myocardial infarctions occur in males between the ages of 35 to 59.

1.1 Incidence

Reported incidence rates vary and reflect data collection methods, athlete demographics, and sporting discipline. Commonly, SCD reports are derived from voluntary reporting or the media. This has been long-standing issue in the young competitive athlete, which has resulted in a wide range of incidence rates (1:23,000 to 1:300,000). The incidence of SCD in Masters athletes is less well studied, however reports in apparently healthy adult joggers, or marathon racers, the rate of SCD is higher (1:7620 to 1:184,000) compared to the younger athlete. Thompson et al., examined the deaths in male joggers from 1975-1980 on Rhode Island and found a death rate of one death for every 7,620 joggers or approximately one death per 396,000 man-hours of jogging (joggers reported jogging at least twice per week). Kim et al. found a lower incidence (1:184,000) rate among 10.9 million joggers that were assessed by interviewing survivors, next of kin of non-survivors, reviewing medical records and analyzing post-mortem data. Rates were higher during marathon (1.01 per 100,000; 95% CI, 0.72 to 1.38) versus half-marathons (0.27; 95% CI, 0.17 to 0.43, P<0.0001). Recently, researchers have examined the incidence of sports related SCDs in recreational athletes because the incidence rates in this population was unknown and it was questioned whether or not they were at the same risk. Although competitive sports are characterized for their high levels of physical exertion, some individuals who participate in recreational sport train similar to competitive athletes and it was thought that they might have a similar risk. Researchers found the prevalence of sports related SCDs to be the same or even higher in non-competitive (recreational) athletes versus competitive athletes. In Germany, for instance 142 (99%) of the cases of SCD occurred in non-elite competitive or recreational athletes versus two cases in young professional elite athletes and, in Switzerland, they found 91% of the sports-related deaths to occur during leisure sport.

Another way to assess, and possibly a more accurate depiction of at risk individuals, is to determine the prevalence of athletes harbouring the disease rather than the prevalence of SCD. Based on the types of CVD present, screening tools should be designed to detect those diseases (Table 1.1). Underlying conditions associated with exercise-related SCD occurs in 1 in 300
young athletes and non-athletes\textsuperscript{24}. In middle-aged active individuals the prevalence of cardiovascular disease and high cardiovascular risk is even higher; 1:36 had a new cardiac diagnosis and 1:25 had a high cardiovascular risk profile\textsuperscript{25}. The SCD rate is much lower than the prevalence of CVD that could potentially cause SCD.

**Table 1.1 Types of cardiovascular disease present in young competitive athletes versus Masters athletes\textsuperscript{10,17}**

<table>
<thead>
<tr>
<th><strong>Young Competitive Athlete</strong> (Inherited)</th>
<th><strong>*Masters Athlete</strong> (Acquired)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Inherited cardiomyopathies</td>
<td>• Coronary artery disease</td>
</tr>
<tr>
<td>o Hypertrophic cardiomyopathy</td>
<td>• Valvular heart disease</td>
</tr>
<tr>
<td>o Arrhythmogenic right ventricular</td>
<td>• Myocarditis</td>
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<tr>
<td>cardiomyopathy</td>
<td>• Atrial fibrillation</td>
</tr>
<tr>
<td>o Dilated cardiomyopathy</td>
<td>• Stroke</td>
</tr>
<tr>
<td>• Coronary artery anomaly</td>
<td>• Dilated cardiomyopathy</td>
</tr>
<tr>
<td>• Wolff-Parkinson-White</td>
<td></td>
</tr>
<tr>
<td>• Long QT syndrome</td>
<td></td>
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<tr>
<td>• Mitral valve prolapse</td>
<td></td>
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<tr>
<td>• Bicuspid aortic valve</td>
<td></td>
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<tr>
<td>• Myocarditis</td>
<td></td>
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<tr>
<td>• Myocardial bridging</td>
<td></td>
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<tr>
<td>• Coronary artery disease</td>
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</table>

*May also present with CVD that is commonly seen in younger athletes

### 1.2 Causes of Sudden Cardiac Death

#### 1.2.1 Presence of Undetected Cardiovascular Disease

Unidentified and asymptomatic CVD is typically the cause of SCD\textsuperscript{26}. The etiology of SCD differs between the Masters and young competitive athlete (< 35 years). In the Masters athlete, the primary cause of sudden cardiac death is acquired CVD (i.e. CAD)\textsuperscript{27}; whereas, in the under 35-year-old athlete, inherited cardiomyopathies, ion channelopathies, coronary artery anomalies are predominately responsible (Table 1.1)\textsuperscript{10,11,28}. The higher incidence of SCD in the middle-aged population is attributable to the atherosclerotic process that occurs with aging. Marijon et al. reported an 84% predominance of CAD amongst known sports-related SCDs\textsuperscript{11}. Canadian researchers examined SCD case autopsies in all persons aged 2-40 in Ontario and reported an incidence of 0.7/100,000 person-years (2-18 year-olds), 2.4/100,000 person-years (19-29 year-
olds) and 5.3/100,000 person-years (30-40 year-olds) 29. Dutch researchers found a similar trend in the general population and added that the incidence increased further in those over 50 to 1:1,000 (median age 72 years, [IQR: 63–80 years]) 30. In contrast, cardiomyopathies have been primarily indicated as the primary cause of SCD in young competitive athletes, with HCM accounting for one-third of fatal deaths and a reported incidence of 1:500 in the United States 18, 31-34, arrhythmogenic right ventricular cardiomyopathy (ARVC) explaining one quarter of SCDs in the Veneto region of Italy, 35, 36 and dilated cardiomyopathy having the highest prevalence in athletes aged 13-77 in Brazil 37.

1.2.2 Gender
Male athletes are at higher risk of SCD versus their female counterparts. Women also have higher likelihood of successful resuscitation 38. Studies have shown up to a 30 fold increase of SCD in males compared to females (10-75 years) 10, 11, 14, 30, 38. This difference was still apparent when sports sudden cardiac arrests were compared to non-sports sudden cardiac arrests, suggesting a potential intrinsic difference, but is likely multi-factorial 11. A greater predominance of males in competition, more intensive training, greater intensity during sports, and inherent sex differences such as substrates (structural and electrophysiological) that act as a trigger for SCA are likely factors 39. Women were less likely to have underlying CAD than men (45% versus 80%), and more likely to have structurally normal hearts or other forms of heart disease (i.e. dilated cardiomyopathy and valvular disease, coronary vasospasm), and less likely to have inducible arrhythmias 40. Coronary artery disease that occurs at a later age for women could also explain the difference 39. Male athletes are characterized by greater cardiac volume and mass, even after adjusting for body composition and size 41. Therefore, when assessing female athletes for possible heart disease, myocardial thickening is more likely to represent a true cardiac abnormality and should be investigated further 41. As more women compete in sport, the proportion of female SCD could continue to rise. Investigations should keep sex differences in mind.

1.2.3 Ethnicity
Differences in the incidence of sudden cardiac arrests and SCDs exist between ethnicities. In the CPR Chicago project, blacks had higher rates (RR 1.3-2.8) of cardiac arrest, lower survival rates
after a cardiac arrest (0.8% versus 2.6%), and were less likely to have a “favourable” rhythm to be resuscitated, compared to whites. Differences in etiologies also exist. Non-whites had a higher incidence of cardiomyopathies and coronary anomalies (20% in non-whites vs. 10% in whites and 10% in non-whites vs. 5%, in whites, respectively). Conversely, deaths attributable to ion channelopathies were more common among whites (2%) versus non-whites (0.3%)

1.2.4 Sport

Previous studies have reported the prevalence of SCD to be higher in certain sports. Marijon et al. reported cycling (30.6%), running (21.3%) and soccer (13%) to have the highest number of sudden deaths during recreational sport and overall, 66.7% of SCDs occurred during individual sports and 33.3% occurred during team sports. The Oregon Sudden Unexpected Death Study in the United States found that among 63 middle-aged individuals (51.1 years ± 8.8, range 35-65 years) SCDs occurred during jogging (27%), basketball (17%), cycling (14%), gym activities (11%), golfing (8%), volleyball (3%), tennis (3%), soccer (3%) and other activities (14%). Chevalier et al. reported similar incidence rates among sports (running, cycling, and swimming were mainly concerned). Comparatively, in the young athlete, SCD most commonly occurred during team sports such as basketball, football, soccer, track and field, and baseball. The fact that SCD occurs more commonly during individual sports in the older athlete (more individuals partake in individual sports as they get older) and in sports that are more commonly practiced (i.e. running), and during team sports in the younger athlete (team sports predominate in the younger athlete) suggests that the number participating in each sport not the sport per se, is the reason for the increased risk during particular sports. Similarly, as the number of individuals in a particular sport increases, such as running, the number of SCDs would also be expected to rise. For example, Kim et al. demonstrated that in the latter part of their 10-year study period the number of total participants in half marathons and full marathons doubled, and the incidence of cardiac arrests increased from a total of 0.42 (CI, 0.25 – 0.66) to 0.63 (CI, 0.45 – 0.86, p=0.15). The intensity of the sport (i.e. cycling versus golf) and the compounded physiological strain of sport (i.e. marathon versus a half marathon) also contribute to the increased prevalence of SCDs in certain sports.
1.3 Elevated Risk with Vigorous Exercise

The transient risks associated with an acute bout of exercise appear to be the greatest in physically inactive individuals (i.e., those unaccustomed to exercise) who engage in vigorous intensity activities/exercises (i.e., ≥6 METS; ≥21 mL/kg/min)\textsuperscript{13, 43}. Moreover, the risk of SCD can be attenuated greatly with regular exercise\textsuperscript{44}. For instance, Siscovik et al. showed the relative risk (RR) of cardiac arrest during exercise (in comparison to rest (no activity)) was 5-fold higher in highly active individuals versus 56-fold higher in those with the lowest activity levels\textsuperscript{43}. Albert et al. also revealed that habitually active men (i.e., those that exercise at least 5 times per week) have a much lower relative risk of sudden cardiac death (RR = 10.9) than men who exercise vigorously less than once a week (RR = 74.1)\textsuperscript{13}. Interestingly, compared to risk during periods of mild or no physical activity, vigorous physical activity transiently increased the risk of sudden cardiac death from a factor of 14 to 45. This risk remained elevated in even the most active men. Importantly, despite these increased risks the evidence is clear that the lifetime risks for adverse cardiovascular-related events are markedly lower in active individuals across their lifespan\textsuperscript{2, 3}. Albert et al, reported the absolute risk of SCD associated with an episode of vigorous exertion to be low at 1 per 1.51 million episodes of person-hours at risk\textsuperscript{13}.

1.4 Mechanisms of SCD

Mechanistic reasons by which intense bouts of exercise precipitates SCD include an increase in arterial wall stress from elevated heart rate and blood pressure, coronary artery spasm in diseased segments, activation of the sympathetic nervous system, increase in circulating catecholamines and a decrease in vagal tone\textsuperscript{12}. Such mechanisms predispose the heart muscle to lethal irregular heart rhythms, whereas regular exercise increases vagal tone and the electrical stability of the heart, protecting against irregular heart rhythms. In previously asymptomatic individuals who experienced a cardiovascular event during exercise, plaque rupture in the artery was the most common pathogenic mechanism. At cessation of exercise, a decrease in venous return, cardiac output, and blood pressure causes a transient reduction in perfusion of the coronary arteries and ischemia, potentially creating a substrate for an arrhythmia. A proper cool down at the end of exercise can protect against this.
1.5 Why Screen Masters Athletes?

Despite the higher incidence of SCD in the middle-aged and older individual (≥ 35 years), research has primarily focused on pre-participation screening (PPS) in young competitive athletes. Since 1982, Italy has mandated screening for all athletes involved in competitive sports. During the 26-year study period Corrado et al. showed an 89% decline in the incidence of SCD\textsuperscript{15}. Similar large-scale studies do not exist in recreational or competitive middle-aged individuals; therefore, data is lacking. Strategies to ensure athletic pursuits are safe and appropriate, such as cardiovascular risk assessment and PPS, in both recreational and competitive Masters athletes, have been suggested to mitigate the risk. PPS is the systematic practice of medically evaluating athletes before participation in sports for the purpose of identifying (or raising suspicion of) abnormalities that could provoke disease progression or sudden death\textsuperscript{45}. The issue of cardiovascular PPS has been the topic of discussion in a number of countries, and most have focused on the young competitive athlete. No published data exist from any notable Canadian Health Organizations.

1.6 Aims:

To evaluate the prevalence of cardiovascular disease (i.e. coronary artery disease, valvular disease) and risk factors and to determine the best screening method for preventing SCD in a group of Masters athletes (recreational and competitive) in British Columbia.

1.6.1 Specific Aim 1:

To determine the prevalence of cardiovascular disease (i.e. coronary artery disease, arrhythmias, valvular disease, hypertrophic cardiomyopathy) that can potentially cause adverse cardiac events in the Masters athlete.

1.6.2 Specific Aim 2:

To determine the prevalence of a high cardiovascular risk profile (i.e. FRS ≥20) and/or a markedly raised single cardiovascular risk factor (i.e. diabetes mellitus, hypertension, > 8 mmol of total cholesterol, strong family history of premature cardiovascular disease) in the Masters athlete.
1.6.3 Specific Aim 3:
To evaluate the effectiveness (positive predictive value) of the screening tools (i.e. AHA cardiovascular personal and family history questionnaire, physical examination, 12-lead ECG, FRS) in detecting cardiovascular disease.

1.6.4 Specific Aim 4:
To determine the prevalence of atrial fibrillation in the Masters athlete (high performance and recreationally competitive) and its association with intensity of sport and volume of lifetime physical activity.

1.7 Hypotheses:

1.7.1 Hypothesis 1:
Approximately 3% of Masters athletes will be diagnosed with new CVD (i.e. coronary artery disease, valvular disease, arrhythmia, hypertrophic cardiomyopathy, long QT syndrome, short QT syndrome, Brugada syndrome, WPW, dilated cardiomyopathy).

1.7.2 Hypothesis 2:
Approximately 5% will have a high cardiovascular risk profile (i.e. FRS ≥ 20%). The recreational Masters athlete will have a higher prevalence of risk factors than the competitive Masters athlete.

1.7.3 Hypothesis 3:
The resting 12-lead ECG will be the most effective screening tool (highest positive predicative value) for detecting coronary artery disease or other indicated CVD in the Masters athlete.

1.7.4 Hypothesis 4:
We predict a 2% prevalence of atrial fibrillation in the Masters athlete with a higher prevalence in the older and endurance-trained athlete.
Chapter 2: Literature Review

The purpose of this chapter is to provide background information on Masters athletes and review the literature on how much exercise is enough and current perceptions on the potential deleterious effects of excessive endurance exercise. A version of this Chapter has been published\textsuperscript{46}.

2.1 History of Masters Athletics

Middle-aged individuals are exercising more and some even participate in sport at national levels\textsuperscript{47}. At the beginning of the 20\textsuperscript{th} century, middle or older aged athletes participating at a national level was unheard of. If they did compete, it was with younger athletes in cross-country and road races. Although, the beginning of Masters sports is unclear, it is generally accepted that its origins were in the mid-1960’s when the USA Masters Track and Field Team was formed in 1965. In 1972, David Pain created the first “Masters Mile” and in 1975 he took 152 U.S. and Canadian athletes to London, Helsinki, Stockholm, Gothenburg, and Cologne for athletic competitions, jump starting the Masters athletics movement. The first World Masters Games were held in 1985 in Toronto with more than 8,305 participants representing 22 sports. Since this first event, participation has continuously increased, with 24,500 participants in 1994, 24,886 participants in 2002, and 28,676 participants in 2009.

2.2 Sport in Canada

More than a quarter of Canadians participate in sport, with numbers highest amongst residents in BC, the Yukon and Northwest Territories\textsuperscript{48}. The rate of sport participation is highest in 15-17 year olds (75%), with numbers decreasing in subsequent decades (45% in 25-44 year olds, 30% in 45-64 year olds, and 20% in greater than 65 year olds). In those aged 18 and older, men are more likely to participate than women\textsuperscript{48}. The sports most frequently played are hockey, golf, baseball, softball, racquet sports, soccer, basketball, volleyball, skiing and snowboarding, with Canadians under the age of 45 more likely to play team sports and those over the age of 45 years more likely to engage in individual sports\textsuperscript{48}. Besides golf, which is the predominant sport of older athletes, participation in endurance sports such as cycling, marathons and triathlons is increasing\textsuperscript{48}. Increased participation in running is likely due to individuals becoming more
health conscious while wanting to take up a sport that requires little skill, is relatively inexpensive, and can be done on one’s own schedule.

2.3 Classification of Sports

Classifying sports according to their physiological (i.e. dynamic or static) impact on the cardiovascular system has been useful when providing sport eligibility recommendations to those who have known CVD. High intensity dynamic exercise requires maximal oxygen uptake, a substantial increase in cardiac output, heart rate, stroke volume, systolic blood pressure, and a decrease in diastolic blood pressure and peripheral resistance. In contrast, static exercise reflects maximal voluntary muscle contraction, causing a marked increase in systolic, diastolic, and mean arterial pressure, with a small increase in oxygen consumption, and little change in total peripheral resistance. Endurance sports typically require high dynamic demand and concomitant volume overload on the left and right ventricles increasing LV mass and chamber size (eccentric remodelling), whereas power sports have a high static demand, and elicit an increase in left ventricular wall thickness, with no change in chamber size, (concentric remodelling). From an energy system perspective, endurance sports involve a greater aerobic component, and power sports are predominately anaerobic. Mixed sports typically involve a combination of these two energy systems, and are frequently team sports. Recently, authors have investigated the type of sport (endurance, power, or mixed) and amount of physical contact, in relation to their impact on conditional survival (quantified additional life expectancy of medalists over the general population). Clarke et al. demonstrated that endurance sports had a relative conditional survival of 1.13, (95% confidence interval (CI) 1.09 to 1.17) and mixed sports (1.11, CI 1.09 to 1.13) had a larger survival advantage over the general population than those in power sports (1.05, CI 1.01 to 1.08). Increased mortality was seen in athletes with high levels of bodily collision (HR 1.1, 1.06 to 1.15) and high levels of physical contact (HR 1.16, 1.11 to 1.22). Similarly, Grani et al. investigated the incidence of sports related SCDs according to their sport category (dynamic versus static). They found that most cases occurred in category IC (33.3%), IIC (18.9%), and IIIA and IIIC (15.9% each), although overall incidence rates were not significantly different, except in the IIA category, owing to the few people in this category. There is also speculation that different types of sport, namely, endurance activities, may have deleterious effects such as atrial fibrillation, atherosclerosis, dilated cardiomyopathy, and
arrhythmogenic right ventricular cardiomyopathy, some of which may be fatal. Therefore, due to higher numbers of sports related SCDs in those with high dynamic and static components and/or possible deleterious effects, classification of sport in healthy individuals is important to consider\(^\text{49, 51}\) (Table 2.1).

**Table 2.1 Classification of sports\(^\text{49}\)**

<table>
<thead>
<tr>
<th>Sport Type</th>
<th>Dynamic Exercise</th>
<th>Static Exercise</th>
<th>Mixed</th>
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<tbody>
<tr>
<td>IIC</td>
<td>Endurance</td>
<td>Power</td>
<td>Endurance/Power (team sports)</td>
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<tr>
<td>Energy System</td>
<td>Aerobic</td>
<td>Anaerobic</td>
<td>Aerobic/Aerobic/Anaerobic</td>
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<tr>
<td>Examples</td>
<td>IIC</td>
<td>IIA</td>
<td>IIC</td>
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<td></td>
<td>Running (≥ 800m)</td>
<td>Bobsledding</td>
<td>Soccer</td>
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<td></td>
<td>Orienteering</td>
<td>Gymnastics</td>
<td>Field hockey</td>
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<td></td>
<td>Race walking</td>
<td>Martial arts</td>
<td>Racquet sports</td>
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<td></td>
<td>IIC</td>
<td>Rock climbing</td>
<td>IIC</td>
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<td></td>
<td>Swimming</td>
<td>Track and Field (throwing)</td>
<td>Basketball</td>
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<td>Cross-country skiing</td>
<td>Sailing</td>
<td>Ice Hockey</td>
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<td></td>
<td>IIC</td>
<td>Weightlifting</td>
<td>Lacrosse</td>
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<td>Cycling</td>
<td>IIB</td>
<td>Team handball</td>
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<td></td>
<td>Rowing</td>
<td>Weightlifting</td>
<td>IIB</td>
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<td>Paddling</td>
<td>Wrestling</td>
<td>Baseball</td>
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<td>Triathlon</td>
<td>Alpine skiing</td>
<td>Volleyball</td>
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<td>Decathlon</td>
<td>Snow boarding</td>
<td>IIB</td>
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<td></td>
<td>Speed Skating</td>
<td>IIC</td>
<td>Rugby</td>
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<td></td>
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<td>Boxing</td>
<td>Track and Field (i.e. sprints, jumping)</td>
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<td></td>
<td></td>
<td>IIA</td>
<td>IA</td>
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<td>Archery</td>
<td>Golf</td>
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<td>Diving</td>
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<td>Equestrian</td>
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<td>Motorcycling</td>
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Adapted from Mitchel et al\(^\text{48}\)

### 2.4 Effect of Aging and Physical Activity on Cardiovascular Function

In addition to the positive health-related dose-response changes that occur with regular exercise, a positive performance dose-response change also occurs in those that train regularly. Cardiovascular function naturally declines with age in both trained and untrained individuals, at approximately 5-12% and 6-8% per decade, after the second and third decades, for the aerobic
and anaerobic systems, respectively. The decline in aerobic capacity, measured by maximal oxygen uptake (VO$_2$max), is mostly attributed to a decline in heart rate max (HRmax) of approximately 0.8bpm/year.

Despite the reduction in HRmax, a concomitant reduction in VO$_2$max is not observed in Masters athletes, suggesting that oxygen pulse increases caused by regular training compensate for the decline in HRmax. For example, in a study comparing Masters long-distance runners and sprinters, both groups had higher levels of aerobic capacity compared to recreationally active individuals, with the endurance runners exceeding both of the other groups. In another study, an Olympic level rower preserved anaerobic exercise capacity to at least the age of 40.

In a cross-sectional study examining the anaerobic and aerobic systems collectively, a decline in anaerobic power and capacity in both sprint and road cyclists (aged 35-64) with no change in aerobic capacity was observed, concluding that age has a greater negative effect on the anaerobic system. Therefore, the probable effects of a decline in exercise capacity are the effects of sedentary lifestyles and co-morbidities rather than age.

Additionally, regular exercise has been shown to have positive effects on the arterial system, whereas age, a sedentary lifestyle, and an unhealthy diet, have negative effects, causing the arteries to become stiff and consequently increasing the workload of the heart. Regular exercise prevents stiffening by improving endothelial function, releasing vasodilators and enhancing the elasticity of the vessels. In a systematic review examining flow-mediated dilation (a measure of vascular health and a predictor of cardiovascular events) in Masters athletes compared to age-matched healthy controls, it was observed that high levels of exercise training attenuated age-related decline in vascular function.

Carrick-Ranson et al. sought to examine lifelong exercise dose on the metabolic and hemodynamic systems, by tracking exercise frequency. They reported four or more weekly sessions (aerobic activity lasting at least 30 minutes) over a lifetime (at least 25 years) was effective in preserving cardiovascular structure and function in seniors (60 years old and older). Specifically, VO$_2$max increased in a dose-dependent manner across the groups of exercisers,
being greatest in those committed to exercising (4-5 sessions/week) and Masters athletes (≥ 6 sessions/wk plus regular competitions). Improved ventricular-arterial coupling (relationship between the heart and arterial system, a determinant of cardiovascular health) and heart rate control (indicator of decreased sympathetic drive) during exercise was also greatest in these groups, with oxygen delivery and extraction improving in all trained groups (at least 2 sessions per week). Peak oxygen uptake and LV mass increased with escalating doses of lifelong exercise, with little change in systolic function. Low doses of casual lifelong exercise did not prevent the decreased compliance (had greater stiffness) and distensibility observed with aging.

These studies reiterate, a dose-response effect to exercise, but in relation to performance measurements, where more exercise elicits greater positive effects on VO₂max and related measurements (autonomic control, peripheral adaptations). For example, a minimum of 4 sessions a week, for at least 30 minutes attenuates the aging process, with greater advances in performance-related measurements when training 6 times or more a week.

2.5 How Much Exercise is Enough?

In addition to physiologic performance improvements that occurs with regular exercise, regular exercise is effective in the prevention and treatment of diseases such as hypertension, coronary artery disease (CAD), heart failure, obesity, and diabetes. According to the World Health Organization, a minimum of 150 minutes of moderate intensity or 75 minutes of vigorous aerobic activity per week is recommended to achieve health benefits. Similarly, the American College of Cardiology suggests moderate to vigorous intense physical activity for 40 minutes, 3 to 4 times per week. Abiding by these guidelines over 12 weeks has been shown to reduce low-density lipoprotein (LDL) cholesterol by 0.08 to 0.16 mmol/L and non–high-density lipoprotein (HDL) by 0.16 mmol/L. Additionally, aerobic physical activity decreased systolic blood pressure by 2–5 mm Hg and diastolic blood pressure by 1–4 mm Hg.

Although there are certainly benefits to exercise, recent research has focused on the high end of the exercise dose-response relationship, suggesting that chronic endurance training can have transient deleterious effects, but whether this translates to long term damage is still unclear. It is well known that vigorous exercise in unfit, sedentary individuals may trigger an adverse cardiac
event, but this remains true even in fit individuals\textsuperscript{13}. While obesity is on the rise in developed countries, there has been a simultaneous increase in the number of individuals participating in ultra-endurance events. Regular physical activity, such as running, is associated with lower mortality\textsuperscript{59, 60}. Recent studies have suggested an upper limit exists where additional physical activity provides no further mortality benefits, and may in fact increase mortality\textsuperscript{59, 61, 62}. Speculation exists that years of endurance training, may lead to long-term consequences, such as myocardial fibrosis, atrial fibrillation (AF), ventricular arrhythmias, and coronary artery calcification\textsuperscript{63, 64}. This leads us to the question - can there really be such thing as “too much exercise”? And on the other side of the coin, what is “enough exercise”?

With obesity and associated co-morbidities on the rise, several prospective studies have investigated ideal “doses” of exercise to decrease risk factors associated with these diseases, as well as the minimum amount required to decrease mortality. Wen et al. examined 416,175 healthy individuals aged 20 years or older who participated in a standard medical screening program with an average follow-up of 8.05 years\textsuperscript{60}. The low-volume activity group (equivalent to about 15 minutes per day) had a 14% reduced risk of all-cause mortality and a 3 year longer life expectancy. Every additional 15 minutes beyond the minimum amount further reduced all-cause mortality by 4%. However, levels more than 100 minutes per day of moderate activity or 50 to 60 minutes of vigorous activity per day saw no additional health benefits.

The Copenhagen City Heart Study observed 1,878 joggers and 10,158 non-joggers for up to 35 years\textsuperscript{65}. They found that joggers had a 44% lower risk of mortality during follow-up for both men and women with an increase in survival of 6.2 years in men and 5.6 years in women. In a subset of 5,048 patients, a U-shaped mortality curve with respect to frequency, pace, and quantity of jogging was observed. Compared to sedentary non-joggers, 1 to 2.4 hours of jogging per week was associated with the lowest mortality (HR 0.29, 95% CI 0.11-0.80). The optimal frequency of jogging was 2-3 times per week, at slow or average pace. Interestingly, the strenuous joggers did not exhibit a mortality rate statistically different from that of the sedentary group.
The Aerobics Center Longitudinal Study reported a similar reduction in mortality in runners versus non-runners. Among 55,137 adults, runners had a 30% lower adjusted risk of all-cause mortality (HR 0.70, 95% CI 0.64-0.77) and a 45% lower adjusted risk of cardiovascular mortality (HR 0.55, 95% CI 0.46-0.65), compared with the non-runners. The mortality benefits amongst runners were similar across quintiles of running time, distance, amount, frequency, and speed. The study found that running up to 51 minutes per week, 6 miles per week, 1 to 2 times, or 6 miles per hour was enough to reduce risk of mortality. In keeping with previous studies, researchers reported a U-shaped mortality curve and noted that the mortality benefit was slightly less with running for more than 176 minutes per week.

2.6 When Does Endurance Exercise Become “Excessive”?
At what point does mortality increase with exercise and what are potential explanations for this? There is no exact definition of “excessive endurance exercise.” Well-known endurance events include marathons (42 km), ultra-marathons (50 to 150 km), ironman triathlons (3.9 km swim, 180 km bike ride, and 42.1 km run), and long distance cycling races (more than 120 km). In preparation for these events, endurance athletes may train for several hours per day, often exceeding 200 to 300 MET (metabolic equivalent) hours per week - 20 to 30 times greater than the recommended amounts for mortality benefit.

2.7 What are the Potential Impacts of Excessive Endurance Exercise?
The effects of long-term endurance exercise are still unclear; however, an increasing amount of data suggests it may be potentially harmful (Figure 2.1). Evidence has revealed impairment of right ventricular (RV) function during and after exercise, RV arrhythmias, left atrial dilation, AF and atrial flutter, and coronary artery calcification in long-term endurance athletes. Although, increased left ventricle (LV) wall thickness is associated with endurance exercise, and to a greater extent in strength-emphasized activities, LV volume and function are not significantly affected. It is believed that the intrinsically thinner walls of the RV and atria could make them more susceptible than the LV to remodeling caused by volume and pressure overload from sustained high-output states.
Figure 2.1 U-shaped curve of mortality with increasing amounts of exercise. What is the point at which "Excessive Endurance Exercise" affects the heart?

RVEF, right ventricular ejection fraction; ARVC arrhythmogenic right ventricular cardiomyopathy

2.8 Myocardial Fibrosis

Extreme exercise has been associated with biochemical and functional evidence of acute myocardial damage and may also be associated with small areas of myocardial fibrosis secondary to episodic volume and pressure overload in the RV. La Gerche et al. investigated the potential relationship between endurance training and the effects on the RV and LV. They observed 40 asymptomatic athletes with structurally normal hearts who either participated in a marathon, endurance triathlon, alpine cycling race, or an ultra-triathlon who participated in at least 10 hours of intense training per week, or had finished in the top 25% in a recent endurance event.

Echocardiography and biochemistry (including cardiac troponin I levels) were performed at baseline (2-3 weeks pre-race), post-race (immediately after), and delayed (6-11 days post-race). Cardiac magnetic resonance imaging (CMR) was performed at baseline. When compared with baseline measurements, RV ejection fraction (EF) decreased significantly by 9% (p<0.0001), while LVEF was preserved. All athletes had detectable cardiac troponin elevations post-race and
levels correlated with depressed RV function. RVEF and biomarkers returned to baseline during the delayed measurements. Interestingly, there was a significant interaction between race duration, race completion time, and changes in RVEF. The change in RVEF correlated inversely with duration (p<0.0001) with the greatest reduction seen in those who completed the longest event. These findings suggest endurance exercise evokes transient declines in RV function.

CMR was used to assess fibrosis as a possible effect of endurance exercise\textsuperscript{64}. Five athletes (12.8\%) had delayed gadolinium enhancement (DGE) of the interventricular septum at the side of RV attachment. These athletes had spent a longer cumulative duration competing in endurance events and had a lower EF than those without DGE. This finding adds to the proposition that repeated bouts of intensive endurance exercise may lead to RV abnormalities. However, the study was not powered for the assessment of clinical events; therefore, it cannot be concluded that the short term changes result in cumulative injury or that the fibrosis in the RV results in a pro-arrhythmic substrate.

### 2.9 Ventricular Arrhythmias

Studies have suggested that long-term high-level exercise might be associated with an increased risk of cardiac arrhythmias, mainly those originating from the RV due to myocardial fibrosis, dysfunction, or underlying arrhythmogenic RV cardiomyopathy (ARVC)\textsuperscript{63, 73-75}. Heidbuchel et al. investigated the prevalence of RV involvement in 46 endurance athletes (median age 31 years, 80\% cyclists) with ventricular arrhythmias\textsuperscript{63}. Eighty percent of the ventricular arrhythmias were of left bundle branch block morphology suggesting an RV origin. Thirty-six athletes presented with symptoms that were attributable to ventricular arrhythmias. Nine were asymptomatic but had a complex ventricular arrhythmia documented (defined as $\geq$1 run of $\geq$3 beats of $\geq$120 bpm of non-sustained ventricular tachycardia [VT]). Twenty-seven athletes met the old diagnostic criteria for definite ARVC while 14 athletes met the criteria for borderline or possible ARVC based on the new criteria\textsuperscript{76}.

Eighteen athletes developed a major arrhythmic event with sudden death in nine - all of whom were cyclists. All but one episode occurred during light or moderate physical activity\textsuperscript{63}. Athletes with inducible sustained VT or ventricular fibrillation (VF) on electrophysiology (EP) study
(n=15) had a significantly higher risk for developing major arrhythmias during follow-up (RR 3.4; p=0.02). This study demonstrates that endurance sport may be related to the development and progression of underlying arrhythmic substrate, and that complex ventricular arrhythmias do not necessarily represent a benign finding.

2.10 Arrhythmogenic Right Ventricular Cardiomyopathy
ARVC has typically been described as an inherited condition. However, RV arrhythmias may exist without underlying genetic abnormalities. The hypothesis of the “unmasking of ARVC” in athletes is that stress is placed on the RV myocardium during vigorous exercise, which in turn disrupts the desmosomal proteins that anchor intermediate filaments between adjoining myocardial cells. This in effect reflects excess stress on the gap junction or desmosome reserve. With abnormal desmosomes, adjacent cardiomyocytes detach from one another and die, gradually being replaced by fat and fibrous tissue. This may result in a decreased RVEF and provide the substrate for malignant reentrant arrhythmias (Figure 2).

**Figure 2.2 Effect of repetitive endurance exercise on the right ventricle. Factors that contribute to the postulated reversible exercise induced RV changes.**

RV, right ventricle; LV, left ventricle
Ector et al. aimed to determine whether RV arrhythmias in 22 endurance athletes were associated with RV abnormalities, compared with matched endurance athletes and non-athletes without ventricular arrhythmias. Athletes with ventricular arrhythmias had a significantly lower RVEF compared to the matched control groups (area length method: 49.1 ± 10.4% vs. 63.7 ± 6.4%, p<0.001). These findings suggest that ventricular arrhythmias in endurance athletes likely originate from a mildly dysfunctional RV. Similarly, La Gerche et al. investigated athletes who performed moderate to intense exercise with complex ventricular arrhythmia of RV morphology. There were lower than expected rates of desmosomal mutations, leading to the conclusion that RV changes from intense endurance exercise can occur independent of a genetic predisposition.

These studies lead to the question of whether these athletes have a forme fruste of ARVC that is unmasked by RV mechanical loading conditions during intense endurance exercise or rather, have developed primary RV abnormalities from endurance exercise itself. In athletes with a genetic predisposition to ARVC, cell adhesion may be more vulnerable to shear stress, which may only become clinically apparent under the conditions of repetitive endurance exercise. The six major genes involved in ARVC have immense natural variability: these allelic differences may predispose to desmosome dysfunction in the context of pressure or volume overload. Recent evidence in both exercise surveys in ARVC patients and animal models support a strong interaction between exercise and severity of disease expression. ARVC is inherited with incomplete penetrance and has variable phenotypic expression, suggesting a role for environmental influences.

When Sawant et al. studied 82 ARVC patients, they found that the 43 patients who did not have desmosomal mutations (i.e. they were diagnosed with gene-elusive, non-familial ARVC) were more likely to be endurance athletes (p<0.001) and to participate in more intense exercise prior to presentation compared with those with desmosomal ARVC (p<0.001).

James et al. sought to determine how exercise might influence penetrance of ARVC among patients with known desmosomal mutations by looking at a group of 87 mutation carriers. After identifying 56 subjects who exercised at >70% VO₂max for at least 50 hours per year, they
found these endurance athletes were more likely to meet the ARVC 2010 Task Force Criteria at last follow-up (82% vs. 35%, p<0.001), and that this finding was associated with increasing hours per year of exercise (p<0.001). Interestingly, a reduction in exercise after initial presentation actually decreased VT/VF risk (p = 0.04). Among the 16 individuals who did the most exercise before presentation and continued to do top quartile exercise after presentation, 6 of 8 (75%) had a first VT/VF in follow-up, whereas only 1 of 8 (12%) who decreased exercise after initial presentation had VT/VF in follow-up. This was one of several findings leading the researchers to conclude that frequent endurance exercise increases the risk of VT/VF and ARVC in desmosomal mutation carriers.

In an animal model, rats exposed to endurance exercise developed eccentric LV hypertrophy, diastolic dysfunction and atrial dilation after 16 weeks of vigorous running. The rats also had significantly greater collagen deposition and fibrosis markers in the RV and atria, and had a higher likelihood of inducible VT (p=0.05). After 8 weeks of detraining, the majority of abnormal cardiac remodeling parameters returned to control levels. However, it is difficult to determine if an animal model can accurately reflect the human response. The human equivalent to the intensity of the rats’ exercise would be approximately 10 years of daily exercise training at 90% of predicted maximal heart rate. Also, the study looked only at complete cessation of exercise rather than with a decreased amount and intensity of exercise. This training and detraining pattern would be less likely to hold true in humans, and thus the reversibility of the changes seen in the rats might not apply to humans.

2.11 Atrial Fibrillation

Recent data has documented a higher prevalence of AF in long-term endurance sport. Most are thought to be lone AF (individuals < 60 years old and without any identifiable etiological factor). Karjalainen et al. were the first to identify a relationship between endurance sport and AF in cross-country runners, with a 5.5 odds ratio for AF associated with vigorous exercise. Elosua et al. demonstrated similar results with a three times higher prevalence of lone AF and five times higher prevalence of vagal AF in those who reported current sport practice versus controls. In a prospective study of high-performance male participants in endurance cross-country ski competitions, there was a 12.8% prevalence of lone AF after approximately 30 years
of follow-up\textsuperscript{84}. Furthermore, a comparison of former professional cyclists (mean age 66 ± 7 years) with a control group demonstrated a 10 % vs. 0 % prevalence of AF\textsuperscript{71}.

The mechanisms proposed for development of AF with excessive endurance exercise appear to be multifactorial. Volume overload, stretching of the thin-walled atria and myocardial damage may result in atrial remodeling and development of fibrosis over time\textsuperscript{85, 86}. Other mechanisms include increased atrial ectopic beats, shifts in electrolytes, increased vagal tone and bradycardia, and inflammatory changes\textsuperscript{81, 86}. The exact relationship between increased atrial size in endurance athletes and AF development has yet to be established in clinical studies\textsuperscript{69}.

The fact that atrial fibrillation is seen predominately in middle-aged athletes engaged in sport activities over a long time period suggests that years of endurance training is necessary to development AF. Lifetime training hours have been used in recent studies examining atrial fibrillation, to determine optimal amounts of exercise and to better understand thresholds or potential ‘overdoses of endurance exercise’\textsuperscript{69, 82}. Brugger et al, studied male amateur runners over 30 years of age and stratified them into 3 groups based on lifetime training hours: low (< 1,500 hours), intermediate (1,500 to 4500 hours) and high (> 4500 hours) training groups\textsuperscript{69} and observations show presence of lone atrial fibrillation with more than 1,500 hours of sport practice\textsuperscript{82}. Stratification of former and current sporting hours will be useful in reporting possible associations with the prevalence of atrial fibrillation and/or other acquired CVD; however, studies quantified lifetime training hours in amateur athletes and endurance sport. Whether or not overall lifetime training hours that includes all types of sports and if it can be adjusted to include individuals who have been lifelong exercisers, remains to be determined.

\subsection{2.12 Atherosclerosis}
Endurance exercise presumably protects against coronary artery plaque formation as marathon running has been shown to reduce cardiovascular risk factors\textsuperscript{72}. However, Mohlenkamp et al. quantified coronary artery calcification using computed tomography and found that despite having Framingham Risk Scores lower than age-matched controls, male marathon runners had calcium scores not significantly different from those of controls\textsuperscript{87}. A coronary artery calcium score \(\geq 100\) was present in 36\% of runners. Similarly, Schwartz et al. assessed 50 veteran male marathon runners and 23 sedentary controls using coronary computed tomographic angiography.
The two groups were similar in age, resting blood pressure, height, smoking history, total cholesterol, and LDL levels. Marathon runners had significantly lower resting heart rate, weight, body mass index, triglyceride levels, and higher HDL levels. However, compared to controls, the marathoners had a higher total plaque volume, calcified plaque volume and non-calcified plaque volume. However, there was no difference in the lesion prevalence, diameter of the stenosis, lesion area, or lesion length\textsuperscript{72}.

The metabolic and mechanical stress to coronary arteries generated by excessive running offers a potential explanation for the increased coronary artery atherosclerosis in the marathoners. Michaelides and colleagues found that exercise prolongation for as long as 60 minutes resulted in higher oxidative stress and vascular endothelial dysfunction with deterioration of vascular elastic properties\textsuperscript{88}. Increased sustained levels of catecholamines, persistent and prolonged tachycardia and blood pressure could also contribute to atherosclerosis\textsuperscript{72}. In addition, many of the runners started marathon running in middle age, which may have reduced their cardiovascular risk factors in terms of FRS, but not their life-long risk exposure to poor lifestyle habits. More than half the runners in the Mohlenkamp et al. study were former smokers and 5% were current smokers\textsuperscript{87}. Marathon runners may also believe that exercise negates a bad diet\textsuperscript{72, 87}. 
Chapter 3: Cardiovascular Pre-Participation Screening and Risk Assessment in the Masters Athlete

The purpose of this chapter is to review current pre-participation screening recommendations, other proposed pre-participation screening tests, methods to assess cardiovascular risk, and other risk-mitigating strategies in the Masters athlete. A version of this Chapter has been published.

3.1 Introduction

Various PPS and risk stratification strategies are currently available ranging from self-administered protocols to those incorporating healthcare professionals. These protocols were developed for use in the general population, but have been incorporated into most athletic settings. Leading agencies such as the American Heart Association (AHA), the American College of Sports Medicine (ACSM), and the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) have created important PPS recommendations for the general population. PPS and risk stratification prior to engaging in physical activity programming and/or exercise testing have been widely considered as a standard of practice with significant medico-legal implications. Recent advancements in PPS and risk stratification strategies (such as the creation of the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and electronic Physical Activity Readiness Medical Examination (ePARmed-X+)) have reduced greatly the barriers to physical activity participation for apparently healthy individuals and individuals with established chronic medical conditions across their lifespan.

3.2 Pre-Participation Screening for Athletes

Owing to the medico-legal implications and importance of PPS the inclusion of simple (often self-administered) surveys (such as the PAR-Q+ and the AHA/ACSM Health/Fitness Facility Pre-participation Screening Questionnaire) is considered to be the standard of practice when working with young and Masters athletes. However, many agencies have recommended more comprehensive risk assessment batteries when dealing with athletes. This is an area of considerable debate with PPS recommendations and protocols varying widely across agencies and countries. For instance, there are clear differences in the PPS recommendations between the European Association of Cardiovascular Prevention and Rehabilitation (EACPR),
and AHA\textsuperscript{7,92} (Table 4.1). The EACPR suggests an individual approach, in which the level of testing required depends on the intended level of physical activity/exercise and self-assessment of risk (i.e. PAR-Q+ or AHA/ACSM questionnaires)\textsuperscript{92}. Comparably, the AHA, recommends selective screening involving a history, physical examination, resting ECG of all Masters athletes and a maximal exercise treadmill test in Masters athletes above the age of 40 years (men) or 50 years (women) with one additional cardiovascular risk factor\textsuperscript{7}.

In a recent longitudinal survey of training and health aspects among runners aged 35 and older, slightly over half who met the criteria for pre-participation evaluation reported a physician visit, and those who did go to a health care provider, the health care provider’s decisions to perform a pre-participation cardiovascular evaluation was only associated with age (OR 1.071; 95\% CI 1.021-1.123) and the provider’s decision to perform an ETT was independently associated with age (OR 1.055; 95\% CI 1.026-2.294) and competitive goals (OR 1.521; 95\% CI, 1.009-2.294)\textsuperscript{94}. Traditional risk factors did not appear to influence pre-participation evaluation decisions.
Table 3.1 Two approaches to recommendations for physical activity clearance and pre-participation screening in athletes

<table>
<thead>
<tr>
<th>Physical Activity Clearance:</th>
<th>Pre-Participation Screening for Athletes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self and Health-Care Professional Administered Questionnaires</td>
<td>Individual Approach (European Association of Cardiovascular Protection and Rehabilitation)</td>
</tr>
<tr>
<td>1. Physical Activity Readiness Questionnaire for Everyone (PAR-Q+)</td>
<td>All adult/senior non-professional engaged in vigorous activity</td>
</tr>
<tr>
<td>2. Electronic Physical Activity Readiness Medical Examination (ePAR-Q+)</td>
<td>Athletes engaged in moderate activity whose physical activity clearance assessment (i.e. results from PAR-Q+ or AHA/ACSM questionnaires) has identified risk</td>
</tr>
<tr>
<td>3. AHA/ACSM Health/Fitness Facility Pre-participation Screening Questionnaire</td>
<td></td>
</tr>
</tbody>
</table>

**Eligibility for pre-participation screening**
- All adult/senior non-professional engaged in vigorous activity
- Athletes engaged in moderate activity whose physical activity clearance assessment (i.e. results from PAR-Q+ or AHA/ACSM questionnaires) has identified risk
- All Masters athletes > 40 years

**Pre-participation screening components**
- History
- Physical examination
- Systematic Coronal Risk Evaluation (SCORE)
- Resting ECG
- History
- Physical examination
- Resting ECG

**Criteria for maximal exercise treadmill testing**
- Presence of alarming symptoms
- Abnormal physical examination results
- High-risk SCORE profile
- Abnormal resting ECG
- Symptoms suggestive of coronary artery disease
- Moderate-to-high cardiovascular risk profile: men >40 years, women >50 years with ≥ 1 risk factor
- All athletes ≥ 65 years
3.3 Pre-Participation Screening Methods

3.3.1 Cardiovascular Risk Factors

Knowing one’s risk factors has shown to be successful with more favourable outcomes\textsuperscript{19, 95}; however, many are unaware they have cardiovascular risk factors such as hypertension, diabetes, or dyslipidemia. In a recent study, men and women were asked to estimate their cardiovascular risk. Only one in four adults were able to accurately estimate their risk\textsuperscript{96}. Women tended to overestimate their risk, while men and older adults were more likely to underestimate their CVD risk. Studies show the greatest improvement on individuals’ cardiovascular risk occurs when risk profiles are discussed and given to the patient\textsuperscript{95}. Calculating one’s cardiovascular risk score is one way to determine one’s risk and has been extensively studied\textsuperscript{92, 95}. Since the 1940’s, when the death rates for CVD had been increasing steadily since the beginning of the 20\textsuperscript{th} century, researchers, with origins in the town of Framingham, Massachusetts, studied the common factors that contribute to CAD. Since its first publication in 1950, there are now a total of 3,221 publications from the Framingham Study. Non-modifiable (i.e. age and sex) and modifiable (i.e. dyslipidemia, hypertension, smoking, diabetes, obesity, physical inactivity) cardiovascular risk factors, have been identified, which has led to the development of the FRS.

3.3.2 Cardiovascular Risk Scores

Cardiovascular risk scores to predict a person’s 10-year risk of cardiovascular disease has been widely accepted and varies slightly in different countries. In Europe, the SCORE system takes into account age, sex, blood pressure, cholesterol and smoking history\textsuperscript{92}. An individual is considered high risk if they have one of the following: a 10 year risk score >5%; elevated total blood cholesterol (>8 mmol); elevated LDL (>6mmol); blood pressure greater than 180/110 mmHg; diabetes with microalbuminuria; family history of premature CVD in first degree relatives < 50 years of age; and/or BMI >28 kg/m\textsuperscript{2}. Similarly, the United States and Canada use the FRS in 30 to 74 year olds with unknown CVD. The FRS includes age, blood pressure, total cholesterol, HDL cholesterol, smoking history, and whether or not medication for blood pressure is taken\textsuperscript{95}. The latest modified FRS also includes history of premature CVD, resulting in a doubling in the FRS in those aged 30-59, if CVD is present in a first-degree relative before 55
years of age for men and 65 years of age for women. The patient’s risk is categorized into one of three categories: 0-9% (low), 10-19% (intermediate), and ≥20% (high). It is highly advocated by consensus groups that cardiovascular risk be assessed routinely, with the frequency depending on the presence and severity of risk markers.

3.3.3 Physical Fitness
Currently, the level of physical activity or physical fitness is not incorporated into the FRS risk assessment. Previous studies show that incorporating level of physical fitness may offer additional information identifying less fit or less active individuals at high risk, similar to the FRS. Metabolic equivalents units (METS) is one way to measure energy expenditure. It is the ratio of the rate of energy expenditure during an activity to the rate of energy expended at rest. One MET is the rate of energy expenditure while sitting at rest and is equal to an oxygen uptake of 3.5 millilitres of oxygen per kilogram per minute. Balady and colleagues showed that for each MET increment in exercise capacity (i.e. from 12 METS to 13METS) reduced risk by 13%. Similarly Blair et al. found that for each minute increase in maximal treadmill time there was a 7.9% decrease in risk of mortality. Myers et al. reported similar risk reduction of 10-25 % for every 1 MET increase (in men and also women). In those with lower aerobic capacities, the risk reduction is reportedly even greater (approximately 30% per 1-MET increase).

Due to the relationship between physical activity and its health benefits, researchers wanted to code physical activity by type and intensity. Ainsworth et al., initially in 1993, and its most recent version in 2011, estimated the energy cost for each individual physical activity by creating a Compendium of Physical Activities. Based on the type of physical activity and intensity of the exercise (assessed using several different methods such as motion sensors (pedometers, accelerometers, activity trackers), heart rate monitors, or physical activity questionnaires and interviews), there is an associated MET value. Absolute intensity of activities can be stratified into three groups: low intensity (1.8-2.9 METS), moderate intensity (3-6 METS) and vigorous intensity (≥ 6METS). Those who participate in Master’s events such as long-distance cycling, city marathons, long distance cross-country skiing and triathlons engage in regular vigorous exercise much above 6 METS, with trained athletes exceeding 12-15 METS for sustained periods. Weekly volume of activity can then be calculated by multiplying intensity (METS) by duration (in minutes or hours). This is also known as metabolic equivalent task hours per week.
Training volumes are useful in determining the extent of cardiovascular physiological adaptations and potential strain on the heart. Marijon et al. reported most incidences of exercise related sudden deaths occurred during moderate (56.4%) and vigorous (39.7%) exercise, versus light activity (3.9%). Due to the increased transient risk of SCD during exercise, consensus documents suggest that those who exercise vigorously (> 6METS), should undergo an exercise treadmill test. One limitation of measuring in absolute METS is that it neglects variations in physical fitness: an activity requiring a particular MET value demands greater exertion from an individual with less physical fitness than someone that is more fit. Absolute intensity was calibrated on the basis of physical effort required by healthy, young to middle-aged adults, therefore relative intensity is useful in older, less physically fit adults. Additionally, the use of 3.5 mL/kg/min as the denominator to denote one MET has been criticized. It represents the resting metabolic rate (RMR), however, the RMR is lower in overweight persons, declines with age, and is lower in females than males. Although there are methods to correct for weight-specific energy costs, Ainsworth et al. report that expressing the energy cost as a “corrected MET” has not been shown to be a superior approach.

3.3.4 Psychological Stress

Psychological stress has been associated with the development of premature CAD. The INTERHEART study showed it is the third highest attributable risk factor for an acute myocardial infarction only behind smoking and lipid concentrations. The INTERHEART study investigated the association of psychosocial risk factors and the risk of MI, by studying 11,119 patients who had one previous MI and 13, 648 age-matched controls free of clinical heart disease from 262 countries. Psychosocial factors included perceived stress (work, home and financial stress), major life events, locus of control, and depression. Locus of control questions were derived from Bobak et al. and the depression questions were an adaptation of the short form DSM-IV CIDI questionnaire for depression. Locus of control and depression are important to consider, as many don’t perceive them as stressors, but negatively affects cardiovascular risk. For instance, those with a low locus of control had an increased risk of MI (OR 0.89, 99% CI; 0.80-0.98) compared to those with a high locus of control (OR 0.68, 99% CI; 0.61-0.76). Perceived stressors such as permanent work (OR 2.14, 99% CI; 1.73-2.64) or home
stress (OR 2.12, 99% CI; 1.68-2.65) had increased risk of MI compared to some work stress (OR 0.95, 99% CI 0.84-1.08) and home stress (OR 1.05, 99% CI; 0.97-1.13).

Reputable organizations such as the ESC recognize the importance of assessing psychological risk factors and recommend systematic screening for psychosocial risk factors such as low socio-economic status (low job status, mandatory education, low income), social isolation, chronic family conflicts, chronic work stress, acute stress (outburst of anger, acute anxiety), negative emotional stress (i.e. depression, vital exhaustion, anxiety, high frequency of anger), and negative personality patterns (i.e. hostility) due to their association with pathogenic mechanisms\textsuperscript{105}. For instance, psychological stress may contribute to CVD risk via activation of the sympathetic nervous system (SNS)\textsuperscript{106}. An increased SNS activity increases heart rate, myocardial contractility, and vascular resistance, which create an increase in arterial pressure and blood flow turbulence. Both an increase in arterial pressure and turbulent blood flow can damage the endothelial lining which is a substrate for the pathogenesis of atherosclerosis\textsuperscript{107}. Permanent injury of the vasculature may occur when there is repeated exposure to short term stress. SNS activation also promotes, catecholamine release, general platelet aggregation, altered plasma viscosity and/or fibrinolytic activity, endothelial dysfunction, release of proinflammatory cytokines, polymorphism of the serotonin transporter gene promoter, and hypercortisolemia\textsuperscript{108}. Therefore, assessment of patients' exposure to both repeated acute mental stress and chronic stress may be useful in determining their risk of developing CV disease\textsuperscript{107}.

### 3.3.5 Lifestyle Factors

Diet (daily consumption of fruits and vegetables and red meat), smoking, and alcohol consumption are risk factors that can be modified to decrease the risk of premature CAD; daily intake of fruits and/or vegetables, less than 2 servings of red meat a week\textsuperscript{100,109}, and less than 7 servings of alcohol per week are protective\textsuperscript{110}. Conversely, heavy drinking (men $\geq$ 21 drinks /week; women $\geq$ 14 drinks/week) have an increased risk of all-cause mortality, possibly due to cirrhosis, cancer and violence\textsuperscript{110}. Current smoking was attributed as the strongest risk factor (odds ratio, 2.95 99% CI) with risk increasing at every increment, with former smoking associated with a smaller risk ratio\textsuperscript{109}.
3.3.6 Personal Symptoms, Family History Questionnaire and Physical Examination

The AHA 14-element and the Pre-Participation Physical Evaluation (PPE) monograph has been used in young competitive athletes to detect or raise suspicion of genetic/congenital abnormalities\textsuperscript{111,112}. The PPE includes 12 personal and family history questions derived from the AHA guidelines and uses slightly different wording and syntax. A history or physical examination that raises suspicion for a potential abnormal screen and requires further evaluation includes: angina during exertion, cardiac-related syncope and/or presyncope during and after exertion for no apparent reason, exertional dyspnea or unusual fatigue out of proportion to the degree of physical effort, palpitations during exercise, unexplained seizures, family history of unexplained SCD before 50 years of age in first or second degree relative (includes unexplained car accident, sudden infant death syndrome or drowning), a family history of CVD in a first degree relative less than 50 years, and/or a family history of HCM, arrhythmogenic right ventricular cardiomyopathy (ARVC), long QT syndrome, short QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia or other potentially disabling CV disease (i.e. bicuspid aortic valve). The physical examination is deemed positive if blood pressure is $> 180/110$ mmHg on more than one reading, mid or end-systolic clicks, abnormal second heart sound (single or widely split and fixed with respiration), any diastolic murmur, systolic murmur $\geq 2$, weak femoral pulses indicative of aortic coarctation, morphological features of Marfan syndrome, and irregular heart rate.

A meta-analysis examining the utility of family history and physical examination in screening for CVD reported a low sensitivity of 20% and 9%, respectively\textsuperscript{113}. Undoubtedly, this leads to high false positive rates and subsequent physician referrals. In the Masters athlete, data to support its effectiveness as a screening tool is non-existent, and therefore, the sensitivity in this population is unknown. Given that the primary cause of SCD in athletes over 35 years is CAD, it is important to elicit, on history, specific symptoms (i.e. angina, syncope and/or presyncope during or after exertion, unusual fatigue, dyspnea, and palpitations) and family history of CVD. The physical examination is important for detecting valvular disease, and hypertension, which has a high prevalence in the Masters athlete\textsuperscript{114-116}. However, studies have shown cardiovascular physical examination to have a high inter-observer variability, which limits its usefulness as an
initial screening tool\textsuperscript{117}. Physician availability and concomitant cost are other barriers to consider.

### 3.3.7 Resting 12-Lead Electrocardiogram

The ongoing debate between European and U.S. Sports Cardiology experts on whether or not to include a resting ECG for PPS resides in the sensitivity and specificity of the test and justification of the cost\textsuperscript{118}. However, most of this debate resides in screening of young competitive athletes, and has yet to be determined in the Masters athlete. The high false-positive concern is a result of training related abnormalities (physiologic) being considered pathologic. As such, ECGs should be analyzed by an expert (i.e. sports cardiologist) and should be considered with respect to age, gender, ethnicity, level of training/competition, workload of the sport, and/or aerobic capacity specific to the sport\textsuperscript{119}. Additionally, they should be evaluated according to the newest criteria. Recommendations for the interpretation of the 12-lead ECG in athletes were initially published by the ESC in 2005 and again in 2010 \textsuperscript{36, 120}. The ‘Seattle Criteria’, released in 2013, made a series of revisions to improve the specificity of ECG screening in athletes. Brosnan et al. compared the ESC criteria to the ‘Seattle Criteria’ and found that the latter reduced the false-positive rate of ECG screening from 17\% to 4.2\% while still identifying the athletes with a cardiac abnormality\textsuperscript{121}.

Training-related ECG abnormalities occur as a result of intense physical training over months or years (minimum of 4h/week). The resultant physiologic ECG patterns can be observed in 60-80\% of athletes and include bradycardia, sinus arrhythmia, first-degree atrioventricular block, early repolarization, incomplete right bundle branch block, and voltage criteria for left ventricular hypertrophy (Appendix H)\textsuperscript{122}. Individuals with left ventricular hypertrophy (seen in both strength and endurance athletes) on 12-lead ECG do not require follow-up unless the pattern of hypertrophy is accompanied by other non-voltage criteria and/or they have other risk factors suggestive of CVD (i.e. long standing high blood pressure) \textsuperscript{122}. These ECG changes have been coined as changes seen in the “athletes heart”. In contrast, ECG training-unrelated changes require follow-up (Appendix H).
Masters athlete specific criteria does not exist, therefore the ‘Seattle Criteria’ has been used in this population. In comparison to the young athlete, where congenital abnormalities are the primary concern, when examining ECG changes in the Masters athlete, ECG changes indicative of CAD should be considered more seriously. Although the resting ECG has limited value of accurately detecting flow-limiting coronary artery disease (CAD), ECG markers such as ST-segment depression, pathological Q-waves, PVCs, ventricular arrhythmias, and criteria for LVH should be considered for further investigation as they are potential indicators for underlying CAD. Subclinical cardiac disease (i.e. prior myocardial infarction, LVH, fibrosis) and many CVDs (i.e. arrhythmias, ion channelopathies, arrhythmogenic right ventricular cardiomyopathy, and hypertrophic cardiomyopathy) may be clinically silent and can be detected by ECG before the onset of symptoms.

The resting ECG can provide further information on the autonomic nervous system (ANS). Autonomic imbalance is a term used to indicate a relative or absolute decrease in vagal activity or an increase in sympathetic activity, which could provide important information in predicting the risk of SCD. There is a significant relationship between abnormalities in the ANS and cardiovascular mortality from arrhythmic and myocardial causes. When sympathetic activity is increased or reflex vagal activities are reduced, risk of death increases. However, at this time an ANS based risk assessment has a predictive value that is likely too low to make such studies useful for first line SCD screening. Well-standardized tests that are easily obtained and can be readily interpreted may allow ANS tests to be used more routinely in the future.

3.3.8 Exercise Treadmill Test

The exercise treadmill test (ETT) is a well-known predictor for arrhythmias and flow-limiting CAD. It has also been advocated as a prognostic tool in risk stratifying those at risk for SCD by considering the degree of ST-segment depression, hypotensive blood pressure response, hypertensive blood pressure response, complex ventricular ectopy, and reduced exercise capacity. The Framingham Offspring Cohort study examined subjects with no history of CAD over 18.2 years and discovered that (after adjustment of their cardiovascular risk score (FRS) and age), failure to reach target heart rate (HR, 1.70; 95% CI, 1.18 to 2.45), ST depression (HR 1.88, 95% CI, 1.21 to 2.95), and exercise tolerance (METS achieved) (HR per MET 0.94; 95% CI 0.89 to
0.99), were strong predictors of CAD risk in men. In women, similar results were seen but were not statistically significant. Mora et al. emphasized the utility of risk stratifying female participants using ETT and confirmed that ST-segment response did not predict future risk for CAD events, whereas low exercise capacity and low heart rate recovery after exercise were independent predictors of death from CAD (RR 3.52) and all-cause mortality (RR 2.11). Jouven et al. also reported the value of examining the heart rate profile during exercise and in recovery in apparently healthy persons. Results showed that the risk of SCD was increased in subjects with: higher resting heart rate that was greater than 75 bpm (RR, 3.92; 95% CI, 1.91 to 8.00) an increase in HR during exercise that was less than 89 bpm (RR, 6.18; 95% CI, 2.37 to 16.11), and in those with a decrease in heart rate of less than 25 bpm per minute in recovery (RR, 2.20; 95% CI, 1.02 to 4.74). These findings suggest there is a greater risk of SCD associated with ability to not only increase vagal but also adjustment of sympathetic activity to appropriate levels.

Despite the ETTs prognostic value in risk stratifying those at risk of SCD, the US Preventative Task Force (USPTF) recommends against routine ETTs to determine the presence of severe CAD or prediction of CAD events in adults with no CAD symptoms or risk factors. They argue that the ETT can detect severe CAD only in a small number of asymptomatic adults and that the potential harms of screening, such as false positives and over treatment, exceed the potential benefits. However, the sensitivity and specificity for CAD has mostly been derived from experience in those with suspected CAD or symptomatic persons. For example, in those with ST depression the ETT detected CAD with a mean sensitivity of 68% (range 23-100%) and a mean specificity of 77% (range 17-100%). Similarly in those with CAD or suspected CAD, the ETT was 79.4% sensitive, 80.4% specific, and had a 75.0% positive predictive value. However, in these studies patients had suspected disease therefore, Froelicher et al. attempted to examine the sensitivity in a group with reduced workup bias, and found a sensitivity of 45% and specificity of 85%. Another study, attempted to examine the predictive value of the ETT in asymptomatic males with and without cardiovascular risk factors. They found the predictive value improves as the number of cardiovascular risk factors increases (i.e. age-adjusted RR of an abnormal ETT for CAD death was 21 in those with no risk factors, 27 in those with one risk factor, 54 in those with 2 risk factors, and 80 in those with ≥ 3 risk factors).
Another potential limitation of the ETT is that a “truly” positive ETT requires the presence of a flow-limiting coronary lesion, whereas most acute coronary events evolve from vulnerable plaque rupture at mild-to-moderate stenosis and are less likely to be detected on such a test. In athletes that have a moderate-to-high risk of CVD, yet a high fitness level (maximal exercise tolerance > 10 METS), CAD and associated symptoms can be potentially silent on an ETT (thereby creating false reassurance), suggesting that imaging tests should be considered even in the setting of a negative ETT. Sofi et al., attempted to evaluate the clinical usefulness of the ETT in examining competitive athletes. They found that the ETT does detect clinically significant CVD and has value in screening. Similarly, Kim et al. examined the clinical characteristics of cardiac arrests by interviews, medical records, and post-mortem data in approximately 10.9 million runners and conferred that the ETT should be included in PPS for high-risk individuals (middle-aged or older men with symptomatic or asymptomatic myocardial ischemia) based on the fact that HCM and ischemic CAD accounted for the majority of deaths.

In Canada, the Canadian Cardiovascular Society recommends secondary testing (i.e. ETT) in those with an intermediate risk (10-19% FRS after adjustment for family history) and who are not candidates for lipid treatment based on conventional risk factors or for whom treatment decisions are uncertain. In those with a low FRS, secondary testing is recommended in those with a strong family history of premature CAD.

### 3.3.9 Biomarkers

Serological markers, such as cardiac troponins I and T and brain natriuretic peptide (BNP) are the accepted standards for identifying myocardial damage and elevated wall stress. Assessment of the presence of biomarkers in athletes has mostly been examined during or directly after a marathon run with numerous studies reporting a significant increase. However, recent findings suggest these normally reduce back to normal levels within 24-48 hours and are representative of transient and reversible alterations of the cardiac myocytes without negative clinical consequences. Postulated reasons for the increase include race duration, intensity, age, training status, but data lacks consistency. Aagard et al. investigated the effect of biomarkers and its association between autonomic tone changes and post-exertional...
high-sensitivity troponin (hsTnT)\textsuperscript{140}. They found that more marked and pronounced changes in autonomic tone were associated with higher levels of hsTnT. This suggests that the magnitude of strenuous exercise may reflect the magnitude of exercise-induced cardiovascular stress. However, adequate rest, especially in those less fit and older individuals, appears sufficient to allow for complete recovery\textsuperscript{140}. Another biomarker, N-terminal prohormone brain natriuretic peptide (NTproBNP) has been studied in patients with heart failure and CAD with associations between BNP and SCD or ventricular arrhythmias\textsuperscript{124, 141}. Collagen turnover and C-reactive protein markers have also been examined in heart failure or post-MI patients, but to a much lesser degree\textsuperscript{142}. Further research needs to examine the value of adding bio and genetic markers reflecting atherosclerosis, coagulation, inflammation, neuro-hormonal status and ventricular function to present cardiovascular risk assessment scores to determine whether and when advanced diagnostics are appropriate\textsuperscript{124}. Therefore, until the long-term effects and predictive capabilities of biomarker assessment is understood, including biomarkers as part of the PPS doesn’t seem feasible.

3.4 Cardiovascular Imaging
Cardiovascular imaging as a first line tool in screening may not be appropriate due to concerns with cost-effectiveness, accessibility and radiation exposure. However, improvements in cardiovascular imaging technology coupled with improvements in therapeutic options for CVD have led to an increased consideration of cardiovascular imaging as possible viable options for pre-participation screening\textsuperscript{133}. Whether or not imaging tests has incremental value over routine risk factors for predicting major adverse cardiovascular events remains to be elucidated.

3.4.1 Echocardiograms
Many professional organizations that are privately funded (i.e. the International Federation of Association Football, the International Cycling Union, and the U.S. National Basketball Association) include echocardiography (echo) as part of the first line screening process, whereas, scientific associations (i.e. European Society of Cardiology (ESC) and AHA) do not recommend the echocardiograms as part of the pre-participation screening process. Echocardiography is relatively inexpensive, accessible, free of any direct adverse effects and can detect disorders not always evident on the ECG (i.e. coronary anomalies, proximal aortic dilation, bicuspid aortic
valve, mitral valve prolapse, some cardiomyopathies, and other forms of left ventricular dysfunction), making it a logical candidate as pre-participation screening modality. However, discriminating between physiological and pathological cardiomyopathies in high level athletes can be difficult and runs the risk of inappropriately excluding athletes and limited or no efficacy in detecting pathological disease with potential for SCD. In attempt to examine the predictive value of the echo in detecting those at risk for SCD, Aagaard et al. included an echo, along with a personal symptoms questionnaire, physical examination, and ECG in screening male endurance runners. They confirmed that the echo did not detect disease at risk for SCD beyond that discovered using the ECG, physical examination and personal symptoms questionnaire. The echo may be of use in younger athletes as it was shown to improve false-positive rates, reduce referrals, and broaden the spectrum of disease captured through pre-participation screening, but it is not currently recommended by consensus groups. The echo could play a prognostic role in identifying age-associated, subclinical CVD (increased epicardial adipose tissue fat, decline in diastolic function, and longitudinal and circumferential-basal left ventricular dyssynchrony) and potentially risk-stratify for atrial fibrillation.

Stress echocardiography has also been used as a non-invasive test to diagnose CAD. It can detect wall motion abnormalities that occur during exercise, myocardial strain that can precede contractile abnormalities, and mild CAD, which may be of use to athletes. Garber et al. assessed its diagnostic capability in patients with intermediate pretest risk for CAD. It had a sensitivity and specificity 76% (range 0.40-1.00) and 88% (range 0.80-0.95) respectively, which is consistent with other stress testing modalities. However, its role in routine PPS has not been examined, and warrants further study as a first line tool.

3.4.2 Cardiac Computed Tomography Angiography and Coronary Artery Calcium Scoring

Currently, coronary computed tomography angiography (CTA) and coronary artery calcium scoring (CACS) is not recommended for PPS, however, consensus groups support its use in asymptomatic individuals with intermediate cardiovascular risk (10-20%), or low risk (<10%) with positive family history for premature CAD. The CTA is a highly sensitive test (99%, 95% credible interval 97 to 99%) for detecting clinical and subclinical CAD (> 50% stenosis), with a
very high negative predictive value (median 100%, range 86-100%)\textsuperscript{146}. Although the CTA is not recommended in low risk populations (i.e. marathon runners) evidence shows it can play a role in detecting low-to-moderate stenosis in an active, fit, asymptomatic population\textsuperscript{149} \textsuperscript{27}. The CTA detected mild-to-moderate CAD in approximately 50% of male marathon runners, while the exercise treadmill test failed to detect these persons\textsuperscript{149}. Both CTA and CACS have prognostic value over routine risk factors for predicting cardiac events, which could be beneficial in risk stratifying and risk management in categories above 10% by altering treatment decision-making (i.e. those suitable for lipid treatment)\textsuperscript{95}. Additionally, the CACS may alter individual lifestyle behaviors and ultimately event rates without incurring significant downstream medical costs\textsuperscript{28}. Radiation exposure has been posed as a limitation; however, new technology has substantially reduced exposure with a mean effective radiation dose of 1.26 mSv and 0.30 mSv for CCT and CACS, respectively, which is approximately one-sixth of the radiation we are exposed to annually\textsuperscript{149}. Larger scale studies need to determine if the inclusion of CTA and/or CACS translates to reductions in morbidity and mortality before it can be implemented as a screening tool. A prospective study (Measuring Athlete’s Risk of Cardiovascular events (MARC) by Braber et al. is currently investigating the additional value of CTA to a routine sports medical evaluation (medical history, physical examination and resting and exercise electrocardiography) in asymptomatic sportsmen ≥ 45 years whose sports medical evaluation revealed no cardiac abnormalities\textsuperscript{150}. The results of this study will provide insight into whether or not the inclusion of the CTA is a valuable and feasible tool in the pre-participation evaluation.

\subsection*{3.4.3 Cardiac Magnetic Resonance Imaging}
Cardiac magnetic resonance (CMR) imaging is the most comprehensive imaging modality for the exclusion of pathology and is the gold standard for examining cardiac function in patients and athletes\textsuperscript{133}. It can distinguish between athlete’s heart, dilated cardiomyopathy and mild forms of hypertrophic cardiomyopathy\textsuperscript{151} and has a potential prognostic role for detecting the presence of subclinical myocardial fibrosis, which is a concern in chronic endurance exercisers\textsuperscript{152}. Numerous studies have used CMR to detect the presence of subclinical myocardial fibrosis in athletes and have had positive findings\textsuperscript{151-153}. Breuckmann et al. found that healthy marathon runners displayed an unexpectedly high rate of myocardial late gadolinium enhancement (LGE)\textsuperscript{153}. Five of the 102 male, non-professional runners had a CAD pattern of LGE and seven had a
non-CAD pattern of LGE. Presence of myocardial LGE was three times higher than age-matched control subjects. During the 2-year follow-up the event-free survival rate was lower in runners with myocardial LGE than in those without myocardial LGE.

Mangold et al. sought to investigate the prognostic significance of the CMR in 95 elite healthy athletes (73 male, 22 female) by quantifying the prevalence of potential risk factors for SCD in those who had an unremarkable pre-participation screen. CMR imaging revealed abnormal findings in 6 (6.3%) of the athletes, including one benign variant of coronary anomaly, another abnormal coursing of a coronary anomaly not typically considered a coronary anomaly but might be affected during exercise, 2 cases of remote myocarditis, one athlete with an ectasia of the ascending aorta, and one athlete had pericardial effusion and pleural effusions who ultimately was identified to have Epstein-Barr virus infection. None of the athletes were restricted from sports competition.

Due to CMR’s limited availability, high cost, and the low pre-test probability for cardiac pathology in the athlete population, this test is less suitable for broad based screening. For athletes with an abnormal ECG, especially when cardiomyopathies, coronary anomalies or myocarditis are suspected, CMR plays a crucial role in diagnosis.

3.5 Automatic External Defibrillators
PPS tools can detect CVD; however, despite our attempts to determine the most effective tool, the art of detecting all individuals at risk for SCD is impossible. Therefore, it is important that automatic external defibrillators (AEDs) are near all sporting venues due to their success in reviving individuals who go into sudden cardiac arrest. They have shown to improve survival rates from 41% to 74% if cardiopulmonary resuscitation (CPR) is provided and defibrillation occurs within 3 to 5 minutes of collapse. The presence and timely access of AEDs at sporting venues provide a means of successful resuscitation for not only the athletes, but also spectators, coaches, event staff, and other attendees. The Vancouver Sun Run, an annual event in British Columbia, is the third largest 10 km run in the world and was introduced in 1985 to promote the benefits of running and improve health and fitness as well as support amateur athletics. Since its inception it has attracted 970,481 runners, with an initial 3,200 participants in its first year,
and in more recent years attracting approximately 50,000 per year. Notably, it has documented no SCDs and only 5 sudden cardiac arrests, all successfully defibrillated (Jack Taunton, MD, personal communication, 2014).

3.6 Previous Literature Evaluating Pre-Participation Screening Methods

To our knowledge, only a few studies exist on PPS in Masters athletes. Aagaard et al. performed a pre-participation evaluation that included a medical history, physical examination, European systematic coronary risk evaluation (SCORE), 12 lead ECG, echocardiogram, blood tests for creatinine, sodium, potassium, and NT-proBNP, in addition to lipid profiles so a risk SCORE could be calculated, in male, middle-aged (51 ± 5, range 45-69 years) long distance runners. Of the 153 individuals, 14 (9%) required further investigations. The medical history and 12-lead ECG identified 12 of the 14 runners requiring further diagnostic evaluation, nine (5.9%) of which were diagnosed with CVD, and 3 (2%) that were discouraged from race participation. The ECG detected long QT syndrome (n=2), the medical history detected third degree atroventricular block (n=1), and atrial fibrillation (n=3), and the physical examination detected hypertension (180/110 mmHg) (n=1). The echocardiogram found the remaining 2 abnormalities, but it did not substantially add to the diagnostic yield. These results demonstrate that the ECG is successful in detecting arrhythmias including ion channelopathies.

Menafoglio et al. performed a similar pre-participation evaluation; however, they strictly followed the European Association of Cardiovascular Prevention and Rehabilitation (EACPR) recommendations for PPS that consisted of a personal and family history questionnaire, physical examination, ECG, and estimation of their cardiovascular risk using the SCORE and did not include an echocardiogram. They evaluated a much larger population, consisting of 785 middle-aged individuals (73% males, 46.8 ± 7.3, range 35-65 years) engaged in high-intensity sports. Individuals with an abnormal screen underwent further examinations according to recommendations for evaluation of athletes with cardiovascular abnormalities. A new CV abnormality was discovered in 22 (2.8%) and 32 (4%) had a high-CV risk profile. Three of the participants with a new CV diagnosis were ineligible for sport for the following discoveries: apical hypertrophic cardiomyopathy; an old asymptomatic myocardial infarction (MI); and an ascending aorta aneurysm. Importantly, all were discovered through an abnormal ECG.
(N=1) was also discovered with the ECG, but the individual was still eligible for sport. The remaining CV abnormalities were discovered with the physical examination: systemic hypertension (n=8); mitral valve prolapse (n=5); bicuspid aortic valve (n=3); and mild pulmonary stenosis (n=1). The history discovered one of the abnormalities (vaso-vagal syncope). No athlete who performed an additional exercise ECG, due to a high risk SCORE or for other abnormal findings were diagnosed with significant CAD, similar to Aagard’s study. Both Aagaard and Menfoglio suggest the ECG plays a pivotal role in detecting serious cardiac disease.

Sofi et al., in a 5-year cross-sectional study of competitive sports participants sought to evaluate the clinical usefulness of complete pre-participation screening, with resting and exercise ECG as their main outcomes. A resting and exercise ECG was performed on 30,065 participants with a mean age of 30.4 (range 5-92). An abnormal resting 12-lead ECG was observed in 1812 (6%) and 1464 (80%) were considered innocent modifications that occur in the athlete’s heart (i.e. sinus bradycardia, incomplete or complete right bundle branch block, early repolarization or type I atrioventricular pattern) and 348 (1.2%) were distinctly abnormal. Of those that were distinctly abnormal, ST-T segment alterations (n=150), premature ventricular (n=120) and supraventricular beats (n=30) were the most common. The other abnormalities were pre-excitation pattern (n=27), left anterior hemiblock (n=6), and atrial fibrillation (n=6). The exercise ECG was abnormal in 1459 (4.9%). In those who had an abnormal ETT, 232 also had an abnormal resting ECG, and 1227 had a normal resting ECG.

A total of 159 were disqualified due to cardiac abnormalities. Personal history, physical examination, or both suggested problems in six (3.7%), and 126 (79.2%) had a normal resting ECG. Almost all those who were disqualified showed some cardiac abnormalities on the ETT. Of note, 56 who had a normal resting ECG showed some potentially fatal cardiac disorder, which led to disqualification. The causes for disqualification were valve diseases (24%), hypertension (19%), arrhythmias (18%), CAD (9%), conduction disorders (7%), and cardiomyopathies (5%). The most prevalent cardiac abnormalities found on ETT, comprised of findings, suggestive of CAD and arrhythmias, which is in line with previous reports. This study demonstrates the value of the resting ECG and the additive value of the ETT as significant CVD was identified, when the resting ECG was normal.
Chapter 4: Thesis Investigation: Evaluation of Pre-Participation Screening and Cardiovascular Risk Assessment in Masters Athletes

The purpose of this chapter is to provide a rationale for the thesis investigation, a detailed description of the methods and results of our findings. This chapter also contains discussions of our findings. A version of this chapter will be submitted for peer review. This research was conducted under the UBC Clinical Research Ethics Board approval certificate number H15-00009.

4.1 Introduction

Middle-aged individuals are exercising more and living longer. With advancing age, the risk of developing atherosclerotic disease increases. In those that have unknown, underlying CVD there is a transient increased risk of a cardiac event during physical exertion\textsuperscript{13, 26, 43, 159}. Additionally, most individuals with underlying CVD are unaware because they don’t experience symptoms until they have a cardiac arrest\textsuperscript{10, 11}. There is undeniable evidence that exercise is preventative medicine for CAD\textsuperscript{4, 6, 59, 65, 66, 87, 160-164}, and perhaps has even led some to believe that exercise makes one exempt from developing disease, but studies show that active individuals are not immune from CVD or fatal cardiac events\textsuperscript{10, 11, 14, 19, 21-23, 51, 25}.

When a fellow athlete collapses during practice or during a competition, individuals reconsider their own risk and question whether or not this could have been prevented. Strategies have been proposed to mitigate the risk of SCD and include pre-participation screening and cardiovascular risk assessment, but such protocols have yet to be systematically and extensively evaluated in Masters athletes. Before screening can be implemented the screening procedures must prove to successfully intervene upon a disease state to prevent morbidity or mortality in a cost-effective manner\textsuperscript{165}. Canada has not studied its own unique, heterogeneous population. Before Canada can make its own recommendations, an understanding of the prevalence of CVD and risk factors as well as the effectiveness of proposed screening procedures must be determined.

We sought to prospectively examine the EACPR recommendations, in addition to the Canadian Cardiology Society (CCS) prevention of cardiovascular disease guidelines to delineate the effectiveness of the screening tools. A modified AHA 14-item cardiovascular personal and
family history questionnaire and physical examination, 12-lead resting ECG, and FRS were the screening tools employed. All athletes, with an abnormal initial screen underwent an exercise stress test and/or further examinations to confirm or exclude an underlying cardiac if they met the criteria, defined a priori. The criteria was largely conformed by the EACPR cardiovascular evaluation of middle-aged/senior individuals and the CCS 2012 guidelines for the prevention of cardiovascular disease in the adult. We included those with an intermediate risk (10-19% FRS after adjustment for family history) because the CCS guidelines states that secondary testing (i.e. exercise treadmill testing) is recommended in those who are not candidates for lipid treatment based on conventional risk factors or for whom treatment decisions are uncertain. In a very active population, treatment may be ambiguous. In those with a low FRS, secondary testing is recommended in those with a strong family history of premature CAD therefore, all those with a premature family history of CAD underwent an exercise test. Lastly, we performed an exercise test in all those 65 years and older, due to the increased risk of CAD with age. The ‘Seattle Criteria’ was used for ECG interpretation. The effectiveness of the screening methods was calculated by the positive predictive value (PPV) of the screening tools (i.e. AHA 14-item cardiovascular personal and family history questionnaire, physical examination, FRS, and 12-lead resting ECG).

Those with an abnormal ETT and/or abnormal initial screen underwent further examinations to confirm or exclude underlying cardiac disease, according to recommendations of athletes with cardiovascular abnormalities. Those that were confirmed to be abnormal, determined the prevalence of cardiovascular disease (i.e. coronary artery disease, valvular heart disease, atrial fibrillation, congenital heart disease). The prevalence of cardiovascular risk factors (i.e. hypertension, dyslipidemia, diabetes), was determined by calculating the FRS and categorizing the individuals as having low, intermediate, or high cardiovascular risk. Additional questions on physical activity, lifestyle, and psychosocial stress were included due to their associations with an increased CVD risk.

The prevalence of atrial fibrillation and its association with intensity of sport and volume of lifetime physical activity was calculated using participants’ lifetime training hours, years spent
being physically active in high intensity sports (> 6 METS), and weekly volume of physical activity (MET-hr/wk).

We hypothesized that approximately three percent of Masters athletes would be diagnosed with new cardiovascular disease (i.e. coronary artery disease, valvular disease, arrhythmia, hypertrophic cardiomyopathy, long QT syndrome, short QT syndrome, Brugada syndrome, WPW, dilated cardiomyopathy) and approximately 5% would have a high cardiovascular risk profile (i.e. FRS ≥ 20%) with the recreational Masters athlete eliciting a higher prevalence of risk factors than the competitive Masters athlete. Due to the fact that participants self-reported their level of competition, we calculated their volume of weekly physical activity (MET-hr/wk) to determine the prevalence of risk factors amongst those who had low, moderate, and high weekly volumes of activity to provide a more objective measure. Furthermore, we hypothesized that the resting 12-lead ECG will be the most effective tool (highest PPV) for detecting CAD or other CVD in the Masters athlete. We predicted a two percent prevalence of atrial fibrillation in the Masters athlete with a higher prevalence in the older and endurance-trained athlete.

4.2 Procedures and Methods

4.2.1 Study Design

This prospective observational screening study was performed in three main demographic areas in British Columbia, with participants attending from surrounding areas (in brackets): Vancouver (greater Metro Vancouver area and Fraser Valley Region); Kelowna (Kelowna, West Kelowna, Penticton, Kamloops, Oliver, Osoyoos, Rossland); and Victoria (Victoria, Nanaimo, Campbell River, Comox Valley, Parksville, Cowichan Valley). The testing sites in the Lower Mainland included: Fortius Sport and Health, the University of British Columbia, medical and physiotherapy clinics, and a local gym. The Kelowna and Victoria testing sites were performed in local physiotherapy clinics.

The duration of the initial recruiting phase was 10 months, from April 2015 to January 2016. Study subjects were self-referred and recruited through TV and radio interviews, social media (Facebook, Twitter), referrals from participants in the study, referrals through Sports Cardiology
BC outpatient clinic, sporting teams, clubs, and organizations, and personal contacts of the study investigators. Those interested contacted the investigator (BM) by email or phone and were provided with a letter of invitation (Appendix B). If the participant wanted to enrol in the study, the same investigator (BM) provided the consent form and details to register for a screening session. Consent forms were provided at least two weeks prior to the scheduled time of initial testing.

In total, 890 athletes were screened, six were excluded because they did not meet physical activity criteria. A total of 884 were eligible and included in the study. There were three cohorts included in the study: Vancouver (n=650), Victoria (n=136), and Kelowna (n=98). A subset of the Vancouver cohort (n=294) is included in this analysis (Figure 4.1).

**Figure 4.1 Study cohorts**

4.2.2 Recruitment and Study Population

We included athletes ≥ 35 years who engaged in a variety of sports. We ensured an equal representation of the broader population of Masters athletes by including a representative sample of athletes from each sport. In Canada, athletes ≥ 35 years typically play individual sports such
as running (i.e. 10km, half-marathon, full marathon), triathlons, golf, cycling (i.e. mountain biking, BMX, track, road), athletics (i.e. track and field, road running, ultra running, cross-country running, race walking), rowing, swimming, and tennis. According to British Columbia sporting body organizations that were able to provide the number of members in their organization (N = members in the organization) the sports most commonly practiced were soccer/SoccerBC (N=3,639), cycling/CyclingBC (N=3,141), athletics/BC athletics (N=1,160), alpine skiing (N=35). We aimed to have an equal sample of both males and females so that gender differences could be observed. Additionally, we targeted all ethnicities, creating a representative sample of British Columbia’s multi-ethnic, multi-racial population.

4.2.3 Inclusion Criteria

Male and female Master (≥ 35 years) competitive athletes (participate in organized team or individual sport that requires systematic training and regular competition against others and places a high premium on athletic performance on athletic excellence and achievement, such as at the provincial, national, international and/or Olympic level).

Male and female Master (≥ 35 years) recreational athletes (participate in a variety of informal recreational sports within a range of exercise levels from modest to vigorous, which does not require systematic training or the pursuit of excellence).

All athletes must engage in a minimum of three days per week of moderate to vigorous activity (the international recommended amount of weekly physical activity) during the previous 3 months.

4.2.4 Exclusion Criteria

Individuals with previously known coronary artery disease (previous stent, coronary artery bypass graft, or coronary artery calcium score ≥ 100).
4.3 Procedures

4.3.1 Initial Screen:
All participants underwent an initial screen that included a cardiovascular physical examination with a physician, anthropometric measurements (height, weight, and waist circumference), a resting 12-lead ECG, a modified AHA 14-item questionnaire (cardiovascular personal and family history), and a lifestyle (smoking status, consumption of fruits and vegetables and red meat)\textsuperscript{100}, physical activity, and psychosocial (locus of control, hostility, perceived stress, life events, and depression)\textsuperscript{102, 103, 105, 109, 167, 168} questionnaire (Figure 4.2). Relevant background information (age, sex, race/ethnicity, country of origin, educational level, marital status, income range, and occupation) was also included. The physical activity questionnaire included questions on frequency, intensity (easy, moderate, vigorous), time (minutes), and type of all physical activities the individual was currently engaged in, subjective fitness level, as well as number of years spent being physically active, and number of lifetime endurance events. A blood lipid profile to calculate the participants’ cardiovascular risk using the FRS calculator was also completed. Prior to the screen, participants were required to complete a blood lipid profile. If this was not complete prior to screening, the study investigators provided them with a requisition on the day of screening and participants were asked to complete as soon as possible. Participants were emailed the questionnaires prior to screening. On the day of screening, questionnaires were collected and the investigator reviewed and probed further if necessary to clarify answers and ensure proper reporting. The initial screen took approximately 30 minutes. Participants were not offered financial incentive to participate.

Figure 4.2 Study procedure
4.3.2 Additional Evaluations

The initial screen results were reviewed by the investigator (BM) and determined if further testing was necessary. If the initial screen was positive displaying at least one of the following pre-determined study criteria (Appendix G) and upon confirmation by the cardiologist, investigator (BM) contacted the participant and informed them further cardiovascular evaluations were necessary. All individuals initially had an exercise treadmill test (ETT), unless it was suggested that they should have a cardiologist consultation before undergoing a maximal ETT and/or the exercise test was not clinically recommended. The ETT was performed at UBC hospital or a satellite location (i.e. Preventum Medical Centre, Kelowna General Hospital or Westheart Cardiology office in Victoria) and took approximately 45 minutes to complete.

A positive or equivocal ETT, a positive family history, positive personal symptoms (i.e. unexplained syncope, chest pain, dyspnea, palpitations) and/or a positive physical examination (i.e. ≥ grade 2/6 systolic murmur, any diastolic murmur, mid or end-systolic click) generated a cardiovascular evaluation with one of four cardiologists (SI, JM, AD, or KP) who have extensive training in evaluating athletes. Follow-up examinations (i.e. echocardiogram, stress echocardiogram, coronary artery calcium score, cardiac computed tomography, cardiac magnetic resonance imaging, myocardial perfusion imaging, and 24 hour ECG Holter monitoring) were ordered at the discretion of the sports cardiologist and confirmed whether or not clinically significant CVD was present according to the recommendations for evaluation of athletes with cardiovascular disease.\textsuperscript{157, 169}

4.3.3 Methods

**Anthropometrics:** Weight, height and waist circumference measurements were taken using a standardized protocol. Students conducting the measurements were provided the standardized measurement protocols and trained prior to the screening (Appendix E). Waist measurements were taken using the National Health and Nutrition Survey anthropometry procedure\textsuperscript{170} with a non-stretchable tape and obtained over the unclothed abdomen at the top of the iliac crest. Height measurements were taken with a portable stadiometer (SECO 213, Chino, CA) according to a standardized protocol and measured to the nearest tenth of a centimeter and recorded to the nearest centimeter, rounding up, when necessary. Weight was electronically measured using a
portable flat scale (SECA 869, Chino, CA) and measured to the nearest tenth of a kilogram, and recorded to the kilogram, rounding up, when necessary.

**Physical Examination:** The physical exam was conducted by a physician (internal medicine resident or a cardiologist). Measurements included heart rate, blood pressure (Welch Allyn, Skaneateles Fall, New York), palpation for regular or irregular pulse, cardiac auscultation for mid- or end-systolic clicks, any diastolic murmur, systolic murmur ≥2/6, abnormal second heart sound (single or widely split and fixed with respiration), examination of a delayed femoral pulse to exclude coarctation of the aorta, and assessment for the physical stigmata of Marfan syndrome (Appendix G). Three measurements of heart rate and blood pressure were taken a minute apart. The lowest measurement was reported and used in calculating the FRS.

**Resting 12-lead Electrocardiogram:** A 10-second, resting, supine measurement was taken using a portable 12-lead electrocardiogram (Mortara Instrument, Milwaukee, WI). All ECGs were taken by a trained, experienced health professional (i.e. kinesiologist, clinical exercise specialist, or physician). They were provided a standardized protocol (Appendix E). All ECGs were interpreted by cardiologists, with expertise in athlete ECG interpretation using the ‘Seattle Criteria’<sup>166</sup>. ECGs were read off-site and the interpreting cardiologist was not aware of findings on the history or physical exam. Only the age and sex of the athlete were made available at the time of ECG interpretation.

**Primary Sport and Level of Competition:** The sport that is played the greatest hours per week and/or the longest number of years was indicated as the individuals’ primary sport. When “running” was reported as a primary sport we specified the type of runner: 1) running (distances less than a half-marathon (< 21km)); 2) marathon (21 – 42km); and 3) ultramarathon (any distance greater than a marathon (>42km). The type of runner was based on the number they had completed and whether or not they had competed in an event within the last 2 years. For example, the primary sport was considered to be an ultramarathon if they had participated in a minimum of one ultramarathon, and had participated in any long distance (≥21km) event within last 2 years, and at least 5 half or full marathons. Marathon was reported as a primary sport, if they reported competing in a minimum of five half or full marathons within the last 2 years. Running was
reported as a primary sport for those who had not participated in any long distance events (i.e. > 20 km) within the last 2 years. Level of competition was based on participants’ response on the questionnaire (i.e. recreational, competitive, provincial, national, international, professional). We reported their highest, current level of competition.

**MET Hours Per Week (MET-hr/wk):** MET-hr/wk was calculated based on type of activity (i.e. running, cycling, swimming) and subjective report of intensity (light, moderate, or vigorous) and matched to the corresponding MET level using the compendium of physical activities classification of energy costs\(^9\). To confirm that they were currently physically active and to ensure an accurate representation of average training volume (not based on one week or one month), a question on much time they were physically active within the last 3 months was included. To determine relative METS achieved from running (pace was not asked) we used the METS associated with age and sex for an average half-marathon race pace and an individual’s reported physical intensity. For example a 45-year-old male average race pace for half marathon is a 9:45 min/mile, which is approximately 10 METS. If they reported moderate running we used 10 METS, if they indicated vigorous running we increased their MET level by one (i.e. 11 METS). We used similar age-approximated METS for cycling (Appendix F). If no specified activity was listed under light physical, or moderate physical activity, three and six METS, were used, respectively. Once METS were determined, we calculated MET-hr/wk by multiplying METS by the number of hours spent doing the activity each week. If hours were provided as a range (i.e. 6-10 hours) the average hours was used (i.e. 8 hours). MET hours per week were then calculated based on the sum of all MET hours.

Example: 45 year-old, male, recreational athlete:
- Cycling (12 METS) x 5 hours/week = 60 MET hours
- Hockey (8 METS) x 3 hours/week = 24 MET hours
- Strength training (5.5 METS) x 1 hour/week = 5.5
- TOTAL = (60 + 24 + 5.5) = 89.5 MET-hr/wk

**Lifetime Training Hours:** Lifetime hours were calculated (based on previous work of Brugger et al.) as follows: average total endurance and strength training hours per week x 52 x training
years\textsuperscript{69}. Number of training years was based on a self-report of years of being physically active. This included sports played as youth, if reported. If they indicated a period in their life when they weren’t regularly physically active, we subtracted these years. When a range of hours for a particular activity was reported (weekly hours can vary greatly, within in a season, and within one’s sporting career), we used average hours provided for each sport during the given time period they participated in the sport (i.e. range was 5-10 hours, we used 7.5 hours). We only included activities that were of vigorous intensity or greater ($\geq$6 METS) (i.e. did not include golf, curling, fishing, walking).

**Psychosocial Reporting:** Locus of control questions were asked according to the extent participants agree/disagree with a statement and answers were obtained using a six-point Likert scale. Based on participant responses to the 6-point Likert scale a combined total score was calculated. A low score (9-18) was associated with a low locus of control, a moderate score (19-36) was associated with a moderate locus of control, and a high score (37-54) was associated with a high locus of control. Hostility was reported based on the number of positive answers (1, 2, or 3). Depression was graded based on the number of questions answered positively to (not depressed, 1 items, 2-4 items, 5 or more items), of which five or more positive responses were defined as clinical depression.

**Exercise Treadmill Test** (if the initial screen was positive): A resting 12-lead ECG and blood pressure in the supine and standing position was performed prior to exercise testing. Maximal exercise treadmill test (ETT) was performed using the Bruce protocol with an initial treadmill speed and grade of 1.7 mph and 10% grade, respectively. Stage 2 is 2.5 mph at a 12% grade, stage 3 is 3.4 mph and 14% grade, stage 4 is 4.2 mph and 16% grade, stage 5 is 5.0 mph and 18% grade, stage 6 is 5.5 mph and 20% grade, and stage 7 is 6.0 mph and 22% grade. Subjects were informed of their age-predicted maximum heart rate and encouraged to exercise until volitional fatigue or a minimum of 100% of their age-predicted maximum heart rate. They were asked what their maximum heart rate achieved was when they exercise. If they were able to go beyond 100% of their age-predicted maximum heart rate, they were encouraged to do so to obtain an accurate representation of their true HR\textsubscript{max} as well as their level of fitness (Max METS achieved). The test was stopped if there were absolute indications for test termination.
based on American College of Sports Medicine absolute contraindications for continuing the exercise test. The ECG and HR were continuously recorded throughout the test and systolic and diastolic blood pressure was measured at 1.5 minutes into each stage. All ETTs were interpreted by cardiologists with expertise in athlete ECG interpretation using the Seattle Criteria. All ETTs were read off-site and the interpreting cardiologist was not aware of findings on the history or physical exam. Only the age and sex of the athlete were made available at the time of ETT interpretation.

**Cardiovascular Disease Diagnoses:** Clinically significant disease was considered as any cardiovascular disease that could potentially cause an adverse cardiac event and included: coronary artery disease (CAD), atrial fibrillation (AF), hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy (ARVC), coronary artery anomaly, myocarditis, Brugada syndrome, pre-excitation syndrome (Wolf-Parkinson-White), Lenegre disease, long and short QT syndrome, catecholaminergic polymorphic ventricular tachycardia, bicuspid aortic valve (BAV), Marfan syndrome, valvular disease (moderate or greater stenosis and/or moderate-to-severe regurgitation of mitral or aortic valves and/or diastolic dysfunction), mitral valve prolapse (MVP), and/or aortic aneurysm.

**Coronary Artery Disease Classification:** The extent of CAD was determined by coronary artery calcium score (CACS) or coronary computed tomography angiography (CTA). It was suggested that individuals with a positive ETT (minimum of 1 mm down-sloping ST depression in 2 adjacent leads) and/or positive cardiac symptoms, underwent CTA and individuals who had a high FRS were encouraged to have a CACS to determine their coronary calcium burden and help decide on treatment management.

The total calcium burden was reported according Rumberger and colleagues in the following manner: Agatson score 0 (no evidence of coronary calcium), 1-10 (minimal evidence of coronary calcium), 10-100 (mild evidence of coronary calcium), 100-400 (moderate evidence of coronary calcium), and > 400 (extensive evidence of coronary calcium) (Table 4.1).
The extent of coronary stenosis determined by CTA was graded as the following: absence of CAD (no coronary plaques), mild coronary atherosclerosis (coronary plaques with luminal narrowing < 50%), moderate coronary atherosclerosis (luminal narrowing > 50%), significant CAD (luminal narrowing > 75%)\textsuperscript{149}. It was further described as single, double, or triple vessel disease and calcified or non-calcified plaque (Table 4.1).

We reported someone has having CAD if they had a minimum of minimal coronary calcium burden (≥ 1 coronary calcium burden) or mild atherosclerosis (luminal narrowing < 50%). Individuals were classified according to the highest degree of CAD present (i.e. if had mild CAD in LAD and moderate CAD in RCA, we indicated them as having moderate CAD).

Table 4.1 Coronary artery disease diagnoses by type of test, number of vessels involved and type of plaque

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<thead>
<tr>
<th>Coronary artery disease diagnoses (CACS)</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>No evidence of coronary calcium</td>
<td>No CCB</td>
</tr>
<tr>
<td>Minimal coronary calcium burden (1-10)</td>
<td>Minimal CCB</td>
</tr>
<tr>
<td>Mild coronary calcium burden (10-100)</td>
<td>Mild CCB</td>
</tr>
<tr>
<td>Moderate coronary calcium burden (&gt;100-400)</td>
<td>Mod CCB</td>
</tr>
<tr>
<td>Extensive coronary calcium burden (&gt;400)</td>
<td>Extensive CCB</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coronary artery disease diagnosis (CTA)</th>
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</thead>
<tbody>
<tr>
<td>Mild CAD (&lt; 50% luminal narrowing)</td>
</tr>
<tr>
<td>Moderate CAD (&gt;50% luminal narrowing)</td>
</tr>
<tr>
<td>Significant CAD (&gt; 75% luminal narrowing)</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Number of vessels involved</th>
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<tbody>
<tr>
<td>One vessel</td>
</tr>
<tr>
<td>Two vessels</td>
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<tr>
<td>Three vessels</td>
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<tr>
<td>Four vessels</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of plaque</th>
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</thead>
<tbody>
<tr>
<td>Calcified</td>
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<tr>
<td>Non-calcified</td>
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<tr>
<td>Mixed</td>
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</table>

**Atrial Fibrillation**

The type of atrial fibrillation (AF) was reported as paroxysmal (AF that begins suddenly and then stops on its own, usually within 24 hour to one week period, with mild to severe symptoms),
persistent (AF than continues for more than one week, is stopped on its own or with treatment),
or permanent (AF that can’t be restored with treatment). Paroxysmal and persistent AF may
become more frequent over time and eventually result in permanent AF.

**High PVC Burden**: High premature ventricular contraction (PVC) burden was considered as >
720 PVCs/24 hours (measured on a Holter). This was based on Sajadleh and colleague’s report
that frequent PVCs (≥ 30/hour) are a significant predictor of combined (HR 2.47, 95% CI, 1.29
to 4.68, p = 0.006) and cardiovascular (hazard ratio 2.85, 95% CI, 1.16 to 7.0, p = 0.023) event
rates, after adjustment for conventional risk factors.\(^{172}\)

### 4.4 Statistical Analysis and Sample Size Calculation

Statistical analysis was performed using SPSS software Version 23.0 (IBM Corp, Armonk, NY).
Continuous variables were expressed as means and standard deviations and were calculated for
all variables of interest. Categorical data was reported as number of subjects (n) and percentage
(%). Differences between two or more groups were performed using the Pearson’s \(\chi^2\) test.

Cardiovascular disease (CVD) that can lead to sudden cardiac arrest/SCD was the primary
outcome. The prevalence (%) of individuals that were determined to have clinically significant
CVD (i.e. coronary artery disease, hypertrophic cardiomyopathy, dilated cardiomyopathy,
coronary artery anomalies, bicuspid aortic valve, mitral valve prolapse, significant valvular heart
disease, ion channelopathies, atrial fibrillation) and the abnormal finding at screening (personal
symptoms, positive family history, physical examination, resting 12-lead ECG, intermediate or
high FRS, previous CVD (excluding CAD), and/or ≥ 65 years old) that indicated further
evaluations is reported. The prevalence of individuals with non-clinically significant
cardiovascular diagnosis (i.e. high PVC burden, mild valvular disease) including clinical
characteristics and abnormal finding at screening (symptoms, family history, physical
examination, 12-lead ECG, intermediate or high FRS, and/or ≥ 65 years old) was also reported,
but not included in the PPV calculation for clinically significant CVD.

The PPV was calculated for each test (physical examination, resting ECG, intermediate FRS,
high FRS, and the personal symptoms and family history questionnaire) to determine the
effectiveness of the screening tools. The PPV for personal symptoms, family history, and presence of previous CVD obtained from the AHA questionnaire were reported together and separately. The PPV for age (> 65 years old) was also calculated. True test positives were considered to be clinically significant CVD. Positive predictive value was calculated by the following formula:

\[
PPV = \frac{\text{True Test Positives}}{\text{True Test Positives} + \text{False Positives}}
\]

The volume of physical activity was reported as MET-hr/wk, which was divided into three groups, low (15-40 MET-hr/wk), moderate (41-75 MET-hr/wk), and high (> 75 MET-hr/wk). The groups were determined based on findings by Arem et al.\(^6\), where the greatest decrease in mortality was from 0.1 to 40 MET-hr/wk, a plateauing effect between 41 and 75 MET/hr/wk, and a potential increase in mortality at > 74 MET-hr/wk. The prevalence of CVD for each volume of physical activity group was reported according to type of CVD (CAD, valvular disease, AF, CHD) and sum of all CVD.

To our knowledge, there have been no other studies testing for the prevalence of CVD in Masters athletes in Canada; therefore, power was not determined. Based on previous literature we hypothesized a sample size of 800 would be sufficient in capturing individuals with cardiovascular risk factors and CVD. For example, Aagaard et al., observed 153 novice, middle-aged long distance runners, and discovered that nine (5.9%) had CVD\(^1\). Similarly, Menafoglio et al. investigated 785 middle-aged athletes engaged in vigorous sports and a cardiovascular abnormality was discovered in 22 (2.8%) and 32 (4%) had a high-risk profile\(^1\). In another study examining the prevalence of risk factors in 623 athletes (529 males) between the ages of 13 and 77 years, the study investigator found 69% of males and 82% of females exhibited at least one cardiovascular risk factor (i.e. dyslipidemia, hyperglycemia, hypertensive)\(^1\). However a direct comparison between these two studies can’t be made because De Matos et al. didn’t calculate a cardiovascular risk score (i.e. SCORE or FRS)\(^1\).
We ensured an equal representative of the broader population of Masters athletes by having a representative sample of athletes from each sport. In Canada, athletes ≥ 35 years typically play individual sports such as running (i.e. 5km, 10km, half-marathon, full marathon), triathlons, golf, cycling (i.e. mountain biking, BMX, track, road), athletics (i.e. track and field, road running, ultra running, cross-country running, race walking), rowing, swimming, and tennis. According to British Columbia sporting body organizations that were able to provide the number of members in their organization (N = members in the organization) the sports most commonly practiced were soccer/SoccerBC (N=3639), cycling/CyclingBC (N=3141), athletics/BC athletics (N= 1160), alpine skiing (N=35). We aimed to have an equal sample of both males and females so that gender differences could be observed.

4.5 Results
A total of 890 athletes were screened, 297 of which have completed all necessary follow-ups and included in the present analysis. The remaining 593 are pending follow-up results. In the initial 297 athletes eight were excluded due to previously known coronary artery disease (previous PCI, CABG, or greater than moderate coronary calcium burden on CACS) and three were excluded because they didn’t meet physical activity criteria. Two-hundred and eighty six (n=286) were eligible for the study. Population characteristics are outlined in Table 4.2 and 4.3. Participants were predominately male (66.8%) and Caucasian (83.2%). A small proportion were Asian (6.2%). Average age was 54.0 ± 8.8 (range 35-81) years for all athletes and 54.7 ± 8.9 yrs and 52.7 ± 8.6 years for males and females, respectively (Appendix A). The number of participants by age group is represented in Figure 4.3.
### Table 4.2 Population characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
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<tbody>
<tr>
<td>Number of athletes</td>
<td>286</td>
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<tr>
<td>Male (%)</td>
<td>191 (66.8)</td>
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<tr>
<td>Female (%)</td>
<td>95 (33.2)</td>
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<tr>
<td>Age (years)</td>
<td>54.0 (8.8)</td>
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<tr>
<td>Height (cm)</td>
<td>173.7 (9.0)</td>
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<tr>
<td>Weight (kg)</td>
<td>75.0 (14.1)</td>
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<tr>
<td>Body mass index (kg/m(^2))</td>
<td>24.6 (3.6)</td>
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<tr>
<td>Waist circumference (cm)</td>
<td>86.9 (9.8)</td>
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<tr>
<td>Resting heart rate (bpm)</td>
<td>58.0 (9.8)</td>
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<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>125.4 (15.1)</td>
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<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>77.1 (8.0)</td>
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**Self-reported ethnicity**

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<tr>
<th>Ethnicity</th>
<th>Value</th>
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<tr>
<td>Caucasian (%)</td>
<td>238 (83.2)</td>
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<tr>
<td>Asian (%)</td>
<td>18 (6.2)</td>
</tr>
<tr>
<td>Other (%)</td>
<td>20 (6.9)</td>
</tr>
<tr>
<td>Not reported (%)</td>
<td>10 (3.5)</td>
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</tbody>
</table>

### Table 4.3 Population blood lipid profile

<table>
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<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Range</th>
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<tbody>
<tr>
<td>LDL – cholesterol</td>
<td>3.01 ± 0.85</td>
<td>1.20 – 5.70</td>
</tr>
<tr>
<td>HDL – cholesterol</td>
<td>1.70 ± 0.52</td>
<td>0.78 – 3.57</td>
</tr>
<tr>
<td>Total Cholesterol:HDL Ratio</td>
<td>3.23 ± 0.90</td>
<td>1.55 – 6.80</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.97 ± 0.46</td>
<td>0.35 – 3.36</td>
</tr>
<tr>
<td>Fasting Glucose</td>
<td>5.14 ± 0.44</td>
<td>4.00 – 7.10</td>
</tr>
</tbody>
</table>
4.5.1 Physical Activity

Participants took part in over 20 sports. The most common primary sports played (most athletes participated in more than one sport) were running sports (41.2%), hockey (14.1%), and cycling (12.7%) (Figure 4.4). The majority of athletes, who participated in running sports, were considered “marathoners” (21.8%). Recreational level of sport participation was the most commonly reported (70.0%), and 10.5% participants reported currently playing at a provincial, national or professional level (Table 4.3a). The participants perceived themselves to be of a high level of fitness with 53% reporting a “very good” and 39% reporting a “good” fitness level. Most participants (52.1%) engaged in moderate to vigorous activity four to five times week and 23.2% engaged in six or more sessions of moderate-to-vigorous activity a week. Based on calculated MET-hr/wk, 40.0% reported a moderate and 44.0% reported a high weekly training volume.
Figure 4.4 Primary sports played

- Field Hockey
- Rugby
- Lacrosse
- Track and field (throwing)
- Basketball
- Swimming
- Baseball
- Rowing
- Golf
- Tennis
- Cross-country skiing
- Soccer
- Alpine Skiing
- Paddling
- Mountain bike
- Other
- Track and field (running)
- Triathlon
- Cycling
- Hockey
- Running
- Ultramarathon
- Marathon
- All running
The current group represents a very active population (Table 4.4). The average time spent engaging in endurance, strength, and/or flexibility-based training activity was 6.9 hours per week. A small subset (n=13) did not report endurance, strength, or flexibility activities which indicates that they only engaged in mixed sports (i.e. tennis, hockey) and did not engage in any additional endurance or strength-based activities. Most athletes reported being physically active most of their life (35.3 years ± 14.2, range 3-67 years). The mean weekly training volume was 78.7 ± 45.3 MET-hr/wk. The majority (90.2%) reported weekly endurance activity, 70.2% participated in weekly strength activities, and 34.3% engaged in weekly stretching, yoga, or pilates.

| Variable | Level of competition | | | | | | Subjective fitness level | | | | | | Average number of moderate to vigorous sessions per week | | | | | | Volume of activity classified by MET-hr/wk group | | | | | | Recreational | 199 (70.0) | | | | | Competitive | 55 (19.3) | | | | | Elite (provincial, national, professional) | 30 (10.5) | | | | | Very Poor | 1 (0.4) | | | | | Poor | 0 (0.0) | | | | | Average | 25 (8.8) | | | | | Good | 110 (38.7) | | | | | Very good | 149 (52.5) | | | | | < 2 sessions per week | 4 (1.4) | | | | | 2-3 sessions per week | 67 (23.6) | | | | | 4-5 sessions per week | 148 (52.1) | | | | | ≥ 6 sessions per week | 66 (23.2) | | | | | Low: 15 – 40 MET-hr/wk | 46 (16.0) | | | | | Moderate: 41- 75 MET-hr/wk | 114 (40.0) | | | | | High: > 75 MET-hr/wk | 126 (44.0) | | | | | | | | | |
Table 4.5 Physical activity characteristics by type of activity

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly minutes spent being physically active (n= 273)</td>
<td>412.3 (233.2)</td>
</tr>
<tr>
<td>Weekly training volume (MET-hr/wk)</td>
<td>78.7 (45.3)</td>
</tr>
<tr>
<td>Total years physically active</td>
<td>35.3 (14.2)</td>
</tr>
<tr>
<td>Total lifetime training hours</td>
<td>11,259 (8005.7)</td>
</tr>
<tr>
<td>Individuals engaged in strength activities (%)</td>
<td>201 (70.2)</td>
</tr>
<tr>
<td>Weekly time engaged in strength activities (min)</td>
<td>99.2 (71.7)</td>
</tr>
<tr>
<td>Number of individuals engaged in stretching/yoga/pilates (%)</td>
<td>98 (34.3)</td>
</tr>
<tr>
<td>Weekly time engaged in stretching/yoga/pilates (min)</td>
<td>73.5 (45.0)</td>
</tr>
<tr>
<td>Number of individuals engaged in endurance activities (%)</td>
<td>258 (90.2)</td>
</tr>
<tr>
<td>Weekly time spent engaged in endurance activities (min)</td>
<td>331.1 (214.4)</td>
</tr>
<tr>
<td>Individuals who had participated in ≥ 1 endurance event</td>
<td>201 (70.3)</td>
</tr>
<tr>
<td>Years since first long distance event</td>
<td>17.8 (12.1)</td>
</tr>
<tr>
<td><strong>Half marathons (n=167)</strong></td>
<td></td>
</tr>
<tr>
<td>Mean number completed</td>
<td>13.4 (15.2)</td>
</tr>
<tr>
<td><strong>Marathons (n=145)</strong></td>
<td></td>
</tr>
<tr>
<td>Number completed</td>
<td>9.9 (13.0)</td>
</tr>
<tr>
<td><strong>Ultramarathons (n=53)</strong></td>
<td></td>
</tr>
<tr>
<td>Number completed</td>
<td>7.0 (8.6)</td>
</tr>
<tr>
<td><strong>Cycling events (n=87)</strong></td>
<td></td>
</tr>
<tr>
<td>Number completed</td>
<td>7.4 (7.8)</td>
</tr>
</tbody>
</table>

4.5.2 Endurance Activities

Most athletes (70.3%) participated in at least one long distance event: 154 (53.8%) ran a half marathon, 145 (50.1%) ran a full marathon, 53 (18.2%) reported running an ultra marathon, 87 (30.4%) reported at least one long distance cycling event, and 19 (6.7%) were currently participating in triathlons (does not include individuals who ran triathlons in the past). The mean number of years of those involved in endurance sport was 17.8 ± 12.1.
4.5.3 Cardiovascular Risk Factors

Only a small proportion presented with known cardiovascular risk factors and additional participants were discovered to have cardiovascular risk factors at screening (Figure 4.5). Approximately 19 (6.6%) were on hypertensive treatment and 11 (4.2%) were taking treatment for dyslipidemia. Two (0.7%) participants were current smokers and 66 (23.2%) were former smokers (quit > 2 years ago). One participant had previously diagnosed type 2 diabetes mellitus. A strong family history of premature CAD was prevalent in 18 (6.3%) of the participants. At screening, an additional 93 (32.5%) were discovered to have dyslipidemia ($\geq 3.5$ mmol/L or total cholesterol: high-density lipoprotein cholesterol ratio $\geq 5.0$), 12 (4.2%) had HDL $< 1.0$ mmol/L, 49 (17.1%) had high blood pressure ($\geq 140/90$ mm Hg), and 37 (12.9%) had hyperglycemia ($>5.5$ mmol/L). Twenty-three (8.0%) participants met the body mass index criteria for obesity ($\geq 30$kg/m$^2$). A moderate and high FRS was observed in 28.0% and 8.7% subjects, respectively. Approximately 43.8% of the population had less than 3 servings of fruits and vegetables a day and a quarter (26.7%) reported consumption of red meat three or more times per week. Most participants self-reported their health as “very good” (52.5%) or “good” (40.0%).

4.5.4 Psychosocial Stress

The prevalence of psychosocial risk factors are displayed in Table 4.6. Most individuals reported being stressed at work (56.0%) and home (65.0%) at least “some of the time”. “Several” to “permanent” levels of stress were reported at work and home (29.8% and 15.6%, respectively). Most (71.4%) individuals had little or none financial stress and 25.8% and 2.8% had moderate or high financial stress, respectively. Stressful life events were reported in 37.6% of the participants (one or more life events). The majority of the population (95.6%) had high perceived control. Hostility was present (positive response to one or more of the three hostility-related questions) in 122 (42.7%) participants. Depression was based on a positive response to having felt sad, blue, or depressed for two weeks or more in a row and a positive response to five of the seven additional questions. Fifteen participants (5.2%) reported yes to five or depression questions.
Table 4.6 Prevalence of psychosocial risk factors (%)

<table>
<thead>
<tr>
<th>Psychosocial risk factor</th>
<th>Stress at work (n=262)</th>
<th>Stress at home (n=283)</th>
<th>Financial stress (n=283)</th>
<th>Stressful life events (n=282)</th>
<th>Perceived control (n=273)</th>
<th>Hostility</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Never</td>
<td>Some of the time</td>
<td>Little or none</td>
<td>None</td>
<td>Mean total score (out of 54)</td>
<td>No positive answers</td>
<td>0 item</td>
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<tr>
<td></td>
<td>37 (14.1)</td>
<td>147 (56.1)</td>
<td>202 (71.4)</td>
<td>175 (62.0)</td>
<td>46.2 (4.9)</td>
<td>164 (57.3)</td>
<td>228 (79.7)</td>
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<td></td>
<td></td>
<td>71 (27.1)</td>
<td>73 (25.8)</td>
<td>77 (27.0)</td>
<td></td>
<td>83 (29.0)</td>
<td>15 (5.2)</td>
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<td></td>
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<td>7 (2.7)</td>
<td>8 (2.8)</td>
<td>30 (10.6)</td>
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<td>25 (8.7)</td>
<td>28 (10.0)</td>
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<td>16</td>
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<td>Low locus of control (9-18)</td>
<td>Three positive answers</td>
<td>14 (4.9)</td>
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<td>Moderate locus of control (19-36)</td>
<td>259 (95.6)</td>
<td>15 (5.2)</td>
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<td>Low locus of control (9-18)</td>
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<td>Moderate locus of control (19-36)</td>
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<td>High locus of control (37-54)</td>
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</tbody>
</table>
4.5.5 Abnormal Findings on Pre-Participation Screening

An initial screening evaluation was abnormal in 167 individuals (58.3%) and they subsequently underwent an exercise treadmill test (ETT) and/or further cardiologist evaluation (Figure 4.6). After ETT and/or cardiology evaluation, further testing (i.e. echocardiogram, stress echocardiogram, Holter, 24-ABP, CACS, CTA, and/or MIBI) was deemed clinically necessary in 85 (29.7%) participants. Table 4.7 outlines indications that prompted further evaluations. The primary indicator for follow-up was an abnormal personal and family history questionnaire (n=87, 30.4%). Palpitations were the primary complaint in 32 (11.2%) individuals. Other indicators for follow-up were an intermediate cardiovascular risk profile (30%), abnormal resting ECG (13.3%), ≥ 65 years of age (10.8%), high cardiovascular risk profile (8.7%), and abnormal physical exam (6.3%). The most common abnormality on resting ECG was left axis deviation (n=11, 3.8%). Select athletes had more than one indicator for further investigations.

Figure 4.6 Further evaluations and diagnoses
### Table 4.7 Indications for further evaluation

<table>
<thead>
<tr>
<th>Abnormal finding</th>
<th>Number of participants (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total 14-item AHA questionnaire</strong></td>
<td>87 (30.4)</td>
</tr>
<tr>
<td><strong>Personal history</strong></td>
<td></td>
</tr>
<tr>
<td>Exertional chest pain</td>
<td>6 (2.1)</td>
</tr>
<tr>
<td>Palpitations with exercise</td>
<td>32 (11.2)</td>
</tr>
<tr>
<td>Exertional fatigue</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Exertional syncope/pre-syncope</td>
<td>15 (5.2)</td>
</tr>
<tr>
<td><strong>Family history</strong></td>
<td>33 (11.5)</td>
</tr>
<tr>
<td>SCD (unexplained) &lt; 50 years in first or second degree relative</td>
<td>11 (3.8)</td>
</tr>
<tr>
<td>Specified heart conditions in first or second degree relative</td>
<td>7 (2.4)</td>
</tr>
<tr>
<td>Premature heart disease &lt; 50 years in first degree relative</td>
<td>18 (6.3)</td>
</tr>
<tr>
<td><strong>Previous CVD (excluding CAD)</strong></td>
<td>16 (5.6)</td>
</tr>
<tr>
<td><strong>Abnormal physical examination</strong></td>
<td>18 (6.3)</td>
</tr>
<tr>
<td>2 or greater out of 6 systolic murmur</td>
<td>15 (5.2)</td>
</tr>
<tr>
<td>Diastolic murmur</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Hypertension (&gt;180/110)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Irregular pulse</td>
<td>4 (1.4)</td>
</tr>
<tr>
<td><strong>Abnormal resting 12-lead ECG</strong></td>
<td>39 (13.3)</td>
</tr>
<tr>
<td>T wave inversions</td>
<td>5 (1.7)</td>
</tr>
<tr>
<td>Significant Q waves</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>ST depression</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>Complete LBBB</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>Complete RBBB</td>
<td>6 (2.1)</td>
</tr>
<tr>
<td>Left axis deviation</td>
<td>11 (3.8)</td>
</tr>
<tr>
<td>Left atrial enlargement</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>Prolonged QT interval</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Atrial tachyarrhythmia (i.e. atrial fibrillation)</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>Premature ventricular contractions</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td><strong>Cardiovascular risk</strong></td>
<td></td>
</tr>
<tr>
<td>High FRS</td>
<td>25 (8.7)</td>
</tr>
<tr>
<td>Intermediate FRS</td>
<td>80 (30.0)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Age 65 or greater</td>
<td>31 (10.8)</td>
</tr>
<tr>
<td><strong>Total participants who required further investigations</strong></td>
<td>167 (58.3)</td>
</tr>
</tbody>
</table>

*selected athletes had more than one abnormal indication

CAD – coronary artery disease; CVD – cardiovascular disease; FRS – Framingham Risk Score; LBBB – left bundle branch block; RBBB – right bundle branch block
4.5.6 New Cardiac Diagnoses

A total of 35 (12.2%) were diagnosed with a new cardiovascular disease. Table 4.8 shows the clinical characteristics including the cardiovascular diagnoses, the abnormal finding on the initial screen, and the follow-up tests that confirmed the diagnoses. The average age of individuals diagnosed with CVD was 61.8 years (range 41-77) and were predominately male (98%). The two females diagnosed with CVD were 68 and 71 years of age, respectively. Only eight (23%) of the individuals diagnosed with CVD reported symptoms. Athletes with significant CVD did not report symptoms, including the four individuals who had significant CAD. All three athletes diagnosed with AF, reported symptoms and had an abnormal ECG. Table 4.9 illustrates exercise treadmill performance (max METS achieved) according to the type of cardiovascular disease.
Table 4.8 New cardiovascular diagnoses: clinical characteristics

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis (n=35)</th>
<th>Abnormal finding on screen</th>
<th>Tests ordered</th>
</tr>
</thead>
<tbody>
<tr>
<td>62</td>
<td>M</td>
<td>Congenital Heart Disease (n=4)</td>
<td>ECG (TWI), FRS-I</td>
<td>ETT, ABP, CTA</td>
</tr>
<tr>
<td>58</td>
<td>M</td>
<td>1. Coronary artery anomaly (low risk)</td>
<td>FH, PE, ECG (LAd+LVH), FRS-H</td>
<td>ETT, ECHO</td>
</tr>
<tr>
<td>41</td>
<td>M</td>
<td>2. BAV with severe AI</td>
<td>ECG (TWI)</td>
<td>ETT, ECHO</td>
</tr>
<tr>
<td>56</td>
<td>M</td>
<td>3. Probable HCM - grossly abnormal ECG with inferolateral TWI</td>
<td>FH</td>
<td>ETT, H, ECHO</td>
</tr>
<tr>
<td>54</td>
<td>M</td>
<td>Mild CAD (n=10)</td>
<td>FRS-I</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>59</td>
<td>M</td>
<td>5. Single vessel, calcified</td>
<td>FRS-I</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>48</td>
<td>M</td>
<td>6. Single vessel, multifocal</td>
<td>FRS-H</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>58</td>
<td>M</td>
<td>7. Minimal CCB</td>
<td>Sx (SYN), ECG (trifascicular block)</td>
<td>ETT, CACS</td>
</tr>
<tr>
<td>68</td>
<td>F</td>
<td>10. Single vessel, calcified</td>
<td>FRS-I</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>59</td>
<td>M</td>
<td>11. Single vessel, calcified</td>
<td>FRS-H, ≥ 65y</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>65</td>
<td>M</td>
<td>12. Single vessel, calcified</td>
<td>Sx (SYN), ECG (RBBB), FRS-H, ≥ 65y</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>65</td>
<td>M</td>
<td>13. Single vessel, mixed</td>
<td>Sx (SYN), ECG (RBBB), FRS-H, ≥ 65y</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>64</td>
<td>M</td>
<td>14. Double vessel, non-calcified</td>
<td>FRS-I</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>59</td>
<td>M</td>
<td>Moderate CAD (n=10)</td>
<td>Sx (pSYN), ECG (ST), FRS-I</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>61</td>
<td>M</td>
<td>15. Mild-mod CAD - double vessel, mixed</td>
<td>FRS-I</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>77</td>
<td>M</td>
<td>17. Mild-mod CAD - triple vessel</td>
<td>FRS-H, ≥ 65y</td>
<td>ETT, ECHO, MIBI, CATH</td>
</tr>
<tr>
<td>64</td>
<td>M</td>
<td>18. Mild-mod CAD - double vessel, minimally calcified</td>
<td>FRS-I</td>
<td>ETT, CTA, MIBI</td>
</tr>
<tr>
<td>59</td>
<td>M</td>
<td>19. Mild-mod CAD - double vessel, mixed</td>
<td>FH, FRS-H</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>68</td>
<td>M</td>
<td>20. Mild-mod CAD - double vessel, mixed</td>
<td>FRS-I, ≥ 65y, AFprev</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>59</td>
<td>M</td>
<td>21. Mod CCB - double vessel</td>
<td>FRS-H</td>
<td>ETT, CACS</td>
</tr>
<tr>
<td>63</td>
<td>M</td>
<td>22. Single vessel, mild diastolic dysfunction, high PVC burden (7178 PVCs)</td>
<td>FRS-I</td>
<td>ETT, H, ECHO, CTA, MIBI</td>
</tr>
<tr>
<td>67</td>
<td>M</td>
<td>23. Mod CCB</td>
<td>Sx (PAL), FRS-H, ≥ 65y, AFprev</td>
<td>ETT, CACS</td>
</tr>
<tr>
<td>69</td>
<td>M</td>
<td>24. Triple vessel, mixed, mild AR</td>
<td>ECG (LAd), FRS-I, ≥ 65y</td>
<td>ETT, ABP, CTA</td>
</tr>
<tr>
<td>61</td>
<td>M</td>
<td>Significant CAD (n=10)</td>
<td>FRS-H</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>71</td>
<td>F</td>
<td>26. Extensive CCB</td>
<td>FRS-I, ≥ 65y</td>
<td>ETT, CACS</td>
</tr>
<tr>
<td>Age</td>
<td>Sex</td>
<td>Diagnosis (n=35)</td>
<td>Abnormal finding on screen</td>
<td>Tests ordered</td>
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<tr>
<td>68</td>
<td>M</td>
<td>27. Single vessel, non-calcified</td>
<td>PE, FRS-H, ≥ 65y</td>
<td>ETT, CTA</td>
</tr>
<tr>
<td>57</td>
<td>M</td>
<td><strong>Valve Disease (n=4)</strong></td>
<td>FRS-I</td>
<td>ETT, H, ECHO, ABP, MIBI</td>
</tr>
<tr>
<td>63</td>
<td>M</td>
<td>29. Mild-mod MR; mild diastolic dysfunction</td>
<td>FH, FRS-I, AFprev</td>
<td>ETT, H, ECHO</td>
</tr>
<tr>
<td>59</td>
<td>M</td>
<td>30. Mild MR, mild diastolic dysfunction</td>
<td>PE, FRS-I</td>
<td>ETT, ABP, ECHO, MIBI</td>
</tr>
<tr>
<td>57</td>
<td>M</td>
<td><strong>Atrial Fibrillation (n=2)</strong></td>
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<tr>
<td>61</td>
<td>M</td>
<td>32. Paroxysmal AF</td>
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<tr>
<td>33.</td>
<td>M</td>
<td>Persistent AF, mild-mod MR</td>
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<tr>
<td>56</td>
<td>M</td>
<td><strong>Multiple CVD (n=2)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>M</td>
<td>34. CAD, valve disease, AF: Mild CAD - double vessel, calcified; Mild MVP, mild MR, mild AR</td>
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<td></td>
</tr>
<tr>
<td>35.</td>
<td>M</td>
<td>CAD, valve disease: Mild-mod CAD – triple vessel, mixed; mod AR, mod AI, diastolic dysfunction</td>
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</tbody>
</table>

ABP – ambulatory blood pressure; AF – atrial fibrillation; AFprev – previous atrial fibrillation; AI – aortic insufficiency; AR – aortic regurgitation; BAV – bicuspid aortic valve; CCB = coronary calcium burden; CTA – coronary computed tomography angiography; CACS – coronary artery calcium score; FH – family history; FRS – Framingham Risk Score; FRS-I – Intermediate Framingham Risk Score; FRS-H – High Framingham Risk Score; ETT – exercise treadmill test; H – Holter; HCM – hypertrophic cardiomyopathy; Hecho – handheld echocardiogram; LAd – left axis deviation; LVH – left ventricular hypertrophy; MIBI – myocardial perfusion imaging; Mod – moderate; MR = mitral valve regurgitation; PE – physical examination; PVC – premature ventricular contraction; RBBB – right bundle branch block; SOB – shortness of breath; SYN – syncope; pSYN – pre-syncope; SSSprev – previous sick sinus syndrome; ST – ST depression; Sx – symptoms; SVTprev – previous supraventricular tachycardia; PAL – palpitations; Q – significant Q waves; TWI – T wave inversion
Table 4.9 Comparison of exercise treadmill performance (Max METS) between cardiovascular disease types

<table>
<thead>
<tr>
<th>Coronary Artery Disease Severity</th>
<th>Max METS Achieved (mean ± SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild CAD (n=10)</td>
<td>14.9 (2.0)</td>
<td>11 - 19</td>
</tr>
<tr>
<td>Moderate CAD (n=10)</td>
<td>11.9 (2.7)</td>
<td>8 - 17</td>
</tr>
<tr>
<td>Significant CAD (n=4)</td>
<td>14.7 (3.8)</td>
<td>11 - 19</td>
</tr>
<tr>
<td>Valve Disease (n=3)</td>
<td>15.6 (2.1)</td>
<td>14 - 18</td>
</tr>
<tr>
<td>Multiple Diagnoses (n=2)</td>
<td>15.3 (4.7)</td>
<td>12 - 19</td>
</tr>
<tr>
<td>Atrial Fibrillation (n=2)</td>
<td>18.4 (0.3)</td>
<td>18 - 19</td>
</tr>
<tr>
<td>Congenital Heart Disease (n=4)</td>
<td>14.1 (4.3)</td>
<td>10 - 19</td>
</tr>
</tbody>
</table>

4.5.7 Participant Characteristics with Congenital Heart Disease

Four cases of congenital heart disease (low risk coronary artery anomaly, bicuspid aortic valve (BAV) with severe aortic insufficiency (AI), mitral valve prolapse (MVP), and a probable case of hypertrophic cardiomyopathy (HCM)) were detected in the screening process. Three of the four cases had an abnormal ECG. The individual with MVP answered positively to family history of MVP, and had no other indicators. No symptoms were reported by any of the four athletes. These individuals had calculated weekly training volumes of low (n=1), moderate (n=1), and high (n=2) (Table 4.13).

A 58-year-old, male, competitive ultra marathoner, diagnosed with BAV and severe AI had multiple criteria for follow-up (borderline left atrial enlargement and borderline voltage criteria for LVH on ECG, a diastolic murmur auscultated during the physical examination, positive family history, and a high FRS). He reported previous recognition of murmur at the age of 16, but had not been evaluated since that time. His average volume of activity per week was 99 MET-hr/wk. On ETT he obtained 90% of his maximum target heart rate and completed 9:47 minutes. The test was terminated due to a hypertensive blood pressure response (max blood pressure = 280/90mmHg). He had a final diagnosis of BAV with severe aortic insufficiency, confirmed by an echocardiogram. At the time of follow-up he did not meet criteria for valve replacement.
A 62-year-old, male, recreational hockey player, diagnosed with a low risk coronary artery anomaly displayed an abnormal ECG (T wave inversion in leads V4- V6) and had an intermediate FRS. His average weekly training volume was 40 MET-hr/wk. On ETT, he displayed 1.5mm ST depression in the inferolateral leads. A subsequent CTA was performed, which coincidently found the circumflex artery to originate from the coronary sinus and course posterior to the aorta. No medical treatment or exercise restrictions were necessary as this type of coronary artery is considered low risk.

A 41-year-old, recreational ultramarathoner, with probable apical HCM, reported a current weekly training volume of 46 MET-hr/wk, displayed a grossly abnormal ECG with inferolateral T wave inversion. He achieved 21:19 minutes on his ETT. Apical HCM is suspected, however, confirmation was not possible as the patient declined a MRI.

A 56-year-old, male cyclist diagnosed with MVP elicited further testing due to a positive family history. He reported a weekly volume of 109 MET-hr/wk. He achieved 16:22 minutes on his ETT and exhibited short runs of supraventricular tachycardia. Subsequently an echo and Holter were performed. His echo displayed normal biventricular function, mild-to-moderate MR, mild-to-moderate AR, mild-to-moderate TR, with no significant gradient across the left ventricular outflow tract. His Holter monitor displayed frequent PACs (578/24 hours), 2 supraventricular ectopic runs (9 beats), and no sustained arrhythmias. No medical treatment or exercise limitations were implemented but he was instructed to be mindful of his symptoms.

### 4.5.8 Participant Characteristics with Significant Coronary Artery Disease

Four new cases of significant CAD were diagnosed. All had an intermediate or high FRS, normal resting ECGs, and no symptoms. Two of the four athletes were > 64 years old. Two athletes were estimated to have a low weekly training volume and the other two had moderate weekly training volumes.

A 61-year-old recreational marathoner, who had competed in 25 half-marathons and 15 full marathons, with an average weekly training volume of 46 METS, met the criteria for an ETT based on a high FRS. He exhibited no symptoms. On his ETT, he went 18 minutes and
demonstrated 1mm inferolateral ST depression with rapid resolution. A subsequent CTA confirmed 100% occlusion in the mid-distal RCA, and mild-to-moderate disease in his proximal RCA, LAD, and left circumflex arteries. His aorta measured 43mm, which is greater than the mean aortic root dimensions size seen in male elite athletes (31.6 mm; 95% CI 30.2-33.1)\textsuperscript{174}. Other risk factors (in addition to a high FRS) included two out of three positive answers on psychosocial hostility questions, and currently taking anti-depressants.

A 71-year-old female, recreational runner, with a weekly training volume of 27 METS, had an intermediate FRS, eliciting an ETT. She did 10 minutes on the Bruce protocol, and had an equivocal ETT (1mm upsloping ST depression). She subsequently had a CACS to determine coronary calcium burden. Her calcium score was 663, putting her in the 94\textsuperscript{th} percentile for her age. She was treated with a statin and was already taking hydrochlorothiazide to control her blood pressure.

Our third case of significant CAD was a 68-year-old recreational runner, with an average weekly training volume of 25 METS. A high FRS, and an abnormal physical exam (grade 2/6 systolic murmur), elicited a follow-up ETT on which he completed 12 minutes and displayed 3mm of horizontal ST depression with incomplete resolution by the end of recovery. This prompted a CTA and a 75% non-calcified lesion in his proximal RCA was detected. He was treated with aspirin, a statin, and a beta-blocker.

The fourth case of significant CAD, was a 55-year-old male, who was a competitive skier and recreational runner and cyclist and obtained a weekly training volume of 45 METS. On screening, he had an intermediate FRS, and a grade 2/6 systolic murmur on his physical exam, generating an ETT. He reached 16 minutes and had 1mm down sloping ST depression in V2 and V3, with occasional PVCs. On further examination, CTA revealed 3-vessel disease. The left circumflex artery had mixed calcified plaque with lesions up to 70%. The RCA had lesions between 25-50% and the LAD had multifocal mixed densely calcified and non-calcified plaque. Additionally, he displayed mild-to-moderate systolic dysfunction, mild mitral valve regurgitation, and mild aortic regurgitation with mild aortic insufficiency.
4.5.9 Participant Characteristics with Moderate Coronary Artery Disease
Moderate CAD was discovered in ten athletes. All athletes had either an intermediate or high FRS. An abnormal ECG was observed in two (20%), one with ST depression and one with left axis deviation. Only two (20%) reported symptoms, and one reported symptoms due to his AF. Two had previous diagnosis of AF, were > 65 years, and had an intermediate or high FRS. Two of the athletes had triple vessel disease, neither reported symptoms, and one had an abnormal ECG (left axis deviation). The individual with left axis deviation also had mild aortic regurgitation. Additionally, there was one case of moderate single vessel disease with mild diastolic dysfunction, and a high PVC burden (7178 PVCs/24 hours). An intermediate FRS, prompted further testing and a PVC triplet was displayed on ETT. The individuals elicited low (n=3), moderate (n=5) and high (n=2) weekly training volumes (Table 4.13).

4.5.10 Participant Characteristics with Mild Coronary Artery Disease
Ten athletes were diagnosed with mild CAD. Seven (70%) of the athletes had an intermediate or high FRS. The three that did not have an intermediate or high FRS, elicited a follow-up due to one or more of the following: symptoms (syncope or shortness of breath), > 64 years, an abnormal ECG (trifascicular block or RBBB), or previous supraventricular tachycardia. A total of three (30%) had a positive resting ECG and three (30%) reported symptoms. These individuals elicited low (n=2), moderate (n=6), and high (n=2) weekly training volumes (Table 4.13).

4.5.11 Participant Characteristics with Multiple Cardiovascular Disease Diagnoses
Two participants presented with multiple CVD diagnoses. Both elicited a follow-up due to an intermediate or high FRS. In addition to an intermediate risk score, one reported symptoms (palpitations) and had an abnormal ECG (significant Q waves), and the other participant had a high FRS and an abnormal physical exam (IV/VI holosystolic murmur).

The 56-year-old, male, recreational runner and hockey player, previously played major junior hockey in the Western Hockey League and was on a university varsity team. A follow-up was prompted due to an abnormal ECG (septal Q waves suggesting an old MI), reported palpitations during exercise, and an average weekly volume of 61 METS. He accomplished 20 minutes on
the ETT (94% of maximal target heart rate), displayed frequent monomorphic PVCs, in isolation and triplets, and 1mm inferolateral ST segment depression with quick recovery. On CTA he displayed < 25% calcified plaque in his LM and LAD arteries, and 25-50% plaque in his RCA. An echocardiogram revealed mild MVP with mild mitral valve leaflet thickening, mild MR, a sclerotic, unrestricted AV, with mild AR. A Holter monitor was ordered to delineate the severity of PVCs and he was diagnosed with paroxysmal AF. He was recommended to start aspirin.

A 70-year-old, male recreational cyclist, and a previous national and provincial cyclist, exercised an average of 120 MET-hr/wk. At screening he was discovered to have a IV/VI holosystolic murmur on physical examination and a high FRS. On exercise testing he had a hypertensive blood pressure response (max BP 240/80), frequent PACs, PVCs originating from the RV not suppressed by exercise, and 1.5mm upsloping ST depression in the inferolateral leads. Consequently, a CTA was ordered and displayed 25-50% narrowing in the RCA, 25-50% mixed plaque in the proximal LAD, < 25%, patchy soft in the mid LAD, < 25% in second proximal marginal branch and no significant plaque in the left circumflex artery. On echo moderate AR, moderate AI, diastolic dysfunction, and a dilated aortic sinus were present.

Subsequent to his initial screen and follow-up tests he went into AF and was cardioverted and treated with apixaban, propranolol, and amlodipine. He does not have any activity restrictions. Interestingly, both of the cases with multiple cardiovascular diagnoses were previous provincial and/or national level athletes.

4.5.12 Participant Characteristics with Atrial Fibrillation

A total of three new cases of AF were discovered (Table 5.7). All reported palpitations and initially displayed abnormal ECGs (one with left axis deviation, one with significant Q waves, and one displayed AF). The two individuals that did not display AF on their initial resting ECG, were discovered during their ETT. Two of the three participants were previous elite athletes, and all three reportedly exercising the equivalent of 60-100 MET-hr/wk. In addition to the three new cases of AF, ten individuals had previously diagnosed AF. Four of the ten (40.0%) cases went on for further testing and were diagnosed with clinically significant CVD (three had CAD and one had mild MR with mild diastolic dysfunction). The individuals with previous AF and newly
diagnosed CVD reported low (n=2), moderate (n=1), and high (n=1) weekly volumes of activity (Table 4.13).

4.5.13 Participant Characteristics with Significant Valvular Disease

Significant valvular disease was discovered in seven participants (one individual with BAV, two with MVP, two with MR and mild diastolic dysfunction, and one with mild AR and mild AI) and four (57.1%) were discovered on physical examination. The remaining three elicited a follow-up due to one or more of the following indicators: an intermediate FRS, positive family history, or history of AF. A positive ETT was found due to arrhythmias (> 7 PVCs/min in recovery, PVC triplet during exercise, SVT) in four participants, marked hypertensive response and failure to reach target heart rate in one participant (BAV), and two were due to ETTs that were positive for ischemia (one of which also had CAD). Consequently, all underwent an echo and were diagnosed with valvular disease, two of which also had CAD. Five individuals had a weekly training volume > 75 MET-hr/wk and two had a weekly training volume between 41-75 MET-hr/wk.

4.5.14 Clinical Diagnoses Not Associated with SCD

An additional 12 (3.8%) had a new clinical diagnoses not associated with SCD (i.e. high PVC burden, mild-to-moderate valvular disease, low systolic function, and positive ETT but low Duke treadmill score) and, therefore, were not included as positive cases found in the positive predictive calculation. There were nine cases of non-clinically significant valvular disease; interestingly four individuals had moderate (41-75 MET-hr/wk) and four had high (>75 MET-hr/wk) weekly training volumes (Table 4.13). Their clinical characteristics can be found in Table 4.10.
### Table 4.10 Non-clinically significant cardiovascular disease diagnoses: clinical characteristics

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diagnoses</th>
<th>Abnormal finding on screen</th>
<th>Tests ordered</th>
</tr>
</thead>
<tbody>
<tr>
<td>62</td>
<td>M</td>
<td>High PVC Burden (2) 1. 6558 PVCs (7%), ETT 5 beat run of VT, two different foci 2. 2019 PVCs (1307 bigeminal cycles)</td>
<td>Sx</td>
<td>ETT, H, ECHO</td>
</tr>
<tr>
<td>40</td>
<td>M</td>
<td>3. Mild MR</td>
<td>PE</td>
<td>ETT, Hecho</td>
</tr>
<tr>
<td>49</td>
<td>F</td>
<td>4. Mild MR</td>
<td>PE</td>
<td>ETT, Hecho</td>
</tr>
<tr>
<td>53</td>
<td>F</td>
<td>5. Mild MR</td>
<td>FH</td>
<td>ETT, Hecho</td>
</tr>
<tr>
<td>58</td>
<td>F</td>
<td>6. Mild MR</td>
<td>Sx, FH</td>
<td>ETT, Hecho</td>
</tr>
<tr>
<td>49</td>
<td>F</td>
<td>7. Mild MR</td>
<td>PE</td>
<td>ETT, ECHO</td>
</tr>
<tr>
<td>67</td>
<td>M</td>
<td>Other 1. Positive ETT</td>
<td>≥ 65y</td>
<td>ETT, no further tests (High DTS, low FRS)</td>
</tr>
<tr>
<td>68</td>
<td>F</td>
<td>2. Low systolic function (EF 55%)</td>
<td>Sx, ECG</td>
<td>ETT, H, ECHO</td>
</tr>
</tbody>
</table>

AFprev – previous atrial fibrillation; DTS – duke treadmill score; FH – family history; FRS – Framingham Risk Score; FRS-I – Intermediate Framingham Risk Score; FRS-H – High Framingham Risk Score; ETT – exercise treadmill test; H – holter; Hecho – handheld echocardiogram; MR = mitral valve regurgitation; PE – physical examination; PVC – premature ventricular contraction; Sx – symptoms; VT – ventricular tachycardia

### 4.5.15 Unconfirmed Cardiovascular Disease Diagnoses

A total of nine individuals have unconfirmed cardiovascular disease diagnoses (Table 4.11).

There was one case of suspected long QT syndrome in a 49-year-old female ultra marathoner. On resting ECG she displayed a QT interval of 529ms. Additionally, she reported a previous presyncopal episode and a positive family history of a premature family death when her brother was in a fatal car accident at the age of 16. When manually corrected using the slope intercept
method the QTc measured 420ms. During ETT, the QT interval did lengthen; however, a definitive diagnosis has not been made and is pending results from the inherited arrhythmia clinic. A 61-year old male had anterolateral T wave inversion on his resting ECG; however, CMR did not display criteria for HCM, and there was no delayed myocardial enhancement. Three individuals had indications for further tests (high FRS, and/or positive or equivocal ETT, and/or high blood pressure (>180/110mmHg), but declined. Lifestyle or medical treatment was suggested. Four individuals are waiting further tests. These nine individuals were not included as true positive cases in the positive predictive value calculation, but were included in the total number of follow-ups indicated for the respective tests that discovered them.

Table 4.11 Unconfirmed cardiovascular disease diagnoses: clinical characteristics

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Unconfirmed Diagnoses</th>
<th>Abnormal finding on screen test</th>
<th>Tests ordered</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>F</td>
<td><strong>Unconfirmed congenital heart disease (2)</strong></td>
<td>ECG, Sx, FH</td>
<td>ETT, pending inherited arrhythmia results</td>
</tr>
<tr>
<td>61</td>
<td>M</td>
<td>1. Long QT syndrome</td>
<td></td>
<td>ETT, H, MRI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Query apical HCM (mildly dilated LV), no MRI criteria of HCM, no delayed myocardial enhancement</td>
<td>ECG (anterolateral T wave inversion), FRS-I</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>M</td>
<td><strong>Unconfirmed CAD</strong></td>
<td>PE</td>
<td>ETT; declined CACS, BP med recommended</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. High blood pressure (&gt;180/110)</td>
<td></td>
<td>ETT; declined CACS, recommended statin</td>
</tr>
<tr>
<td>77</td>
<td>M</td>
<td>2. FRS &gt;30%, equivocal ETT</td>
<td>FRS-H, ≥ 65y</td>
<td>ETT; declined CTA</td>
</tr>
<tr>
<td>70</td>
<td>M</td>
<td>3. FRS &gt; 20%, positive ETT</td>
<td>FRS-H, ≥ 65y, PVDprev</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Waiting Tests</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57</td>
<td>M</td>
<td>1. Waiting further tests</td>
<td>FRS-H</td>
<td>ETT, pending CACS</td>
</tr>
<tr>
<td>61</td>
<td>M</td>
<td>2. Waiting further tests</td>
<td>FRS-H</td>
<td>ETT, pending CACS</td>
</tr>
<tr>
<td>67</td>
<td>M</td>
<td>3. Waiting further tests</td>
<td>FRS-H, ≥ 65y</td>
<td>ETT, pending CACS</td>
</tr>
<tr>
<td>39</td>
<td>M</td>
<td>4. Waiting further tests</td>
<td>Sx, PE</td>
<td>ETT, pending ECHO</td>
</tr>
</tbody>
</table>

CACS – coronary artery calcium score; FH – family history; FRS – Framingham Risk Score; FRS-I – Intermediate Framingham Risk Score; FRS-H – High Framingham Risk Score; ETT – exercise treadmill test; H – holter; Hecho – handheld echocardiogram; HCM – hypertrophic cardiomyopathy; LV – left ventricle; MR = mitral valve regurgitation; MRI – myocardial resonance imagining; PE – physical examination; PVC – premature ventricular contraction; Sx – symptoms; VT – ventricular tachycardia
4.5.16 Positive Predictive Value

The prevalence of clinically significant cardiovascular disease in this population of Canadian Masters athlete was 12.2% (n=35). Positive predictive value was used to calculate the effectiveness of screening tools. A high FRS was the single most effective tool in detecting CVD (PPV = 56.0%). Age (≥ 65 years), physical examination, resting ECG, intermediate FRS, and the AHA modified personal and family history questionnaire, had 38.7%, 33.3%, 28.2%, 20.0%, and 18.4% PPV, respectively (Table 4.12). Table 4.11 lists the individuals that did not have their diagnoses confirmed. There were five individuals with a high FRS and one had a high blood pressure (>180/110), and two of these individuals had a positive or equivocal ETT. These cases were not included in “positive cases found” in the PPV calculation; however, their indications were included in “follow-ups indicated”. Therefore, the PPV for high FRS, age, and physical examination could be greater than the reported 56.0%, 38.7%, and 33.3%, respectively, and would increase the number of Masters athletes with clinically significant CVD to 14.3%. Similarly, if the Long QT syndrome case (unconfirmed diagnoses) is deemed positive, the PPV for ECG will be increased to 30.8% and would increase the prevalence of clinically significant CVD.

Table 4.12 Positive predictive value of screening tools used for clinically significant cardiovascular disease diagnoses

<table>
<thead>
<tr>
<th>Screening Tool</th>
<th>Follow-ups indicated</th>
<th>Positive cases found</th>
<th>PPV (%)</th>
<th>False-positive %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Questionnaire</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal symptoms</td>
<td>103</td>
<td>19</td>
<td>18.4</td>
<td>81.6</td>
</tr>
<tr>
<td>Family history</td>
<td>54</td>
<td>8</td>
<td>14.8</td>
<td>85.2</td>
</tr>
<tr>
<td>Previous CVD (excluding CAD)</td>
<td>33</td>
<td>5</td>
<td>15.1</td>
<td>84.9</td>
</tr>
<tr>
<td>FRS-Intermediate</td>
<td>16</td>
<td>6</td>
<td>37.5</td>
<td>62.5</td>
</tr>
<tr>
<td>12-lead resting ECG</td>
<td>80</td>
<td>16</td>
<td>20.0</td>
<td>80.0</td>
</tr>
<tr>
<td>Physical examination</td>
<td>39</td>
<td>11</td>
<td>30.0</td>
<td>70.0</td>
</tr>
<tr>
<td>≥ 65 years old</td>
<td>18</td>
<td>6</td>
<td>33.3</td>
<td>66.7</td>
</tr>
<tr>
<td>FRS-High</td>
<td>31</td>
<td>12</td>
<td>38.7</td>
<td>61.3</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>14</td>
<td>56.0</td>
<td>44.0</td>
</tr>
</tbody>
</table>

*select cases had a positive response to more than one tool (ie. murmur + irregular HR, or 2 abnormalities on ECG)
4.5.17 Framingham Risk Score

Prevalence of CVD categorized by FRS is displayed in Figure 4.7. The prevalence of CVD increased with an increasing FRS. A total of 181 participants had a low FRS and 62 (34.5%) went on for further evaluations because they met one or more of the criteria for follow-up (i.e. symptoms, family history, abnormal ECG, age ≥ 65, previous CVD). After further evaluations, five participants (8.1%) were diagnosed with CVD. Eighty participants had an intermediate risk score and went on for further evaluations, of which 16 (20.0%) were diagnosed with clinically significant CVD, two of which were diagnosed with significant CAD. Notably, an intermediate FRS was the single indicator in six (17.1%) of the total cases diagnosed with CVD (Table 4.6). A high FRS was present in 25 participants and 14 (56.0%) were diagnosed with CVD. Five athletes elicited a high FRS as their only indicator for follow-up. Two were diagnosed with mild CAD, two with moderate CAD, and one with significant CAD.

Figure 4.7 Associations between cardiovascular risk and cardiovascular disease

4.5.18 Physical Exam

The physical examination was abnormal in six cases, but was an indicator for follow-up in 18 individuals, eliciting a 33.3% PPV and 66.7% false-positive rate (Table 4.10). In addition, there
were a total of seven cases of clinically significant valvular disease (all had an echo), of which the physical examination detected only three (42.0%). In other words, the physical examination had a 58.0% false-negative rate in the cases that were found to be positive. The individuals that were found to have valvular disease went on for further testing due to an intermediate or high FRS, and/or positive family history, and/or symptoms (not due to an abnormal physical exam). Similarly, five of the nine non-clinically significant valvular diseases were not detected on physical examination, producing a 55.6% false-negative rate. These five cases had additional evaluations primarily due to a positive family history, and/or symptoms, and/or intermediate FRS.

4.5.19 Resting ECG
The resting ECG had a PPV of 28.2% and played an important role in detecting CHD and AF, whereas it had little value in detecting CAD; only six of the 26 (23.1%) cases with CAD had a positive resting ECG, whereas three of the four cases (75.0%) with CHD, and all three cases of AF (100.0%) displayed an abnormal resting ECG.

4.5.20 Personal and Family History Questionnaire
The modified AHA questionnaire, including personal and family cardiovascular history, and previous diagnoses of CVD (excluding CAD) was the least effective in detecting clinically significant CVD, with a PPV of 18.4%. Only eight (22.9%) of the clinically significant cases of CVD exhibited symptoms, whereas it was indicated in 54 follow-ups. A positive family history indicated 33 follow-ups, whereas only five (15.1%) were true positive cases. A positive family history was the sole indicator in one individual with CVD (mild MVP). An abnormal 4th heart sound was also heard in this individual, but is not considered an indicator for follow-up according to the AHA criteria. Importantly, all four cases of significant CAD, and all four cases of CHD, did not exhibit symptoms. Symptoms were reported in only two (20%) cases of mild, and three (30%) cases of moderate CAD. Conversely, all three cases of AF reported symptoms. Individuals with previous CVD (excluding CAD) had a PPV of 37.5%.

4.5.21 Exercise Treadmill Test
Thirty of the 35 (85.7%) cases of new CVD diagnoses had an abnormal stress test (ST depression or PVC indicator). Specifically, 21 of the 35 cases had ST depression, and eight cases
had either $\geq 7$ PVCs/minute or a minimum of one PVC triplet during the test, and one had an abnormal resting ECG (probable HCM subject). Additionally, 10 individuals who had a high FRS and were diagnosed with CVD, elicited a positive ETT.

4.5.22 Associations of Cardiovascular Disease and Risk with Physical Activity

The association between cardiovascular risk and cardiovascular disease with weekly training volumes is displayed in Table 4.13. The majority of participants reported a high (44%) or moderate (40%) weekly training volume (MET-hr/wk) (Figure 4.8). When examining the relationship between weekly training volume and cardiovascular risk (FRS), there was a significant association ($x^2=11.162; \text{df}=4; p<0.025$) (Figure 4.9). A significant difference was seen between the low and intermediate FRS groups ($x^2=7.981; p=0.018$) and the low and high FRS groups ($x^2=6.145; p=0.046$), but not between the intermediate and high FRS groups ($x^2=0.387; p=0.824$). The lowest weekly training volume group (15-40 MET-hr/wk) had the greatest prevalence of individuals with a high FRS (13.0%), and the high volume group had the lowest (5.6%) prevalence of individuals with a high FRS volume groups. Similarly, the prevalence of new CAD was highest in the low volume group (15.1%) and lowest in the high volume group (3.2%). The moderate volume group had the highest absolute number of total new cases of CAD (n=13). There were a total of four (3.2%) new cases of CAD in the high volume group (two cases of mild and two cases of moderate CAD). The prevalence of total new clinically significant CVD (excluding non-significant valvular disease) followed a similar pattern: the group who had the highest prevalence of clinical significant CVD was highest in the low MET group (17.4%), followed by the moderate volume group (15.0%), and the high volume group (8.0%) (Figure 4.10). Interestingly, diagnoses of valvular disease (significant and non-clinically significant), was the highest in the high volume group (5.6%). Similarly, new diagnoses of AF and the two cases of multiple diagnoses were in the moderate and high volume groups. The four cases of new CHD were divided amongst the weekly training volume groups. Interestingly, the two valvular diagnoses (BAV and MVP) were high volume exercisers. The case of probable HCM was a moderate volume exerciser. Overall, the presence of CVD decreased with increasing volumes of physical activity.
The association between CVD and type of sport (endurance vs. mixed vs. power) is displayed in Table 4.14. Endurance sports had the most number of participants (n=24) with CVD; however, most participants’ primary sport was endurance (n=190). There were a total of seven power sport athletes, two of which had CAD. Interestingly, there were eight endurance athletes (4.2%) who had mild CAD, compared to two (2.4%) power athletes. All cases of AF, multiple diagnoses and valvular disease were in endurance athletes.

**Figure 4.8 Number of participants categorized by weekly training volume**
Table 4.13 Cardiovascular risk and cardiovascular disease association with weekly training volumes (n, %)

<table>
<thead>
<tr>
<th>Cardiovascular risk</th>
<th>LOW 15-40 MET-hr/wk</th>
<th>MODERATE 41-75 MET-hr/wk</th>
<th>HIGH &gt;75 MET-hr/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>46 (16)</td>
<td>114 (40)</td>
<td>126 (44)</td>
</tr>
<tr>
<td>FRS-L</td>
<td>25 (54.3)</td>
<td>63 (55.3)</td>
<td>93 (73.8)</td>
</tr>
<tr>
<td>FRS-I</td>
<td>15 (32.6)</td>
<td>39 (34.2)</td>
<td>26 (20.6)</td>
</tr>
<tr>
<td>FRS-H</td>
<td>6 (13.0)</td>
<td>12 (10.5)</td>
<td>7 (5.6)</td>
</tr>
</tbody>
</table>

Cardiovascular disease

 Coronary artery disease

<table>
<thead>
<tr>
<th></th>
<th>LOW 15-40 MET-hr/wk</th>
<th>MODERATE 41-75 MET-hr/wk</th>
<th>HIGH &gt;75 MET-hr/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>2 (4.3)</td>
<td>6 (5.3)</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (6.5)</td>
<td>5 (4.4)</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Significant</td>
<td>2 (4.3)</td>
<td>2 (1.8)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>7 (15.1)</td>
<td>13 (11.4)</td>
<td>4 (3.2)</td>
</tr>
</tbody>
</table>

 Valve disease

<table>
<thead>
<tr>
<th></th>
<th>LOW 15-40 MET-hr/wk</th>
<th>MODERATE 41-75 MET-hr/wk</th>
<th>HIGH &gt;75 MET-hr/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant</td>
<td>0 (0.0)</td>
<td>1 (0.9)</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Non-significant</td>
<td>1 (2.2)</td>
<td>4 (3.5)</td>
<td>4 (3.2)</td>
</tr>
<tr>
<td>Total</td>
<td>1 (2.2)</td>
<td>5 (4.4)</td>
<td>7 (5.6)</td>
</tr>
</tbody>
</table>

 Multiple diagnoses

<table>
<thead>
<tr>
<th></th>
<th>LOW 15-40 MET-hr/wk</th>
<th>MODERATE 41-75 MET-hr/wk</th>
<th>HIGH &gt;75 MET-hr/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>0 (0.0)</td>
<td>1 (0.9)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>1 (2.2)</td>
<td>1 (0.9)</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Total</td>
<td>8 (17.4)</td>
<td>17 (15.0)</td>
<td>10 (8.0)</td>
</tr>
</tbody>
</table>

*One additional participant has AF, and is included in the multiple diagnoses group (moderate volume)

Figure 4.9 Association between cardiovascular risk and cardiovascular disease
Figure 4.10 Types cardiovascular disease and association with weekly training volume

![Graph showing prevalence of cardiovascular disease (%)](image)

Table 4.14 Association between type of sport and cardiovascular disease

<table>
<thead>
<tr>
<th></th>
<th>Running (n=21)</th>
<th>Marathon (n=62)</th>
<th>Ultra-marathon (n=35)</th>
<th>Cycling (n=36)</th>
<th>Triathlon (n=19)</th>
<th>Cross-country ski (n=5)</th>
<th>Total endurance sports (n=190)</th>
<th>Total mixed sports (n=82)</th>
<th>Total power sports (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild CAD</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8 (4.2)</td>
<td>2 (2.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate CAD</td>
<td>2</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
<td>3 (1.6)</td>
<td>6 (7.3)</td>
<td>1 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Significant CAD</td>
<td>2</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
<td>3 (1.6)</td>
<td></td>
<td>1 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Valve disease</td>
<td>1</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
<td>3 (1.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 (1.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple diagnoses</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td>2 (1.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>2</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td>3 (1.6)</td>
<td>1 (1.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>8</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>24 (12.6)</td>
<td>9 (11.0)</td>
<td>2 (28.6)</td>
</tr>
</tbody>
</table>

CHD – congenital heart disease; CAD – coronary artery disease
4.5.23 Association of Atrial Fibrillation, High PVC Burden and Previous Coronary Artery Disease with Volume of Physical Activity and Lifetime Training Hours

Table 4.15 demonstrates the association between AF, including the three new cases of AF (new), the four cases of previously known AF who were diagnosed with new CVD (known, new CVD), and the six cases of previously known AF with no new CVD diagnoses (known, no new CVD), with current weekly training volumes and lifetime training hours. The mean lifetime training hours of the current population was 11,259 (±8005.7), which was lower than the group newly diagnosed with AF (17,489 ±5153.6) and the total group with AF (14,958 ±8613.4). The group with new AF, was also on average, younger than those with known AF (58.0, ± 2.6 vs. 63.9 ± 6.1). Those who had a high PVC burden had lower lifetime training hours compared to the study population (10,356 ± 6045.5 versus 11,259 ±8005.7) and were either moderate (n=2) or low (n=1) volume exercisers.

Although we did not include those with previously known CAD we examined their volume of activity and lifetime training hours. Interestingly, five individuals with previously diagnosed CAD engaged in high weekly physical activity volumes, and three engaged in moderate weekly volume activity levels. However, their lifetime training hours was less than the study population (10,075 ±11,399.5 versus 11,259 ±8005.7).

Table 4.15 Association of atrial fibrillation, high PVC burden, and previous coronary artery disease with volume of physical activity and lifetime training hours

<table>
<thead>
<tr>
<th>Atrial Fibrillation (n=13)</th>
<th>Age (mean ±SD)</th>
<th>LOW 15-40 MET-hr/wk</th>
<th>MODERATE 41-75 MET-hr/wk</th>
<th>HIGH &gt;75 MET-hr/wk</th>
<th>Lifetime Hours (mean ±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>-</td>
<td>46</td>
<td>114</td>
<td>126</td>
<td></td>
</tr>
<tr>
<td>New (n=3)</td>
<td>58.0 (2.6)</td>
<td>0 (0.0)</td>
<td>2 (1.8)</td>
<td>1 (0.8)</td>
<td>17,489 (5153.6)</td>
</tr>
<tr>
<td>Known, new CVD (n=4)</td>
<td>67.9 (4.9)</td>
<td>2 (4.3)</td>
<td>1 (0.9)</td>
<td>1 (0.8)</td>
<td>12,727 (8908.8)</td>
</tr>
<tr>
<td>Known, no new CVD (n=6)</td>
<td>59.8 (7.3)</td>
<td>1 (2.2)</td>
<td>3 (2.6)</td>
<td>2 (1.6)</td>
<td>14,660 (11,777.1)</td>
</tr>
<tr>
<td>Total</td>
<td>61.9 (4.9)</td>
<td>3 (6.5)</td>
<td>6 (5.3)</td>
<td>4 (3.2)</td>
<td>14,958 (8613.4)</td>
</tr>
<tr>
<td>High PVC Burden (new)</td>
<td>63.6 (2.0)</td>
<td>1 (2.2)</td>
<td>2 (1.8)</td>
<td>0 (0.0)</td>
<td>10,356 (6045.5)</td>
</tr>
<tr>
<td>Previous CAD</td>
<td>65.1 (7.4)</td>
<td>0 (0.0)</td>
<td>3 (2.6)</td>
<td>5 (4.0)</td>
<td>10,075 (11,399.5)</td>
</tr>
</tbody>
</table>
4.6 Discussion

This study sought to investigate the prevalence of CVD and cardiovascular risk in a sample of Canadian recreational and competitive Masters athletes, and determine the most effective method for detecting CVD. To our knowledge, this is the first study to extensively examine population characteristics, prevalence of CVD, and screening tools to detect CVD, in a prospective study of highly active middle-aged Canadians. However, despite high levels of physical activity new CVD and high cardiovascular risk scores (FRS) were discovered in 12.2% and 8.7% individuals, respectively. The presence of cardiovascular risk factors is higher than previous reports examining active individuals, but lower compared to a representative sample of Canadians. CAD was the most frequent diagnosis of clinically significant CVD (9.1%). In addition, there were four (1.4%) cases of congenital heart disease, five (1.7%) cases of clinically significant valvular disease, and three cases (1.0%) of atrial fibrillation. There were two (0.7%) individuals who had multiple diagnoses (AF, CAD, valvular disease). A high cardiovascular risk score (FRS) was the single most effective tool in detecting CAD (56.0% PPV). The modified AHA-14 item questionnaire produced the greatest number of false-positives. The physical exam had the second highest PPV (33.0%). Age (≥ 65 years), was also an important predictor for CVD, with a PPV of 38.7%.

4.6.1 Prevalence of Cardiovascular Disease and Risk Factors

Before recommendations can be made on implementing a screening program, an understanding of the risk in the population being studied must be determined. In Canada, heart disease and stroke accounts for approximately 20% of all deaths, and is the leading cause of hospitalizations. In British Columbia the mortality rate for heart disease and stroke is 141.9 per 100,000 deaths per year. The cardiovascular risk and mortality in Masters athletes is unknown and because they represent a very active population (exercise is a factor that can prevent the development of CAD), it would be postulated their risk would be lower; however, whether or not that translates into decreased CVD is not known. Our results did indicate that Masters athletes have a lower prevalence of risk factors compared to the Canadian population; however, dyslipidemia (36.4% vs 38.0%) and inadequate servings of fruits and vegetables (43.8% vs. 54.9%) were similar. As would be expected in a very active population, there was a lower
prevalence of smokers (0.7% versus 21.0%), diabetes mellitus (0.3% versus 5.5%), and obesity (8.0% versus 20.4%). Surprisingly, a greater proportion (5.2% versus 4.3%) of individuals in the present study presented with depression (a positive response to having felt sad, blue, or depressed for two weeks or more in a row and a positive response to five of the seven additional questions). In the Canadian literature, higher reports of depression are seen in youth and women; however, our study was comprised mostly of males over 50 years of age. The sample size in our study is relatively small; therefore, whether or not this holds true for a greater population remains to be elucidated.

**Figure 4.11 Cardiovascular risk factors compared to the Canadian population**

We also sought to compare the prevalence of risk factors in our present study to other literature, to determine if Masters athletes in British Columbia are at greater risk. To date, there are only two studies that have prospectively evaluated the prevalence of CVD and implications of PPS in
adult athletes, with clear differences in their methodology. In Switzerland, Menafoglio et al. strictly followed the EACPR guidelines in a group of highly active individuals from a variety of sports disciplines, and in Stockholm, Aagaard et al. examined a group of novice runners that, in addition to the EACPR guidelines included an echocardiogram. In comparison to Menafoglio’s study, our study had four times the number of new clinical diagnosis (12.2% versus 2.8%) and twice as many as Aagaards’ study (12.2% versus 5.9%). Additionally, 25 athletes (8.7%) in our sample had a high FRS, which is double the prevalence evidenced in Menafoglio’s and Aagaards’ studies (4.1% and 0.65%, respectively). Age and sex are powerful predictors of both cardiovascular risk and CVD. In the present study, the average age was 54.0 years (± 8.8, range 35-81) and the majority were male (66.2%). Thirty-one (10.8%) participants were 65 years or older. In comparison, the mean age of Menafoglio’s study was 48.6 (± 7.3, range 35-65 years) with a 72.7% male predominance, and in Aagaard’s study the population was entirely male with a mean age of 51 (± 5.0 range, 45-69 years). In our present study, 12 individuals ≥ 65 were diagnosed with clinically significant CVD. Adjusting for age (removing those ≥ 65 years from the analysis), 23 (8.0%) individuals presented with new CVD, which is still greater than reported in both Menafoglio (2.8%) and Aagaard’s (5.9%) studies. Similarly, if we excluded those ≥ 65 years with a high FRS, 12 (4.2%) individuals <65 years presented with a high FRS, which is in alignment with Menafoglio’s study, but still higher than Aagaard’s study. Because of the higher prevalence of cardiovascular risk factors in our study population, it is not surprising that we observed a greater number of individuals with CAD (n=26). In Menafoglio’s study, only one individual was diagnosed with CAD, and none were diagnosed with CAD in Aagaard’s study.

A potential explanation for a higher prevalence of CVD in the present study is the inclusion of an intermediate risk score, those who had previously diagnosed CVD (excluding CAD), and individuals ≥ 65 years, in the criteria that necessitates a follow-up. Additionally, 30 of the 35 new diagnoses exhibited a positive ETT. An intermediate FRS was present in 16 (20%) cases of new CVD and was the sole indicator for further testing in six (17.1%) of the cases. Although individuals with previously diagnosed CVD (excluding CAD) were included, five of them had additional indicators for follow-up (family history, symptoms, ≥ 65 years). Importantly, unlike findings by Menafoglio and Aagaard’s studies, where no athlete who performed an additional
ETT due to a high-risk score was diagnosed with significant CAD, our study discovered ten cases of CVD who had a high FRS and a positive ETT. Those who had a negative ETT, went on for further testing if they had a high FRS, positive physical examination, positive symptoms during ETT, and/or positive family history.

A total of 7 (2.4%) participants were diagnosed with significant valvular disease. The prevalence of valvular disease in our study is similar to Menafoglio’s study in which nine (1.1%) were diagnosed with valvular disease (5 cases of MVP, 3 cases of BAV, and one case of pulmonary stenosis) accounting for nearly half of their total diagnoses. Sofi et al., in 30 065 competitive sports participants reported valvular disease in 23.9% of participants and Aagaard et al. did not report any valvular disease. Interestingly, Aagaard’s study population consisted of novice runners, whereas in our study, Menafoglio’s, and Sofi’s studies, the participants were active approximately four to six hours a week, and included seasoned athletes. Valvular regurgitation is frequently detected in athletes with reports showing 90% of athletes displaying single valve regurgitation and 20% having triple-valve regurgitation, with the vast majority having no clinical significance. A potential explanation for increased valvular regurgitation, in particular MR, includes increased left atrial pressure due to increased heart rate and cardiac output with intensive, prolonged exercise. Enlargement of the left atrium in well-trained athletes could also be the reason why MR and AF are often seen together. When determining the severity of MR in athletes, LV end-systolic volume should be used to distinguish the clinical significance of LV enlargement. Exercise generally doesn’t affect the regurgitant fraction because of reduced systemic resistance; however, in those with an elevated systemic blood pressure, exercise may cause an increase in the volume of regurgitation and pulmonary capillary pressures.

A possible explanation for AR in athletes (excluding congenital BAV) is systemic hypertension. Therefore, high blood pressure readings in athletes should not be ignored and further examinations to determine the severity of hypertension (24-hour ambulatory blood pressure).

### 4.6.2 Abnormal Findings Elicited with Pre-participation Screening

Over half of the study participants (58.3%) required additional examinations (ETT and/or cardiology consult) according to pre-determined criteria. This proportion is substantially greater.
than Menafoglio (14.3%) and Aagaard’s (9.0%) studies; however, they are not comparable due to the inclusion of participants with an intermediate risk score, previous cardiovascular disease (excluding CAD), and those > 64 years in our present study and the inclusion of an echocardiogram in Aagaard’s study (more participants with abnormal ECGs may be have required further work-up). There were also a substantially greater proportion of adults requiring additional examinations compared to our young competitive athlete study (8.3% in phase 1 and 4.4% in phase 2), which is primarily due to concern of CAD in the present population. Our study results are similar to the findings by Abbatemarco et al. when they recently applied the AHA 2001 Masters guidelines to 1,457 athletes 35 years and over. They found that 34.0% were eligible for an ETT (compared to 58.3% in our present study); however, they did not include individuals with an abnormal resting ECG and abnormal physical exam, which would have contributed to a higher number or individuals requiring further testing in our study.

In the present study, an abnormal personal or family history was indicated in 103 (36.0%) of the follow-ups, which is much higher than in Menafoglio (3.0%) and Aagaard’s (2.0%) studies. Palpitations (11.2%) and positive family history (11.5%) were the most common indicators that elicited a follow-up, compared to 0.3% and 1.5%, respectively in Menafoglio’s study, and 1.3% for palpitations in Aagaard’s study. A lower rate of negative personal history in Menafoglio and Aagaard’s studies could owe to a more extensive review of the participants’ history to exclude non-clinically relevant symptoms. In the current study, qualified physicians performed the screening and were instructed to exclude palpitations that occurred at rest, but include palpitations that occurred during exercise (according to the AHA guidelines, palpitations during exercise warrant further investigation), even if they thought they were not clinically significant. If the physician completed a more thorough review to exclude non-clinically significant symptoms, it is likely fewer follow-ups would have occurred. However, we wanted to mimic the protocol set forth by the AHA to determine the true sensitivity of the questionnaire. Selection bias may have contributed to a higher rate of positive family history in the present study.

According to the ‘Seattle criteria’, an abnormal resting ECG was considered abnormal and required follow-up in 39 (13.3%) participants. This is greater than in Menafoglio’s (5.1%), Aagaard’s (3.9%), and Sofi’s (1.2%) studies. Left axis deviation accounted for 3.8% ECG
abnormalities in our study versus 1.1% in Menfoglio’s study. In Aagaard’s study, left axis deviation in isolation was not deemed to require further work-up. A possible explanation for the higher number of individuals who exhibited left axis deviation on their ECGs in our study could be due to the very active, lifelong exercisers in our current study. Iskander et al. reported a 4.1mm greater left atrial diameter in elite athletes compared to controls\textsuperscript{174,177}. Since the commencement of this study, the refined Seattle criteria was released and reported that left axis deviation in isolation, correlates extremely poorly with serious cardiac pathology\textsuperscript{178,179}. Similarly, if right atrial enlargement, left atrial enlargement, right axis deviation, and right ventricular hypertrophy are seen in isolation, further evaluations aren’t necessary. Notably, these studies were performed in highly trained young athletes (14-35 years); therefore, whether or not this can be extrapolated to our current population remains to be determined considering the differences in types of CVD that exist amongst these two populations. In our current population left axis deviation was evident in three individuals diagnosed with CVD. A revised version of the “Seattle Criteria” for Masters athletes may be warranted.

4.6.3 Effectiveness of the Screening Tools
In addition to an understanding of the prevalence of disease the effectiveness of proposed screening procedures must be determined. The utility of a screening test is a function of its ability to successfully intervene upon a disease state to prevent morbidity or mortality in a cost-effective manner\textsuperscript{165}. The presence of risk factors, particularly a high FRS (PPV = 56.0%), appropriately flagged individuals that were at risk for CAD. The physical examination had the second highest PPV (33.3%) and a high false-positives rate (66.7%). Additionally, in the individuals that were diagnosed with valvular disease, the physical exam only picked up 42.0% (3/7 of the cases), which suggests a 58.0% false-negative rate in this sub-group that went on for further testing due to other indicators. We did not perform an echocardiogram in all study participants; therefore, the false-negative rate of the physical examination in the entire population is unknown. Interestingly, a positive ETT (PVC indicators) in those who had significant valvular disease was observed. Whether or not other studies have seen a positive ETT (due to significant arrhythmias/PVCs) in the presence of valvular disease is unknown. Menafoglio et al. flagged nine individuals with the physical examination who were ultimately diagnosed with valvular disease, but whether or not other indicators such as cardiovascular risk
factors, family history and/or symptoms were present in addition to an abnormal physical examination is unknown. The physical examination requires a highly trained (i.e. cardiologist) to properly detect pathological CVD, and even in the setting of a trained professional, there is high inter-observer variability, which limits its usefulness as an initial screening tool. Therefore, due to its low sensitivity and specificity, and the availability of a highly trained professional to properly administer the exam, it may not be the most cost-effective tool for pre-participation evaluations. However, inclusion of blood pressure measurements (to detect hypertension) and a pulse check (to detect irregular heart rates) should remain. Both can easily be performed by a trained allied health professional at low cost.

4.6.4 Effectiveness of the Electrocardiogram
Contrary to our hypothesis, the resting ECG had an overall low PPV (30.0%) in detecting CVD. It particularly had a low PPV (23.1%) in the detection of CAD; however, it did play an important role in detecting CHD and AF, with 75.0% PPV and 100% PPVs, respectively. Sofi et al. also discovered that the ECG does not detect all those with significant CVD (79.2% of those who were disqualified from sport had a normal resting ECG). However, other studies have shown that the ECG does play a role in detecting CHD and AF as well as in our study in the YCA (in the detection of CHD).

4.6.5 Effectiveness of the Questionnaire
The 14-point AHA questionnaire had a low PPV (18.4%) and a high false-positive rate (81.6%). Although no other studies have examined the sensitivity and specificity of the questionnaire in Masters athletes, it has been studied extensively in young competitive athletes. In a recent meta-analysis, the sensitivity and specificity for the cardiovascular history was 20% and 94%, respectively. Although the PPV yielded low results in the present study, proper history taking for clinically relevant symptoms (i.e. angina, syncope and/or presyncope during or after exertion, unusual fatigue, dyspnea, and palpitations) and family history is important given that the primary cause of SCD in athletes over 35 years is CAD. Additionally, the prevalence of AF increases with age and in lifelong endurance exercisers. Although AF does not contribute to SCD, it can cause stroke in those that are not properly medically managed if their risk is high. In the Aagaard et al. study, four individuals elicited a positive medical history (palpitations and
syncope) and were diagnosed with CVD (AF and third degree AV block), illustrating that the medical history can detect clinically significant CVD. Similarly, in our current study, all three individuals with AF reported palpitations on their medical history; however, a total of 32 (11.2%) individuals reported symptoms and only four were diagnosed with CVD. The high number of follow-ups (n=103) for the personal symptoms and history questionnaire, and the 85.2% false-positive rate for personal symptoms, is high and warrants a more sensitive questionnaire. The questionnaire should be able to appropriately rule-out insignificant palpitations, determine cardiac syncope from non-cardiac syncope, and delineate concerning chest pain from chest pain that is not due to angina. A potential solution would be an algorithm that considers the palpitations in context of other risk factors such as syncope, unusual fatigue, and/or chest pain and a positive family for SCD and/or premature CAD, and/or inherited CHD. An abnormal ECG in the setting of palpitations should also elicit further examinations. Another potential solution would be training of allied professionals in medical history taking to appropriately confirm or rule-out CVD.

4.6.6 Exercise Treadmill Test
The ETT was positive in 85.7% of those diagnosed with new CVD, which is in congruence with findings by Sofi et al. as they also found that the most prevalent cardiac abnormalities on stress testing comprised of abnormalities suggestive of CAD and arrhythmias. This is contrary to previous reports where the ETT has been criticized for its use in individuals in whom there is a low likelihood of CAD, such as in an active, physically fit population\textsuperscript{158,165}. Additionally, it has been suggested that in those who can achieve greater than 10 METS, CVD and symptoms can be masked and, therefore, reduces the likelihood of detecting CAD. Contrary to this belief, our study did not find that CAD was masked in those who achieved > 10 METS (Table 4.7). The ETT detected 22 of the 26 individuals that were positive for CAD, and all individuals except one achieved > 10 METS. Notably, all individuals with moderate-to-significant CAD and seven (70%) individuals with mild CAD had an intermediate or high FRS, which is known to increase the likelihood of a positive ETT in males\textsuperscript{132}.
**4.6.7 Cardiovascular Risk and Volume of Weekly Activity**

The marked improvement in health, risk reduction of CVD, and overall mortality that occurs in those that are physically inactive and become active, is well documented, 1, 3, 60, 61, 65, 66, 163, 164, 182. Lately, attention has been paid to the potential adverse cardiovascular effects that occur with greater amounts of exercise, 63, 71, 72, 183-186. There appears to be a law of diminishing returns as exercise volume increases, and there is almost certainly a J-shaped curve with adverse cardiac effects at the highest levels of exercise duration and intensity, 59-61, 66, 187. The reason some athletes are affected and others are not is likely multifactorial with genetic, lifestyle and environmental influences all playing a part. Whether or not this translates to increased CVD and overall mortality is unknown. Arem et al., in a recent detailed pooled analysis of 661,137 men and women, concluded that the longevity benefit threshold occurs around three to five times the recommended minimum, with maximal risk reduction occurring at 41 MET-hr/wk, and no increase in mortality risk at levels > 75 MET-hr/wk, 61. Notably, only 0.6% of their total population was in the > 75 MET-hr/wk category and they excluded individuals reporting > 100 MET-hr/wk. The majority of their population fell in the 0.1 to < 7.5 (26.1%) and 7.5.0 to < 15.0 MET-hr/wk (25.8%) categories. The Copenhagen City Heart study, found similar results where the strenuous joggers did not exhibit a mortality rate statistically different from that of the sedentary group, 59. Similar to Arem et al. they had a small number of deaths and a wide confidence interval in the moderate and strenuous categories. Lee et al. attempted to correct this by organizing the runners into quintiles of weekly running time, 66. They found a lower mortality rate in running > 150min/week, but reported a U-shaped mortality curve and noted that the mortality benefit was slightly less when running for more than 176 minutes per week. Wen et al., reported an even lower threshold (> 100 minutes per day of moderate activity or 50 to 60 minutes of vigorous activity per day) where additional activity produced no additional health benefits, 60.

Contrary to these studies, our current investigation represents a very active population and includes all type of sports, not just running. Most of the individuals exercised a minimum of 4 times a week with an average of 6.5 hours of physical activity a week. Additionally, we calculated a mean weekly volume of physical activity of 78.7 MET-hr/wk (± 45.2), which is 10.5 times higher than the recommended international guidelines (7.5 MET-hr/wk). Interestingly,
only 85 (29.7%) athletes considered themselves as either competitive (n=55, 19.3%) or elite (n=30, 10.5%). Therefore, we classified the level of activity by MET-hr/wk instead of subjectively reporting recreational versus competitive (MET-hr/wk is a better objective measure). When we grouped the population according to low, moderate, or high weekly training volumes, 126 (44%) exercised > 75 MET-hr/wk, suggesting that recreational athletes have weekly training volumes at the same level or greater than their competitive counterparts.

Several studies have demonstrated the dose-response relationship where greater health benefits occur with more exercise\textsuperscript{1, 161, 182, 188}. This dose-response relationship was demonstrated in our study with the greatest prevalence of new CVD diagnoses in the low volume group versus the high volume group (17.4% vs. 8.0%) (Figure 4.12). Notably, this also shows that even in those who exercise more than 10 times the recommended amount of weekly exercise, they are not exempt from disease. However, more research is needed to determine if the presence of CVD in very active individuals translates to increased risk of mortality. The Runners database examined runners ≥ 50 years of age and found that compared to matched non-runners, there was a 39% lower risk of all-cause and CVD mortality in the running group\textsuperscript{160}. In comparison, the Aerobics Center Longitudinal Study found a 29% lower mortality risk in a sample of runners ≥ 50 years of age\textsuperscript{66}. Although both studies saw a lower mortality risk, the greater benefits in the study from the Runners database could be due to a generally more health conscious population. Although a healthier diet and overall risk factors were lower in our population versus the rest of Canadians, whether or not this confers a lower mortality risk is unknown.
4.7 Study Limitations

This study has innate flaws due to its observational study design. Because there is no control population or randomized process, we were not able to show if these clinical evaluations are effective in reducing the risk of SCD or incidence of adverse cardiac events during sports participation. Second, there were many inherent flaws in measuring physical activity using a questionnaire: 1) We relied on subjective reporting of physical activity; however due to the prospective design of the study, recall bias was minimized; 2) Relative METS were estimated based on intensity and type of activity and its associated MET value from the physical activity compendium. We did not inquire about distance and pace because we did not feel that we could rely on all athletes knowing their values and because we examined athletes from a large variety of sports in which the pace can be largely variable. Although we could not accurately account for inter-individual variation we did our best to ensure consistency amongst athletes by estimating relative intensity using approximate age-associated pace in their respective sports when available (i.e. marathon), subjective level of competition (recreational versus competitive), and gender; 3) The questionnaire has not been validated in a very active, middle-aged population; however we did our best to adapt the questionnaire to this population as described in our second limitation noted above. Thirdly, the accuracy in years spent being physically active and the associated lifetime hours we calculated based on these years, may not be consistent amongst all participants.
We noticed that some individuals indicated their current age as years spent being physically active. In these individuals, we tried to correct for this by using 10 years to keep it consistent. Additionally, some reported only the years that they have been active in their later years (did not account for sports played as youth), whereas others did, and we cannot be certain that all individuals excluded years that they weren’t physically active (i.e. if there was a period of less physical activity). Fourth, as in all screening studies, there is a selection bias in which those who had previous concerns about their cardiovascular risk (symptoms, strong family history) are more likely to self-refer. Fifth, we cannot accurately report that we detected all CVD (true prevalence) and account for the false-negative rate of the PPS methods because we did not perform gold-standard cardiovascular examinations (i.e. CACS, CTA, echocardiogram) on all athletes. However, our pre-determined criteria for further evaluations was quite extensive utilising recommendations from two consensus organizations (EACPR and CCS) and only required one criteria to be present to undergo further evaluations. Lastly, our current sample of athletes is limited by a small sample size from a wide variety of sports and a relatively low prevalence of CVD. Despite grouping athletes by weekly training volume (low, moderate, high), which takes into consideration the type and intensity of all physical activities performed, we cannot accurately determine what volume of activity is optimal or whether or not a specific sport type (endurance versus power versus mixed) is associated with a greater risk for CVD. Similarly, it is possible that PPS may be warranted in some athletic populations over others (i.e. marathon running) but cannot be determined in this subset of athletes. Due to the small number of individuals with new AF, the significance of volume of physically activity could not be determined; however, those with newly diagnosed AF did report higher weekly training volumes and higher lifetime hours than the rest of the study population.

4.8 Conclusion

Masters athletes are not immune to cardiovascular risk factors and significant CVD exists despite being physically fit and regularly active. Most individuals are unaware of their risk factors and report no symptoms when underlying disease is present. Although the modalities are still a matter of debate, presence of significant CVD and risk factors, in light of having very high levels of physical activity, suggest that PPS may be warranted. Our study demonstrated that the individual screening methods have a low PPV in reliably detecting CVD; however, when
combined, CVD was detected. The current methods need to be refined to alleviate unnecessary evaluations and associated costs if this is to be applied to a universal health care plan. Removing the physician from the initial screen, a more specific questionnaire that trained allied health professionals such as physiotherapists, athletic trainers, and coaches could administer, and a Masters athlete specific ECG interpretation criteria, are possible solutions. The low PPV of the physical examination, high false-negatives seen in a subset of study participants, and inter-individual variability in performing physical examinations, provides rationale for removing the physician from the PPS process. Due to a high cardiovascular risk profile exhibiting the highest PPV, suggests that the low cost and easily accessible blood lipid profiles is a viable tool for PPS. Whether or not specific blood markers are more reliable predictors for CAD than others in a very active population was not examined in this analysis; however, further investigation is warranted. Lastly, the prevalence of CVD and high risk factors was lower in those who reported greater weekly training volumes, which is consistent with current literature on the benefits of exercise (more exercise elicits greater health benefits). However, there was a higher prevalence of AF, valvular heart disease, and multiple diagnoses (AF, valvular disease, CAD) in those with increasing volumes of weekly physical activity, higher fitness (max METS on ETT), and greater lifetime hours. Whether or not this finding is significant remains to be determined.
Chapter 5: Discussion, Future Directions, and Conclusions

5.1 General Discussion

Regular physical activity improves all modifiable risk factors for CAD including, weight (prevention of obesity), blood pressure, lipid levels, blood glucose, development of Type II diabetes, and psychosocial factors (stress, anxiety, depression)\(^{186}\); however, previous studies have proven that even in those who are highly active and physically fit are not immune to cardiovascular risk factors and CAD \(^{72, 87, 149, 185}\), which is consistent with our findings. Some studies even suggest that long-term excessive exercise may be associated with increased coronary artery calcification \(^{72, 87, 149, 185}\). Furthermore, Mohlenkamp et al. reported that runners did not have less coronary calcium compared to aged-matched controls (CACS ≥100 was present in 36% of runners), despite runners having lower FRS scores\(^{87}\). Potential explanations for similar prevalences of CAD and risk factors in controls and active individuals could be due to an increase in vascular oxidative stress and an influx of inflammatory cytokines from regular exhaustive exercise during marathons and training and because current risk factor tools do not reflect life-long exposure to poor lifestyle habits such as diet and previous smoking (more than half the runners were former smokers)\(^{87}\). Marathon runners may also believe that exercise negates a bad diet. Similarly, Schwartz et al., found that despite marathon runners having significantly lower resting heart rate, weight, body mass index, triglyceride levels, and higher HDL levels, the marathoners had a higher total plaque volume, calcified plaque volume and non-calcified plaque volume than the controls\(^{72}\). Although we did not have controls in our study, we compared risk factors of study participants to the Canadian population and found that study participants had lower risk factors (except depression). However, CAD was still discovered in 11 marathon runners and an overall total of 14 endurance athletes (Figure 4.12). Interestingly, three individuals who had a low FRS and went for further testing (due to the presence of other indicators) displayed mild CAD. When Tsiflikas et al. examined male marathon runners using a CTA, the only predictors for CAD, were age and family history (OR 6.60, CI 1.92-22.62). Traditional risk factors did not differ between those with and without CAD\(^{149}\).

Although 85.7% of the participants in our study that were diagnosed with CVD had a positive ETT, the number of false-negatives is unknown because further examinations were not performed in all of these individuals. Additionally, only those who had an indicator for follow-up
went for further testing so we cannot conclude that all CVD was detected. The inclusion of CTA in all individuals would accurately determine the true prevalence of disease and those at potential risk as the CTA can identify low-to-moderate stenosis that an ETT would otherwise not detect. This could be important in athletes who have mild CAD that are at risk for plaque rupture during exercise. The inclusion of the CTA would also confirm whether an individual is at risk or not. The absence of CAD is associated with excellent outcome and the risk of death increases with the extent of CAD\(^{189}\). Mohlenkamp et al. reported that runners with mild (< 100), moderate (100-399) and ≥ 400 coronary calcium had event rates of 1.5%, 12.0%, and 21.4%, respectively (p=0.002), and were not different than the control group\(^{87}\). All-cause mortality was similar in marathon runners (2.8%) and controls (3.0%). Hou et al. confirmed the prognostic value of CTA and CACS for major adverse cardiac events by following up with 4,425 out-patients suspected of having CAD. They found both have incremental value over routine risk factors for predicting major adverse cardiovascular events and CTA is superior to CACS. Another important factor to consider is that a CACS of zero suggests there is no detectable coronary calcium, but it does not consider the presence of soft, lipid filled plaque that is vulnerable to plaque rupture; therefore, a score of zero does not exclude the risk of CAD events. In fact, plaque characteristics are predictive for major events with unfavourable outcomes for mixed plaque\(^{190}\).

Additionally, CACS may serve in altering individual lifestyle behaviours and ultimately event rates, without incurring downstream costs\(^{191}\). Rozanski found that subjects, who underwent CACS, had a significantly greater reduction in systolic blood pressure, LDL cholesterol, and reduction in waist circumference (for those with increased abdominal girth at baseline) at 4-year follow-up\(^{191}\). These findings contributed to a stable FRS, whereas in the no-scan group, the FRS increased. Overall rates of downstream medical testing and procedures did not differ among the groups and medication costs were mildly higher in the scan group, with a 25% greater reduction in medical costs in the normal CACS scan group and 37% reduction in procedure costs. In the scan group, downstream medical testing increased in proportion to baseline CACS score, but the frequency of 4-year rates of cardiac catheterization and coronary revascularization were substantially lower. The reduced medical costs, and high sensitivity and specificity \(^{190,191}\) that guides risk factor management beyond traditional methods leans in favour of conducting CACS; however, whether or not the inclusion of CACS translates to reductions in morbidity and
mortality remains to be elucidated. Similarly, the cost that it would incur in imposing as a mass screening test does not seem prudent at this time.

A potential solution in identifying at risk individuals without imaging tests may be to investigate what risk factors are more concerning (i.e. family history, age, low HDL) to further define which individuals with an intermediate risk score warrant further evaluations (i.e. CTA or CACS). Our study discovered CVD in five individuals who had an intermediate risk score as their only risk factor. Delineating which factors put them at higher than their intermediate risk counterparts would be a worthwhile investigation. Additionally, because a resting ECG is relatively inexpensive and allied health professionals can be easily trained to administer one, it should be included in the screening process. However, refined Masters athlete specific ECG criteria might be appropriate. Additionally, a more specific questionnaire could assist in decreasing the number of follow-ups. In developing a new questionnaire, it will be important to ask specific question to delineate what palpitations are true-positive versus false-positive. Palpitations are included in the questionnaire due to their association with genetic ion channelopathies, supraventricular tachycardias (atrial fibrillation, atrial flutter), ventricular pre-excitation, ARVC, HCM, ischemic heart disease, and myocarditis. It will be important to differentiate between palpitations that are not clinically significant (PVCs and PACs) from those that have a more concerning clinical cause. The ability to confirm a potential pathological cause from a non-pathological one requires thorough history taking and a trained professional. Typically more lethal diseases are partnered with other symptoms and/or a family history of SCD. If we were to apply this rule to our current population, all individuals who reported palpitations and were diagnosed with CVD, had additional indications (i.e. family history, and/or abnormal ECG). This includes the individuals who were diagnosed with AF. Therefore, a potential remedy to decrease the amount of false-positives would be an algorithm that takes into account additional symptoms (syncope, shortness of breath), a positive family history of SCD and inherited or structural heart disease, rather than palpitations in isolation. In our young competitive athlete study, we modified the AHA questionnaire by adding evidence-based questions to delineate between benign and potential pathological symptoms, without the presence of a physician\textsuperscript{194}. Removal of the physician was done to make the screening process a more feasible approach so that if screening were to implemented in a publically funded health care system, it would reduce the cost of having a
physician present. The young athlete SCBC screening questionnaire was found to be successful, reducing the total number of false positives in phase 2 (implementation of the questionnaire) versus phase 1 (AHA questionnaire). Application of this questionnaire to the current population would not be a reasonable solution as the etiologies of CVD between the two populations differ.

5.2 Future Research
The low PPV and high false positive rates of the screening tools suggests future research is needed to further refine the PPS in a reasonable cost-effective fashion. Differentiating those who are potentially at risk and require secondary testing (i.e. CTA and CACS) and/or medical management from those who do not, determining if removal of the physician from the screening process will miss clinically significant disease, and designing a Masters athlete-specific questionnaire that differentiates symptoms associated with clinically relevant disease from benign symptoms is suggested.

Active individuals who are truly at risk is likely multifactorial, and includes previous and current lifestyle, genetics, and environmental influences. Although the evaluation of cardiovascular risk using the FRS is a widely accepted tool for accessing 10-year cardiovascular risk, it has shown to overestimate the risk in some and underestimate it in others. Analysis of true-negative and true-positive CACS and CTA examinations to determine associations between risk factors and volume of physical activity to CVD would be a worthwhile investigation to gain a better understanding of those at greater risk. Additionally, a large prospective longitudinal study to define false-negatives is necessary to improve the effectiveness of the PPS methods.

Future research needs to assist in medical decision-making, such that if two patients had the exact same lipid profiles, but one exercised more than the other, should they both be treated medically the same. Similarly, whether or not those that are very physically active and have high physical fitness but have CVD, translates to an increased mortality risk, needs to be examined. Such research will also assist exercise professionals in providing the best training recommendations to prevent the development of CVD and possible SCD. Additionally, optimal training suggestions would need to consider total training years, current training regime, intensity of sport, adequate recovery time after a competitive event (varies depending on intensity,
duration, and type of sport), as well as proper hydration, electrolyte supplementation, and dietary requirements. Additionally, it will be important to determine if there is a greater risk in certain sports, and if so, what are the underlying factors (i.e. higher prevalence of at risk persons, high training volumes), and optimal training suggestions to lessen the risk. Mohlenkamp et al. examined correlations between weekly volume of activity, number of marathon races completed, and training mileage with coronary calcium in runners, and found no associations. To my knowledge, no other studies have confirmed this, and whether or not this translates to all sports is unknown, suggesting further research is needed in this area. A prospective, longitudinal, repeated measures study that examines the effects of different training regimes (directly measured intensity and duration) on cardiovascular morphology, pathology, and function may assist in answering these questions.

Future research also needs to determine if PPS would reduce the cost of health care. In Canada, CVD is the second leading cause of death (after cancer) and costs the Canadian government (physician services and hospitalizations) and the individuals afflicted with the disease (lost wages and decreased productivity) a total of approximately $20.9 billion every year. PPS (and early detection) of CAD, other cardiovascular diseases (i.e. atrial fibrillation, valvular disease), and cardiovascular risk factors (i.e. high cholesterol, high blood pressure), could potentially reduce the cost of health care as well as losses to the athlete (i.e. lost wages, decreased productivity, decreased quality of life, and psychological impact to the participant) if cardiovascular disease was detected early versus having an event. Similarly, whether or not PPS is effective in reducing the risk of SCD or incidence of cardiac accidents in sports participation needs to be determined. Determining if those that are regularly active do confer an increased risk, and if they do, how can we guide them to be safer during activity. Also, if a highly active population is provided with their cardiovascular risk profiles, despite already achieving optimal fitness, is a reduction in risk factors achievable? The psychological impact of PPS to the athlete and whether or not they think it is worthwhile should be examined.

5.3 Conclusion

Exercise is vital to preventing CVD. However, it is undeniable that SCD occurs in those we least expect it to. From the evidence presented and that confirmed by previous studies,
asymptomatic CVD is present in those that we consider to epitomize health, suggesting underlying CVD is the likely culprit for sports-related SCDs. Therefore, PPS may be warranted in some individuals.

Although optimal training methods and recovery recommendations to prevent CVD could potentially decrease ones’ risk of SCD, whether or not the evidence gathered so far would change the way endurance athletes train and practice is uncertain given that most high-level athletes do not engage in their sports for health benefits alone. They may be motivated more by the need for an adrenaline “high”, a desire to reduce stress, or a commitment to competition. Exercise addiction is not well-defined in the literature; however, it can co-occur with other psychological disorders, such as substance addiction or eating disorders. In addition, there may be other exogenous factors not yet addressed in these studies, such as doping, that may have long-term adverse cardiac effects. As with most things, based on the evidence to date, some exercise is good, but more is not always better.

In addition to PPS potential strategies to reduce the risk of SCD include: 1) Appropriately modifying exercise for high-risk individuals; 2) Promptly reporting and evaluating new and unusual symptoms; 3) Ensuring emergency procedures are in place; 4) Placement of AEDs in all sporting venues; and 5) Educating athletes on safe exercise participation and other preventative strategies (i.e. monitor blood pressure and lipids, maintain healthy body weight, proper diet).
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## Appendix A: Population characteristics by gender (mean ± SD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number or athletes (%)</td>
<td>191 (66.8)</td>
<td>95 (33.2)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.7 (8.9)</td>
<td>52.7 (8.6)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>178.1 (6.5)</td>
<td>164.9 (6.2)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>81.3 (11.4)</td>
<td>62.5 (10.2)</td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>25.6 (2.9)</td>
<td>22.7 (4.1)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>90.0 (8.8)</td>
<td>80.6 (8.7)</td>
</tr>
<tr>
<td>Resting heart rate (bpm)</td>
<td>57.9 (10.0)</td>
<td>58.0 (9.3)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>129 (13.5)</td>
<td>118.2 (15.4)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>78.5 (7.2)</td>
<td>74.3 (8.7)</td>
</tr>
</tbody>
</table>
Appendix B: Letter of Invitation

The University of British Columbia
Sports Cardiology B.C.

Letter of Invitation

Title of Project: Evaluation of Pre-Participation Screening and Cardiovascular Risk Assessment in Masters Athletes in British Columbia

Investigators:
Dr. Saul Isserow – Director of Cardiology Services, UBC Hospital
Barbara Morrison (Master’s student) - Faculty of Experimental Medicine, UBC
Dr. Jack Taunton – Professor, Faculty of Medicine, UBC
Daniel Lithwick (Master’s student) – School of Population and Public Health, UBC
Dr. Brett Heilbron – Clinical Assistant Professor, UBC
Dr. Darren Warburton (Ph.D.) – School of Human Kinetics, UBC

To the participant,

You are being contacted because a research team from Sports Cardiology B.C. is recruiting male and female masters athletes older than or equal to 35 years of age that participate in sport (competitively or recreationally) to partake in a research study to evaluate the cardiovascular risk and the best screening method for detecting cardiovascular disease in British Columbia masters athletes in order to prevent adverse cardiac events. We will also examine the prevalence of atrial fibrillation and its association with intensity of sport and volume of lifetime training.

The sample population for this study is 1000 athletes across British Columbia. Participation in the study is voluntary and non-invasive. It consists of attending a screening session that includes a family history, personal health, and lifestyle questionnaire, physical examination and resting 12-lead electrocardiogram (ECG). The screen takes 30 minutes/athlete. Prior to the initial screen you will be required to complete a lipid blood profile. If you have not completed a recent blood lipid profile (within one year of the screen), please consult with your physician to acquire a laboratory requisition (i.e. lipid profile and fasting blood sugar). If this is not possible or not complete on the day of screening you may acquire a requisition from the research team.

If any abnormalities are found in the initial testing, a follow up exercise stress test will occur. If the exercise stress test is abnormal or inconclusive, additional testing will be done in order to make a proper diagnosis. This could include echocardiogram (ultrasound of the heart), cardiac computed tomography (test that uses x-rays and contrast dye to create detailed pictures of the heart), coronary artery calcium score (test that detects calcium deposits in heart arteries), cardiac catheterization (test that uses a long, thin flexible tube inserted into a blood vessel of arm or groin and threaded to the heart to take x-ray pictures), cardiac magnetic resonance imaging (test that uses radio waves, magnets, and a computer to take pictures of your heart), endomyocardial biopsy (biopsy of the heart muscle), 24 hour blood pressure monitoring and/or 24 hour Holter test (electrocardiogram monitor that is worn for 24 hours).

Each subsequent year for 5 years you will be asked to complete a follow up questionnaire, redo your blood lipid profile, and come to UBC hospital (or the location where you were initially screened) to have the resting ECG re-administered. The questionnaire will be used to observe changes in your cardiovascular risk profile as well as to document any adverse cardiovascular events. The resting ECG will observe the presence of new cardiovascular disorders. Re-administration of the ECG and questionnaire will take approximately 30 minutes of your time.

If after reading the study description carefully, you would like to participate in this study, please email Research coordinator Barb Morrison – bmorrison@sportscardiologybc.org. Thank you for your interest in this investigation.

Sincerely,
Dr. Saul Isserow, M.D., Principal Investigator

Screening in Masters Athletes
Version 2.0 – March 10th, 2015
Appendix C: Participant consent form

Participant Information and Consent Form

**Title of Project:** Evaluation of Pre-Participation Screening and Cardiovascular Risk Assessment in Masters Athletes in British Columbia

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Vancouver, B.C.

Dr. Jack Taunton  
Professor, Faculty of Medicine  
University of British Columbia  
Vancouver, B.C.

Dr. Darren Warburton  
Professor, School of Human Kinetics  
University of British Columbia  
Vancouver, B.C.

Dr. Brett Heilbron  
Clinical Associate Professor, Division of Cardiology  
University of British Columbia  
Vancouver, B.C.
**Invitation:**
You are being invited to participate in this study because you are considered a Masters athlete older than or equal to 35 years of age that is physically active or participates in sports (competitively or recreationally) at least 3 times per week. We want to evaluate the cardiovascular risk and the best screening method in Canadian masters athletes in order to prevent sudden cardiac arrest (SCA) and/or sudden cardiac death (SCD).

**Your Participation is Voluntary**
Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

You should be aware that there is a difference for both you and your doctor between being a patient and being a research participant. As a patient all medical procedures and treatments are carried out for your benefit only according to standard accepted practice. As a research participant you and your doctor also must take into account the requirements for the research study. These may include procedures and treatments that are not part of standard practice or are not yet proven. This consent form describes the diagnostic and treatment procedures that are being carried out for research purposes. Please review the consent document carefully when deciding whether or not you wish to be part of the research and sign this consent only if you accept being a research participant.

If you wish to participate in this study, you will be asked to sign this form.

Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

This study is funded by Sports Cardiology B.C., a Vancouver Coastal Health program, funded by the University of British Columbia and Vancouver General Hospital foundation.
Background

Sudden cardiac death (SCD) or a sudden adverse cardiovascular event in sport is traumatizing and shocking. Athletes are considered healthy and fit, two factors considered cardio-protective. However, although there are certainly benefits to exercise, the risk of myocardial infarction, aortic dissection, arrhythmias, sudden cardiac arrest and/or sudden cardiac death (SCD) is increased during and briefly after exercise. The exercise paradox emerges from evidence that vigorous exercise simultaneously triggers and protects against SCD. Both regular trainers (i.e. competitive athletes) and non-habitual but vigorous exercisers (i.e. weekend warriors) have a two to three fold increase risk of SCD versus non-athletes. Sudden cardiac death is often the first clinical expression of cardiovascular disease because many do not have symptoms (asymptomatic) and are unaware they have cardiovascular disease (CVD). Screening for cardiovascular disease has the potential to detect these disorders and those with cardiovascular risk factors in order to prevent such devastating events.

Though pre-participation screening has the capacity to detect cardiovascular disease, it lacks systematic evaluation. In particular, pre-participation screening has received considerable attention in the young competitive athlete, whereas limited data exists on Masters athletes despite the higher risks for coronary artery disease. Currently, there is no official mandate in Canada for pre-participation screening in the Masters athlete and the prevalence of risk factors in this population is unknown. Previous research, outside of Canada, found a new cardiovascular abnormality in approximately 3% of athlete and 4.1% had multiple cardiovascular risk factors, putting them at risk for developing CVD.

This study could have implications on future care of athletes in Canada. Pre-participation screening has the potential to decrease the risk of death by detecting CVD, as well as the capacity to detect disorders related to SCD. It creates an awareness of risk factors, which has the potential to decrease the risk of developing disease, and ultimately slowing the atherosclerotic process and subsequent cardiac events. Surprisingly, many athletes are unaware they have cardiovascular risk factors (i.e. high blood pressure, diabetes, or dyslipidemia). Therefore, use of pre-participation screening may provide the greatest reductions in cardiovascular risk by
assessing and reviewing one’s own health profile. Finally, the pre-participation evaluation can be used as a vehicle to educate Masters athletes on the nature and significance of warning signs for CVD.

**Purpose**
The purpose of this study is to determine the prevalence of cardiovascular risk factors and disease in masters athletes in B.C using a heart health questionnaire, physical examination, Framingham Risk Score, resting 12-lead electrocardiogram (ECG), and a maximal exercise treadmill test when indicated. The effectiveness of these screening methods will also be evaluated. Additionally, we will inquire about your physical activity level (past and current), lifestyle (i.e. diet, alcohol consumption and smoking) and stress, as it relates to cardiovascular risk.

**You are eligible to participate in this study if:**

1. You are a male or female Master (≥ 35 years) high performance athlete (participate in organized team or individual sport that requires systematic training and regular competition against others and places a high premium on athletic performance on athletic excellence and achievement, such as at the provincial, national, international and/or Olympic level) who perform exercise sessions at least 6 times per week.

2. Male and female Master (≥ 35 years) recreational competitive athletes (participate in a variety of informal recreational sports within a range of exercise levels from modest to vigorous, which does not require systematic training or the pursuit of excellence) who perform exercise sessions at least 3 times per week.

**Study Procedures:**
If you agree to take part in this study, the procedures and visits you can expect will include the following:

One of the researchers will schedule the initial screening session, which includes a questionnaire, a resting 12-lead ECG and a cardiovascular physical examination. Prior to the initial screen you
will be required to complete a lipid blood profile. The screening will take place at either the University of British Columbia Hospital or your sporting facility (your preference). Additional testing (if the initial screen is positive) will be conducted at the University of British Columbia Hospital, or one of its satellite locations.

This study will require 15-20 minutes of your time and up to 90 minutes of additional time if the initial screen discovers anything that is potentially abnormal.

Each subsequent year you will be asked to complete a follow-up questionnaire, similar to the initial heart health questionnaire, redo your blood lipid profile, and come to UBC hospital to have the resting ECG re-administered. The questionnaire will be used to observe changes in your cardiovascular risk profile as well as to document any adverse cardiovascular events. The resting ECG will observe the presence of new cardiovascular disorders. The ECG and questionnaire will take approximately 10-20 minutes of your time.

The consent form will be reviewed at the initial screening session and your written consent will be sought should you decide to participate.

#1 – Before you begin the study

If you have not completed a recent blood lipid profile (within one year of the screen), needed to complete the Framingham Risk Score, please consult with your physician to acquire a laboratory blood lipid requisition (i.e. total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, fasting blood glucose) and complete prior to your screening session. If this is not possible or not complete on the day of screening you may acquire a requisition from the research team. Please complete this as soon as possible and inform your research coordinator, Barb Morrison at 604-719-2825 once it is complete.

Laboratory Blood Analysis

A hospital chart review will be performed to acquire your recent blood work or you may bring a copy of your recent blood lipid profile (within the last year) with you on the day of screening.
#2 – Screening Visit

On the day of testing, you will be asked to refrain from exercise and smoking for 2 hours prior to testing, and caffeine/alcohol on the day of the test.

Questionnaire
Two weeks prior to the screening date, you will be sent a questionnaire and will be asked to bring it with you on your screening date. You will not have to answer any questions that you are not comfortable with on any of the questionnaires. This questionnaire should take about 10 minutes to complete.

The health history questionnaire asks about aspects of your family history and personal symptoms relevant to this study, your educational background, your approximate income and your ethnic background. It also includes information on your past and current physical activity, psychological stress, and lifestyle (i.e. smoking, alcohol consumption, diet).

Electrocardiogram
The study will involve a resting electrocardiogram (ECG), which records your heart rate and rhythm and will be performed by a trained professional. Areas on your arms, legs and chest, where the ten electrodes will be placed, will be cleaned with alcohol wipes and you may need to be shaved to provide a clean, smooth surface to attach the electrode discs. Participants will be asked to remove their top garment for this test so that the electrodes can be placed on the proper areas of the chest. This is required for a proper reading of the electrical conductivity of the heart. Some ECG leads need to be place on the body near the breasts. When dealing with female participants a female research associate, will be available to place the leads on these individuals. We will have private areas available for testing. This is painless and non-invasive. These measures should take 5 minutes to complete.

Physical Examination
This will include measurements of heart rate and blood pressure. A physician will also listen to your heart and assess for other cardiovascular risk features. This is painless and non-invasive and should take 5 minutes to complete.

#3 - Additional testing (if the initial screen is positive):

**Exercise Stress Test**

If you are 65 years or older, and/or the initial screen is positive as deemed by a cardiologist, you will be contacted to complete an exercise stress test. This test assesses your exercise capacity and your heart rate and rhythm while exercising. This will be determined by walking and/or running on a treadmill. You will be instructed to initially walk at a speed and grade of 1.7 mph and 10% grade, respectively. Every 3 minutes the speed and incline increases. Stage 2 is 2.5 mph at a 14% grade, stage 3 is 3.4 mph and 14% grade, stage 4 is 4.2 mph and 16% grade, stage 5 is 5.0 mph and 18% grade and stage 6 is 5.5 mph and 20% grade. This is known as the Bruce Protocol. You will be encouraged to exercise until you are too tired to continue, unless you experience symptoms that would cause you or the research team to terminate the test early. Your heart rate and rhythm will be continuously recorded throughout the test and your blood pressure will be measured at 2.5 minutes into each stage. This test takes approximately 30 minutes.

#4 - Diagnostic Testing (If the exercise stress test is positive or inconclusive)

If the exercise stress test is positive or inconclusive you will be contacted for additional diagnostic testing, to make a diagnosis, including but not limited to: an echocardiogram (ultrasound of the heart), cardiac computed tomography (test that uses x-rays and a contrast dye to create detailed pictures of the heart), calcium artery score (test that detects calcium deposits found in atherosclerotic plaque in your heart arteries), cardiac catheterization (procedure that uses a long, thin flexible tube inserted into a blood vessel in your arm or groin and is threaded to your heart to take x-ray pictures and is used to make diagnosis of heart conditions or provide treatment), cardiac magnetic resonance imaging (test that uses radio waves, magnets and a computer to take pictures of your heart), endomyocardial biopsy (biopsy of the heart muscle), 24 hour blood pressure monitoring and/or 24 hour Holter test (electrocardiogram monitor that is worn for 24 hours). These tests can take an additional hour.
#5 – Follow-up Questionnaire and Resting Electrocardiogram

Each subsequent year you will be asked to complete a follow-up questionnaire, redo your blood lipid profile, and come to UBC hospital (or we can come to your training facility) to have the resting ECG re-administered. The questionnaire will be similar to the initial heart health questionnaire and will also include questions on whether or not you have experienced a new cardiovascular event. Two weeks prior to the date of your ECG being re-administered, you will be sent the questionnaire and will be asked to bring it with you on your screening date. The questionnaire and resting ECG will take approximately 10-20 minutes.

What are my responsibilities?

1. Please see your doctor and acquire a blood lipid profile requisition (i.e. total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, fasting blood glucose) and have this complete (and bring a copy with you) prior to screening. If this is not feasible, you can obtain a requisition from us on the day of screening, and notify us as soon as it is complete.
2. Complete a yearly questionnaire, blood lipid profile and resting ECG for 5 years.

Risks

There is no potential harm to the participant in the initial screen; however, there is a chance of a false-positive test result, which could lead to further testing and could cause an inconvenience to the patient, or unnecessary alarm. Although there is a small chance of a false-positive test (4.2%), the potential benefits could be considered to outweigh the potential unnecessary concern because in the case of a correct diagnosis; appropriate treatment, safe exercise/sport guidance, and saved lives could result.

The initial screen will be conducted by a physician and a qualified professional will administer the ECG in order to minimize the chance of false-positives.

There is a slight chance that the some of the questions included in the questionnaire (i.e. psychological assessment) my cause minimal distress in some individuals. However, recent
research reported that pre-participation screening does not cause excessive anxiety and could create an ease of mind knowing their cardiac risk.

If a high psychological stress profile is revealed on your heart health questionnaire, we will inform you of this and offer you counseling resources, but we will not be responsible for providing counseling.

The exercise stress test (if required) could cause you to become tired and short of breath. There are no known permanent adverse side effects that have resulted from these exercise sessions. Data from individuals with or without heart disease indicates that the likelihood of having a heart attack or dying during an exercise stress test is 1 in 10,000 tests. All exercise testing will be performed under the supervision of a Certified Stress Lab technician or a Certified Exercise Physiologist. These individuals have received the most advanced exercise training in Canada; have performed a minimum of 100 stress tests under direct supervision, and are certified in first aid, CPR and the use of an automated external defibrillator (AED). All stress testing sites will be under the supervision of a physician at all times. A crash cart with defibrillation, suction, blood pressure monitoring, oxygen, etc. is within 10 meters of the stress machine. Distance from the emergency room is less than 10 kilometers.

Since there is a variable response from individuals during exercise, unanticipated complications may occur that would require treatment. Few problems have been associated with exercise testing, and the shortness of breath and muscular soreness usually clear quickly with little or no treatment. Every effort will be made to conduct the test in such a way as to minimize discomfort and risk. However, there exists the small possibility of potential risks from maximal exercise such as vomiting (5%), abnormal blood pressure, such as low blood pressure or hypotension following exercise (less than 1%), disorders of heartbeat, or arrhythmia (0.1%), and very rare instances of heart attack (less than 0.001%). Having trained professionals implement the tests will further reduce the risks associated with exercise testing.
Each participant will be required to have a lipid blood analysis. The risks of taking blood include pain, a bruise at the point where the blood was taken, redness and swelling of the vein and infection, and a rare risk of fainting.

In the event that further diagnostic testing (individuals with a positive screen and exercise treadmill test) few risks are involved and are described as follows:

- **Cardiac computed tomography (CCT):** CCT is a non-invasive test, however, there is a small amount of radiation, similar to the amount that you are naturally exposed to over 1-5 years. New methods reduce the amount of radiation and the benefit of an accurate diagnosis outweighs the risk. CCT is painless, however, some people have side effects from the contrast dye that might be used during the scan. An itchy feeling or rash may appear after the contrast die is injected. These side effects don’t normally last long.

- **Coronary artery calcium score (CACS):** CACS has very few risks. This is a non-invasive test, however a small amount of radiation is used, which is equivalent to the amount you are naturally exposed to in a single year. No dye is used.

- **Cardiac catheterization:** An invasive, common medical procedure that rarely causes serious problems but complications that can occur include: bleeding, infection, pain at the catheter insertion site, damage to blood vessels, an allergic reaction to the dye, abnormal heart rhythm, kidney damage caused by the dye, blood clots, low blood pressure, a buildup of blood or fluid in the sac that surrounds the heart.

- **Endomyocardial biopsy:** An invasive procedure, and follows the same procedure as cardiac catheterization, with the same risk and complications (rare).

- **Cardiac magnetic resonance imaging (CMR):** This is a non-invasive test that uses magnetic fields and radio waves and does not have side effects. It does not carry the risk of causing cancer or birth defects. Serious reactions to the contrast agent are very rare, but are possible and include: headache, nausea, dizziness, changes in taste, and allergic reactions.
**Benefits:**

No one knows whether or not you will benefit from this study. There may or may not be direct benefits to you from taking part in this study.

Potential benefits from participating in this study include diagnosis of an underlying cardiovascular disease that can cause significant harm. Information collected from this study can be used in the future to benefit athletes with cardiovascular disease.

Athletes with general concerns about health and well-being while participating in competitive sports may gain comfort in the knowledge that they have undergone testing that indicates they have no indications of a cardiovascular disorder.

The participants will receive a cardiovascular risk profile of their results and recommendations for their positive risk factors.

By evaluating Masters athletes, we could potentially decrease the incidence of SCA/SCD, and improve the health profile of active individuals and subsequently lessen the burden on the health care system and save lives.

We hope that the information learned from this study can be used in the future to benefit other people with a similar disease.

**Confidentiality**

Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of the Investigator or his or her designate by representatives of Sports Cardiology BC and the clinical research ethics board for the purpose of monitoring the research. Your date of birth will also be provided if requested by the sponsor or responsible regulatory agency. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.
You will be assigned a unique study number as a subject in this study. This number will not include any personal information that could identify you (e.g. it will not include your personal health number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected. You also have the legal right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

Participants with positive results for cardiovascular disease will be notified. Participants who wish to view their ECG results can do so upon by contacting the number seen above.

**Disclosure of Race/Ethnicity**
This study involves collecting information on race, ethnicity, sex and age as these characteristics may indicate a predisposition to certain cardiovascular disease and will be important to note for future research. Providing this information is voluntary.

**Study withdrawal**
You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, you have the right to request the withdrawal of your information collected during the study. This request will be respected to the extent possible. Please note however that there may be exceptions where the data will not be able to be withdrawn for example where the data is no longer identifiable (meaning it cannot be linked in
any way back to your identity) or where the data has been merged with other data. If you would like to request the withdrawal of your data, please let your study doctor know. If your participation in this study includes enrolling in any optional studies, or long term follow-up, you will be asked whether you wish to withdraw from these as well.

**What will this study cost me?**

All research-related medical care and treatment and any related tests that you will receive during your participation in this study will be provided at no cost to you.

**Reimbursement**

You will receive no financial reimbursement or remuneration for your participation in the study.

**Legal Rights**

By signing this form, you do not give up any of your legal rights against the investigators, or anyone else, and you do not release the study doctor or other participating institutions from their legal and professional duties. There will be no costs to you for participation in this study. You will not be charged for any research procedures. If you become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you. The costs of your medical treatment will be paid by your provincial medical plan.

**Contacts**

I understand that if I have any questions or need any further information about this study, I should contact Dr. Saul Isserow at ____ or Barb Morrison at ____.

If you have any concerns or complaints about your rights as a research subject and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at ________ or by phone at ________. 
☐ Yes, I grant the study investigator to obtain relevant cardiovascular related tests from my primary care physician(s) or specialist(s). My primary care physician(s) and/or specialist(s) name(s) is/are: ________________________________

The name of the medical clinic I attend is: ________________________________

Participant Initials: ______

PARTICIPANT CONSENT TO PARTICIPATE

My signature on this consent form means:
- I have read and understood the information in this consent form.
- I have had enough time to think about the information provided.
- I have been able to ask for advice if needed.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I understand that all of the information collected will be kept confidential and that the results will only be used for scientific purposes.
- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive.
- I authorize access to my laboratory lipid blood profile as described in this consent form.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.
- I understand that there is no guarantee that this study will provide any benefits to me.

I will receive a signed copy of this consent form for my own records.

I consent to participate in this study.

Subject Consent:

__________________________________________  __________________________________________  __________
(Participant Signature)  (Printed Name)  (Date)

Signature of Person Obtaining Consent:

__________________________________________  __________________________________________  __________
(Signature of person obtaining consent)  (Printed Name/Study Role)  (Date)
Appendix D: Health history questionnaire

**Health History Questionnaire**

Please take the time to answer the following questions about you and your health. This questionnaire is voluntary and you are free to leave any questions unanswered. Please be assured that all information will be coded and will remain strictly confidential and only be available to the researchers.

1. **Regarding you:**
   1.1. What is your sex? M/F/T
   
   1.2. What is your birthdate (day/month/year)? ____________________________
   
   1.3. What is your country of origin? _______________________
   
   1.4. What is your ethnicity? European/Chinese/South Asian (e.g. East Indian, Pakistani, Sri Lankan)/Southeast Asian (e.g. Vietnamese, Cambodian, Malaysian, Laotian)/Japanese/Korean/Filipino/Black/Latin American (e.g. Central and South America)/West Asian (e.g. Iranian, Afghan), Middle Eastern (Arabic)/Aboriginal/Other:___________________
   
   1.5. What is your primary sport?
   
   1.6. At what level do you play:
   competitive/provincial/national/international/collegiate/professional/ recreational
   
   1.7. What is your current marital status? Please check only one.
   o Single, never married
   o Married
   o Living common-law
   o Separated
1.8. What is your highest level of education that you completed? Please check only one.
- 8th grade or less
- Some high school
- High school diploma
- Vocational school or some college
- Undergraduate degree
- Graduate degree
- Doctorate or professional degree

1.9. What is your work situation?
- Homemaker
- Paid full-time employment
- Paid part-time employment
- Temporarily unemployed
- Retired
- Part time student
- Full time student

1.10. Type of work: ______________________________________________________

1.11. What is your annual personal income? Please check only one:
1) $5000 or less
2) $5501 to $10,000
3) $10,001 to $20,000
4) $20,001 to $40,000
5) $40,001 to $75,000
6) More than $75,000

2. Personal Heart Health History Questions
2.1. Do you have known heart disease: coronary artery disease (blocked arteries), angina, cerebrovascular disease (stroke), heart valve disease, cardiomyopathy (enlarged heart), peripheral vascular disease, congenital heart disease, atrial fibrillation or other arrhythmia (abnormal heart rhythm), or any other known heart disease?
- Yes / No
○ If yes, which disease:

_____________________________________________________

○ If yes, date of diagnoses:

_____________________________________________________

○ If yes, did you have a procedure to correct this (please circle which one(s):
Percutaneous coronary intervention (stent), coronary artery bypass grafting (heart
surgery for blocked arteries), valve surgery, cardiac catheterization (test that uses
a catheter and x-ray to examine arteries), heart transplantation, ablation or other?

__________________________________________________________________

______________

○ Date of the procedure:

_____________________________________________________

2.2. Has a doctor ever told you that you have any heart problems (high blood pressure, high
cholesterol, a heart murmur, a heart infection, Kawasaki disease, or other)?

○ Yes / No

○ If yes, please explain: -

_____________________________________________________

2.3. Have you ever been restricted from participation in sports due to heart problems?

○ Yes / No

○ If yes, please explain: -

_____________________________________________________

2.4. Has a doctor ever ordered a test for your heart? If yes, please circle which tests(s):
ECG/EKG, Echo/echocardiogram, cardiac magnetic resonance imaging (CMR), cardiac
computed tomography (CCT), stress test, other: ________________?

○ Reason for
test? ________________________________________________________
2.5. Have you ever passed out or nearly passed out during or after exercise?
   o Yes / No
   o If yes, please explain: -

2.6. Have you had discomfort, pain, tightness, or pressure in your chest during exercise?
   o Yes / No
   o If yes, please explain: -

2.7. Do you feel more shortness of breath than expected during exercise or do you easily feel fatigued with exercise?
   o Yes / No
   o If yes, please explain: -

2.8. Does your heart ever race or skip beats (irregular beats) during exercise?
   o Yes / No
   o If yes, please explain: -

2.9. Do you take any heart medications?
   o If yes, name of medication(s): -
2.10. Do you have any other non-cardiac conditions (i.e. asthma, arthritis, cancer, diabetes, neurological condition, endocrine condition, digestive condition, respiratory disease, or kidney disorders)?
   o If yes, please describe:__________________________________________

3. Family History Questions
3.1. Does anyone in your family have a heart problem, pacemaker, or implanted defibrillator?
   o Yes / No
   o If yes, what heart problem do they have?
     __________________________________________
   o Which family member was affected?
     __________________________________________
   o How old were they? ________________

3.2. Has any family member or relative died of heart problems or had any unexpected or unexplained sudden death before 50 years of age, including drowning, unexplained car accident, or sudden infant death syndrome?
   o Yes / No
   o If yes, which of the above occurred: -
     __________________________________________
   o Who did this happen to (relation)? _____________________________
   o How old were they? ___________________________________________

3.3. Does any family member have: Hypertrophic Cardiomyopathy (enlarged heart), Dilated Cardiomyopathy (enlarged heart), Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (disorder of the heart muscle), Long QT Syndrome (irregular heart rhythm), Short QT Syndrome (irregular heart rhythm), Brugada Syndrome (irregular heart rhythm), Wolf-Parkinson-White Syndrome, Marfan Syndrome,
Catecholaminergic Polymorphic Ventricular Tachycardia (rhythm disorder of the large chambers of the heart), or other (i.e. bicuspid aortic valve)?
- Yes / No
- If yes: Which disease? ____________________________________________
- How old were they? __________
- Who did this happen to (relation)? __________________________________

4. Physical Activity Questions

4.1. In a general fashion, would you say that your current physical fitness is:
- Very good
- Good
- Average
- Poor
- Very poor

4.2. Weekly Activity

- On average, during the week, how many hours per day are you sedentary (i.e. sitting at desk, sitting while commuting, watching TV)?
  - I spend less than 1 hour being sedentary
  - I am sedentary for 1 to 3 hours
  - I am sedentary for 4 to 6 hours
  - I am sedentary for 7 to 8 hours
  - I am sedentary for more than 8 hours

- How many times a week do you engage in physical activity that is sufficiently prolonged and intense to cause sweating and a rapid heart beat?
  - ≤ 2 exercise sessions/week
  - 2-3 exercise sessions/week
  - 4-5 exercise sessions/week
  - ≥ 6 exercise sessions/week
On average, how many minutes a week do you train?

- Strength training: _______ minutes/week
- Endurance training: _______ minutes/week
- Flexibility Training (i.e Yoga/Pilates): _______ minutes/week

Intensity – During the last month, on average, how many minutes per week do you do:

a) Light physical activity (minimal effort, no perspiration – e.g. Easy walking, yin yoga, bowling, archery, fishing, horseshoes, golf, snow-mobiling)
   - _______ minutes/week

b) Moderate physical activity (not exhausting, light perspiration – e.g. Fast walking, baseball, power yoga, tennis, easy bicycling, curling, volleyball, badminton, easy swimming, alpine skiing, dancing)
   - _______ minutes/week

c) Vigorous physical activity (heart beats rapidly, sweating – e.g. running, jogging, hockey, soccer, football, squash, basketball, cross country skiing, judo, roller skating/blading, vigorous swimming, vigorous long distance bicycling, vigorous aerobic dance classes, heavy weight training)
   - _______ minutes/week

4.3. Last 3 Months

How many minutes a week have you endurance trained in the last 3 months?
   - _______ minutes/week

How many minutes/week have you strength trained in the last 3 months?
   - _______ minutes/week

4.4. Lifetime Activity

4.4.1. How many years have you been physically active? _______ years

4.4.2. Which sports have you practiced and for how many years?
Example: Sport: Hockey Dates practiced: 1997-2005 Hours/week: 3
1. Sport: ___________ Dates practiced: _______ Hours/week: ______
2. Sport: ___________ Dates practiced: _______ Hours/week: ______
3. Sport: ___________ Dates practiced: _______ Hours/week: ______
4. Sport: ___________ Dates practiced: _______ Hours/week: ______

4.5. **Long Distance Events:**

4.5.1. Do you participate in long distance events (>20 km running, > 50 km cycling)?

**Yes / No**

- If YES:
  - When was your first long distance event? _______ years ago
  - When (date) was your last long distance event you participated in?
    ____________________________
  - How many half-marathons have you participated in? _________
    - What was your personal minimum time? __________
  - How many marathons have you participated in? __________
    - What was your personal minimum time? __________
  - How many ultra-endurance marathons have you participated in? _______
  - How many Grand Fondos or other long-distance cycling events have you participated in? _______
  - Have you been involved in other competitive events? If so, please describe (event, number, years involved):
    ______________________________
    ______________________________
5. **Lifestyle Questions**

5.1. What is your menopausal status *(women only)*?
- Have not yet started menopause (still get regular periods)
- Am pregnant
- Started menopause less than 10 years ago (stopped having regular periods less than 10 years ago)
- Started menopause 10+ years ago (stopped having regular periods 10 or more years ago)

5.2. How many servings of fruits and vegetables do you have?
- ≤ 6 servings/week
- 1-2 servings/day
- ≥ 3 servings/day

5.3. How many servings of red meat do you eat?
- ≤ 3 servings/month
- 1-2 servings/week
- ≥ 3 servings/week

5.4. What is your smoking status? (Please check all that apply)
- Never Smoked
- Smoke **10 or less** cigarettes a day
- Smoke **11 to 20** cigarettes a day
- Smoke **20 or more** cigarettes a day
- Quit **MORE** than 2 years ago
- Quit **LESS** than 2 years ago
- Am exposed to 2nd hand smoke
- Use chew tobacco
- Smoke a pipe or cigar
- If yes do you inhale? Y/N
- If yes, how often? ___

5.5. During the past 12 months, how often did you drink alcoholic beverages?
- Never
- Less than once a month
5.6. On average, how many drinks per week do you have (1 drink = 12 oz. beer, 5 oz. wine, 1.5 oz. of spirits (40% alcohol), 8-9 oz. malt liquor)?

- Former drinker, don’t drink anymore
- Abstainer
- <7 drinks
- ≥7 up to 14 drinks
- ≥14 up to 21 drinks
- ≥21 drinks

5.7. How often in the past 12 months have you had 5 or more alcoholic drinks on one occasion?

- Never
- Less than once a month
- Once a month
- 2 to 3 times a month
- Once a week
- More than once a week
6. **Psychosocial Questions**

➢ **During the last 12 months how would you rate the following?**

6.1. How do you rate your health over the last 12 months?

- Very good
- Good
- Average
- Poor and very poor

6.2. How often do you feel stressed at work?

- Never experience stress
- Experience some periods of stress
- Experience several periods of stress
- Experience permanent stress

6.3. How often do you feel stressed at home?

- Never experience stress
- Experience some periods of stress
- Experience several periods of stress
- Experience permanent stress

6.4. Do you have financial stress?

- Little or none
- Moderate
- High or severe

6.5. Have you experienced any specified life events in the past year (i.e. marital separation, divorce, loss of job or retirement, loss of crop or business failure, violence, major intra-family conflict, major personal injury or illness, death or major illness of a close family member, death of a spouse, or other major stress)?

- No life events
- 2 or more life events

6.6. At home, I feel I have control over what happens in most situations:

- Strongly Disagree
- Moderately Disagree
- Slightly Disagree
- Slightly Agree
- Moderately Agree
6.7. I feel that what happens in my life is often determined by factors beyond my control:
   - Strongly Disagree
   - Moderately Disagree
   - Slightly Disagree
   - Slightly Agree
   - Moderately Agree
   - Strongly Agree

6.8. Over the next 5-10 years I expect to have more positive than negative experiences:
   - Strongly Disagree
   - Moderately Disagree
   - Slightly Disagree
   - Slightly Agree
   - Moderately Agree
   - Strongly Agree

6.9. I often have the feeling that I am being treated unfairly:
   - Strongly Disagree
   - Moderately Disagree
   - Slightly Disagree
   - Slightly Agree
   - Moderately Agree
   - Strongly Agree

6.10. In the past 10 years my life has been full of changes without knowing what will happen next:
   - Strongly Disagree
   - Moderately Disagree
   - Slightly Disagree
   - Slightly Agree
   - Moderately Agree
   - Strongly Agree

6.11. I gave up trying to make big improvements or changes in my life a long time ago:
   - Strongly Disagree
   - Moderately Disagree
   - Slightly Disagree
   - Slightly Agree
   - Moderately Agree
   - Strongly Agree

6.12. Keeping healthy depends on things that I can do:
   - Strongly Disagree
   - Moderately Disagree
6.13. There are certain things I can do for myself to reduce the risk of heart attack:
- Strongly Disagree
- Moderately Disagree
- Slightly Disagree
- Slightly Agree
- Moderately Agree
- Strongly Agree

6.14. There are certain things I can do for myself to reduce the risk of getting cancer:
- Strongly Disagree
- Moderately Disagree
- Slightly Disagree
- Slightly Agree
- Moderately Agree
- Strongly Agree
6.15.  Do you frequently feel angry over little things? Y/N
6.16.  If someone annoys you, do you regularly let him/her know? Y/N
6.17.  Do you often feel annoyed about habits other people have? Y/N

6.18.  During the past 12 months, have you felt sad, blue, or depressed for 2 weeks or more in a row? Y/N, if YES, please answer the following questions:
  o  Have you lost interest in things? Y/N
  o  Do you feel tired or low on energy? Y/N
  o  Have you lost or gained weight? Y/N
  o  Do you have trouble falling asleep? Y/N
  o  Do you have trouble concentrating? Y/N
  o  Do you think of death? Y/N
  o  Do you have feelings of worthlessness? Y/N
Appendix E: Screening protocols

Masters Athlete Screening Protocols

Blood Pressure

Equipment: Welch Allyn ProBP 3400 Blood Pressure Device


Procedure
1. Participant should be seated comfortably with back supported and the upper armed bared without constrictive clothing. The legs should not be crossed.
2. The arm should be supported at heart level.
3. Attach an appropriate sized cuff to the participant (sitting) on their non-dominant arm. The lower end of the cuff should be 2-3cm above the antecubital fossa.
4. Neither the patient nor observer should talk during the measurement.
5. Perform 3 measurements, 1 minute apart.

Waist Circumference

Equipment: K-E Anthropometric tape or equivalent

(Ref: http://www.csep.ca/english/view.asp?x=724&id=84; originally published in the CSEP member newsletter, Communiqué, November 2008)

1. Clear the client’s abdomen of all clothing and accessories. Position the client with feet shoulder width apart and arms crossed over the chest in a relaxed manner. Take a position to the right side of the client’s body on one knee.
2. Using the NIH protocol, the waist circumference measurement should be taken at the top of the iliac crest. To find this landmark, palpate the upper right hipbone of the client until
you locate the uppermost lateral border of the iliac crest. Draw a horizontal line at this landmark at the midline of the body.

3. Position the tape directly around the abdomen so that the inferior edge of the tape is at the level of the landmarked point. Use a cross-handed technique to bring the zero line of the tape in line with the measuring aspect of the tape.

Ensure that the measuring tape is positioned in a horizontal plane around the abdomen. Apply tension to the tape to ensure it is snug, without causing indentation to the skin. At the end of a normal expiration, take the measurement to the nearest 0.5cm.

Height

**Equipment:** SECO 213 Portable Stadiometer


**Procedure:**

1. The patient stands barefoot (if possible) with his/her back to the wall
2. With feet together, ensure the heels are touching the wall
3. The body is erect and centered on the measuring rod
4. Confirm the corner of the eyes and the top of the ears are level
5. To measure, the user places the headpiece against the scalp and locks it.
Weight
Equipment: SECA 869 Portable Flat Scale

1. Press the start button.
2. Ensure the measurement is set to kg.
3. Patient steps on.
4. Record weight.

12-lead Electrocardiogram (ECG)

Equipment: Mortara, Eli 10
(Ref: http://www.emtresource.com/resources/ecg/12-lead-ecg-placement/)
(You Tube video: https://www.youtube.com/watch?v=HK1NHr0JcqQ)

Procedure:

I. Patient Positioning:

1. Place participant in a supine position.
2. Instruct participant to place their arms down by their side and to relax their shoulders.
3. Make sure participants legs are uncrossed.
4. Move any electrical devices (i.e. cell phones) away from participant.

II. Skin Preparation:

1. Ensure the skin is dry.
2. Shave any hair that interferes with electrode placement.
3. Rub an alcohol pad on the skin to remove any oils and help with electrode adhesion

III. Electrode Application
1. V1: 4th intercostal space to the right of the sternum
2. V2: 4th intercostal space to the left of the sternum
3. V3: Midway between V2 and V4
4. V4: 5th intercostal space at the midclavicular line
5. V5: Anterior axillary line at the same level as V4
6. V6: Mid axillary line at the same level as V4 and V5
7. RL: Anywhere above the ankle and below the torso (for our study purposes, place just above ankle)
8. RA: Just above the wrist
9. LL: Anywhere above the ankle and below the torso (for our study purposes, place just above ankle)
10. LA: Just above the wrist

IV. Machine Data Entry:
1. Once electrodes have been placed, push button “Patient ID” on ECG
   a. Enter name (will be on consent form), clarify with patient if writing is illegible
b. Enter participant ID (study ID on questionnaire)

c. Enter birthdate – each machine is different in the order of entry – either
day/month/year or month/day/year - we will inform you the order for each
machine
d. Enter sex of patient (M/F)
e. *(Correct entry of this information is crucial, so please double check once all
information is entered)*
f. Allow the ECG to record for a minimum of 10 seconds (we need 10 seconds of
artifact-free data, so do not start counting until there is no artifact and if the
patient moves during this time, restart the count).
   i. To ensure the signal is adequate you can push the button “leads” to look
      at the various signals
g. Push the button “auto”
h. “Save ECG”
### Appendix F: MET CHART

<table>
<thead>
<tr>
<th>Activity</th>
<th>METS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Intensity (absolute)</td>
<td>1.8-2.9</td>
</tr>
<tr>
<td>Low intensity (no activity indicated)</td>
<td>3</td>
</tr>
<tr>
<td>Moderate intensity (absolute)</td>
<td>3.0 - 6.0</td>
</tr>
<tr>
<td>Moderate intensity (no activity indicated)</td>
<td>6</td>
</tr>
<tr>
<td>Vigorous intensity (absolute)</td>
<td>&gt; 6</td>
</tr>
</tbody>
</table>

#### Walking

<table>
<thead>
<tr>
<th>Activity</th>
<th>METS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow walking (2.5 mph)</td>
<td>2.5</td>
</tr>
<tr>
<td>Moderate walking (3.0 mph, level)</td>
<td>3</td>
</tr>
<tr>
<td>Walking (3.5 mph, level surface)</td>
<td>4</td>
</tr>
</tbody>
</table>

Badminton

<table>
<thead>
<tr>
<th>Activity</th>
<th>METS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Competitive</td>
<td>7</td>
</tr>
<tr>
<td>Doubles, social</td>
<td>4.5</td>
</tr>
<tr>
<td><strong>Cardio</strong></td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>-----</td>
</tr>
<tr>
<td>General, gym</td>
<td>8</td>
</tr>
<tr>
<td>Coaching (football, soccer, basketball, baseball, swimming)</td>
<td>4</td>
</tr>
<tr>
<td>Curling</td>
<td>4</td>
</tr>
<tr>
<td><strong>Cycling</strong></td>
<td></td>
</tr>
<tr>
<td>Light effort (10-11.9 mph, 16-19km/hour)</td>
<td>6</td>
</tr>
<tr>
<td>Moderate (12-13.9 mph, 19-22.5 km/hr)</td>
<td>8</td>
</tr>
<tr>
<td>Vigorous (14-15.9 mph, 22.6-25.7 km/hr)</td>
<td>10</td>
</tr>
<tr>
<td>Racing, (16-19 (25.7 - 30.6) not drafting or &gt;19 drafting)</td>
<td>12</td>
</tr>
<tr>
<td>Racing &gt; 20 (32.2km/hr) not drafting (<strong>Fit rider</strong>)</td>
<td>16</td>
</tr>
<tr>
<td>BMX or mountain</td>
<td>8.5</td>
</tr>
<tr>
<td>Dance (ballet or modern, twist, jazz)</td>
<td>4.8</td>
</tr>
<tr>
<td>Field hockey</td>
<td>8</td>
</tr>
<tr>
<td>Golf</td>
<td>4.5</td>
</tr>
<tr>
<td>Hiking</td>
<td>6</td>
</tr>
<tr>
<td>Hockey (ice)</td>
<td>8</td>
</tr>
<tr>
<td>Kick Boxing, Judo, Jujitsu, Karate, Tae Kwan Do</td>
<td>10</td>
</tr>
<tr>
<td>Jazzercise</td>
<td>6</td>
</tr>
<tr>
<td>Lacrosse</td>
<td>8</td>
</tr>
<tr>
<td>Moto-cross</td>
<td>4</td>
</tr>
<tr>
<td>Rollerblade (skate)</td>
<td>7</td>
</tr>
<tr>
<td><strong>Rowing</strong></td>
<td></td>
</tr>
<tr>
<td>Stationary - light</td>
<td>3.5</td>
</tr>
<tr>
<td>Stationary - moderate</td>
<td>7</td>
</tr>
<tr>
<td>Stationary - vigorous</td>
<td>8.5</td>
</tr>
<tr>
<td>Stationary - very vigorous</td>
<td>12</td>
</tr>
<tr>
<td><strong>Running</strong></td>
<td>7 to 18</td>
</tr>
<tr>
<td>-------------</td>
<td>---------</td>
</tr>
<tr>
<td>Jogging</td>
<td>7</td>
</tr>
<tr>
<td>Cross Country</td>
<td>9</td>
</tr>
<tr>
<td>12 min mile (5mph)</td>
<td>8</td>
</tr>
<tr>
<td>10 min mile (6mph)</td>
<td>10</td>
</tr>
<tr>
<td>9 min mile (6.7mph)</td>
<td>11</td>
</tr>
<tr>
<td>8 min mile (7 mph)</td>
<td>12.5</td>
</tr>
<tr>
<td>6.5 min/mile (9mph)</td>
<td>15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Soccer</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>7</td>
</tr>
<tr>
<td>Competitive</td>
<td>10</td>
</tr>
<tr>
<td>Softball</td>
<td>5</td>
</tr>
<tr>
<td>Squash</td>
<td>12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Skiing</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>7</td>
</tr>
<tr>
<td>Cross-country (light)</td>
<td>7</td>
</tr>
<tr>
<td>Cross-country (moderate)</td>
<td>8</td>
</tr>
<tr>
<td>Cross-country (vigorous)</td>
<td>12</td>
</tr>
<tr>
<td>Downhill (light)</td>
<td>5</td>
</tr>
<tr>
<td>Downhill (moderate)</td>
<td>6</td>
</tr>
<tr>
<td>Downhill (vigorous)</td>
<td>8</td>
</tr>
<tr>
<td>Snowshoe</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Swimming</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Swimming, leisure</td>
<td>6</td>
</tr>
<tr>
<td>Laps, freestyle, light effort</td>
<td>8</td>
</tr>
<tr>
<td>Activity</td>
<td>METS</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Laps, freestyle, vigorous</td>
<td>10</td>
</tr>
<tr>
<td>Crawl, vigorous</td>
<td>11</td>
</tr>
<tr>
<td><strong>Strength Training</strong></td>
<td></td>
</tr>
<tr>
<td>Vigorous (i.e. pullups, pushups, situps)</td>
<td>8</td>
</tr>
<tr>
<td>Vigorous (circuit training, some aerobic)</td>
<td>8</td>
</tr>
<tr>
<td>Vigorous (free weights, power lifting)</td>
<td>6</td>
</tr>
<tr>
<td>Light/moderate weight lifting</td>
<td>3</td>
</tr>
<tr>
<td>General</td>
<td>5.5</td>
</tr>
<tr>
<td><strong>Tennis</strong></td>
<td></td>
</tr>
<tr>
<td>Singles</td>
<td>8</td>
</tr>
<tr>
<td>Doubles</td>
<td>6</td>
</tr>
<tr>
<td>General</td>
<td>7</td>
</tr>
<tr>
<td><strong>Track and field (team, practice)</strong></td>
<td>10</td>
</tr>
<tr>
<td><strong>Volleyball</strong></td>
<td></td>
</tr>
<tr>
<td>General, noncompetitive</td>
<td>3</td>
</tr>
<tr>
<td>Competitive</td>
<td>4</td>
</tr>
<tr>
<td>Beach</td>
<td>8</td>
</tr>
<tr>
<td><strong>Water Sports (use these METS for dragon boating)</strong></td>
<td></td>
</tr>
<tr>
<td>Canoeing, rowing light</td>
<td>3</td>
</tr>
<tr>
<td>Canoeing, rowing moderate</td>
<td>7</td>
</tr>
<tr>
<td>Canoeing, rowing vigorous (&gt;6mph)</td>
<td>12</td>
</tr>
<tr>
<td>Canoeing, rowing, in competition, or crew or sculling</td>
<td>12</td>
</tr>
<tr>
<td>Kayaking</td>
<td>5</td>
</tr>
<tr>
<td>Paddleboat</td>
<td>4</td>
</tr>
<tr>
<td>Sailing</td>
<td>5</td>
</tr>
<tr>
<td><strong>Yoga</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Average Half marathon pace by age (miles per hour)</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------------------------------------------</td>
</tr>
<tr>
<td>Age</td>
<td>Men</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>12:26</td>
</tr>
<tr>
<td>60-64</td>
<td>11:09</td>
</tr>
<tr>
<td>55-59</td>
<td>10:34</td>
</tr>
<tr>
<td>50-54</td>
<td>10:10</td>
</tr>
<tr>
<td>45-49</td>
<td>9:45</td>
</tr>
<tr>
<td>40-44</td>
<td>9:36</td>
</tr>
<tr>
<td>35-39</td>
<td>9:42</td>
</tr>
</tbody>
</table>
## Age-associated cycling METS

<table>
<thead>
<tr>
<th>Age</th>
<th>Vigorous</th>
<th>Moderate</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-45</td>
<td>15</td>
<td>13</td>
<td>-2 for women</td>
</tr>
<tr>
<td>45-50</td>
<td>14</td>
<td>12</td>
<td>-1-2 for recreational</td>
</tr>
<tr>
<td>50-55</td>
<td>13</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>55-60</td>
<td>12</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>60-65</td>
<td>11</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>&gt; 65</td>
<td>10</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>
Appendix G: Criteria for exercise testing and further evaluation

1. **Personal History**
   - Cardiac-related syncope and/or presyncope during and after exertion for no apparent reason
   - Angina during exertion
   - Dyspnea during exertion
   - Unusual fatigue during exercise
   - Palpitations during exercise
   - History of Rheumatic Fever

2. **Family History**
   - Family history of SCD or any unexpected or unexplained sudden death before 50 years in first or second degree relative (i.e. drowning, car accident, or sudden infant death syndrome)
   - *Family history (first or second degree relatives) of hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, Marfan syndrome, long QT syndrome, short QT syndrome, Brugada syndrome, Wolf-Parkinson-White Syndrome, catecholaminergic polymorphic ventricular tachycardia, dilated cardiomyopathy, thoracic aorta aneurysm, bicuspid aortic valve, or other potentially disabling CV disease
   - Family member with cardiovascular disease in first degree relative < 50 years (i.e. premature CAD, CV disease that requires implanted defibrillator)

3. **Physical Examination**
   - >180/110 mmHg on more than one reading
   - Mid or end-systolic clicks
   - Abnormal second heart sound (single or widely split and fixed with respiration)
   - Any diastolic murmur
   - Systolic murmur grade ≥ 2
   - Abnormal femoral pulses indicative of aortic coarctation
   - Morphological features of Marfan syndrome
- Irregular heart rate

4. **Framingham Risk Score**
   - Moderate (10-19%) to high (≥ 20%) risk
   - **Markedly Raised Single Cardiovascular Risk Factor**
     - Diabetes mellitus (≥ 7.0 mmol/L or post-prandial ≥ 11.1 mmol/L)
     - > 8 mmol/L blood cholesterol
     - Elevated (>180/110 mmHg) systemic blood pressure irrespective of treatment

5. **Age ≥ 65 years**

6. **Abnormal resting 12-lead ECG (see appendix 3)**

7. **Known CVD** (i.e. AFIB, CAD)

*A follow-up is required with a family history of autosomal dominant disorders in first and second degree relatives.*
Appendix H: ECG interpretation

**Normal ECG Findings in Athletes**

- Common training-related ECG alterations
- Physiological adaptations to exercise
- Do not require further evaluation
- Sinus bradycardia (≥ 30bpm)
- Sinus arrhythmia
- Ectopic atrial/junctional escape rhythm
- 1° AV block (PR interval > 200 ms)
- Mobitz type I (Wenkebach) 2° AV block
- Incomplete RBBB
- Early repolarization (ST elevation, J-point elevation, J waves, or terminal QRS slurring)
- Convex (“domed”) ST segment elevation combined with T wave inversion in leads V1-V4 in black/African athletes
- Isolated QRS voltage criteria for LVH
  - Except: QRS voltage criteria for LVH occurring with other non-voltage criteria for LVH such as left atrial enlargement, left axis deviation, ST segment depression, T wave inversion or pathological Q waves
Abnormal ECG Findings in Athletes

- Unrelated to regular exercise
- Require further diagnostic evaluation
- T wave inversion (excluding III, aVR, VI)
- ST-segment depression (≥ 0.5mm in two or more leads)
- Q-waves (excluding III and aVR)
- Complete left bundle branch block
- Intraventricular delay (any QRS ≥ 140ms)
- Left atrial enlargement
- Left axis deviation
- Right ventricular hypertrophy pattern
- Ventricular pre-excitation syndrome (WPW) (PR interval <120ms with a delta wave) and wide QRS (>120ms)
- Long (≥470ms (male) ≥ 480ms (female) or short QT interval (≤320ms))
- Brugada-like ECG pattern
- Profound sinus bradycardia (<30 bpm or sinus pauses ≥ 3 s)
- Supraventricular tachycardia, atrial flutter or atrial fibrillation
- PVC’s (≥2 PVCs per 10s tracing)
- Ventricular arrhythmias (couplets, triplets, and non-sustained ventricular tachycardia)