PHYSICAL ACTIVITY AND CARDIORESPIRATORY FITNESS IN THE MANAGEMENT OF CARDIOVASCULAR DISEASE IN PREVENTIVE CARDIOLOGY

A REVIEW OF THE EVIDENCE

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The global scale of physical inactivity is a major health concern with current estimates suggesting that 31% of the world's adult population (aged 15 years or older) are physically inactive[1]. The frequency of inactivity varies across different regions from 17% in Southeast Asia to around 43% in the Americas and the eastern Mediterranean regions[1]. In general, women are more inactive (33.9%) than men (27.9%) and inactivity increases with age[1]. Physical activity (PA) is a behaviour defined as 'any body movement produced by the skeletal muscles that causes energy expenditure' and includes commuting, domestic, occupational and leisure-time physical activity (LTPA). Physical inactivity alone causes substantial morbidity and mortality with around 9% of all deaths from non-communicable diseases being attributed to this unhealthy behaviour[2]. Further, physical inactivity causes 6% of the burden of disease from coronary heart disease (CHD), 7% of type 2 diabetes, 10% of breast cancer and 10% of colon cancer[2]. The causes of physical inactivity are multifactorial and are strongly influenced by occupation, financial income and living environment[3]. For example, increasing urbanisation and rapid economic growth have been linked to reductions in overall and occupational PA levels in adults living in China and similar trends have been observed in African communities migrating from rural to urban areas[3].

To tackle the rising issue of physical inactivity, several national and international organisations have developed guidelines and recommendations on the dose-response relationship between the total volume of PA (frequency, duration and intensity) needed for the prevention of non-communicable diseases[4-7]. Table 1 gives an overview of PA recommendations. The general consensus is that all adults should minimise the amount of time spent being sedentary (sitting) and most (if not all) adults should participate in at least 150 minutes of moderate-intensity PA each week or 75 minutes of vigorous-intensity PA per week or equivalent combinations of moderate and vigorous-intensity activities[4-7]. In addition, all healthy adults should perform muscle-strengthening activities working the larger muscle groups on 2 or more days per week[4-7].

In accordance with these recommendations, many preventive cardiology programmes (including cardiac rehabilitation) offer PA guidance and structured exercise as a central component along with educational sessions on smoking cessation, lifestyle management and cardio-protective medication[8]. The effectiveness of these programmes has been demonstrated in randomised controlled trials in patients stratified at high cardiovascular disease (CVD) risk and in patients with established vascular disease[8,9]. Therefore, the purpose of this review article is to discuss the evidence for PA and cardiorespiratory fitness (CRF) in the prevention and management of CVD in a preventive cardiology setting.

Table 1

- *150 minutes of moderate-intensity aerobic physical activity throughout the week or at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate- and vigorous-intensity activity.*
- *Aerobic physical activity should be performed in bouts of at least 10 minutes duration.*
- *Eight to 10 different muscle-strengthening activities involving all large major muscle groups should complement aerobic exercise and should be performed on two or more non-consecutive days each week. A resistance should be selected that brings about local muscular fatigue after 8–12 repetitions of each exercise.*
- *Prolonged sedentary activities (i.e. sitting) should be kept to a minimum.*

Table 1: Physical activity recommendations for all healthy adults[4-7].

LITERATURE SEARCH

Since the 1950s, a wealth of research has been published on the benefits of PA in CVD risk and a recent Google Scholar search conducted on 1 September 2014 using the search terms 'PA and CVD prevention' and 'CRF and CVD prevention' resulted in over 1,830,000 and 28,300 articles, respectively. Therefore, this review article will focus on a selection of key studies that have been published on the benefits of PA and CRF in CVD prevention. However, it is worth noting that CVD is a single family of diseases, which presents itself as CHD, transient cerebral ischaemia or peripheral artery disease. In the literature, most studies refer to the benefits of PA on CVD or CHD mortality or risk. Therefore, this review article will use CVD and CHD interchangeably throughout the text.

EVIDENCE FOR PHYSICAL ACTIVITY IN THE PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE

The evidence for PA in promoting longevity has been apparent throughout the ages and Plato in 380BC was one of the first to advise that the "lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save it and preserve it". These early findings were supported in 1768 by Herberden's descriptions of a patient who set himself a task of sawing wood for half an hour every day and was nearly cured from his symptoms of angina[10]. However, it was not until the 1950s that modern-day exercise research entertained the notion that deaths from non-communicable diseases such as CVD were attributed to physically inactive occupations. This notion was first described by Professor Morris and colleagues who compared the death rates of physically active transport workers to their sedentary counterparts[11]. From this seminal study it was noted that men who participated in active occupations experienced half the CHD mortality rates when compared to their sedentary counterparts who spent most of their working days sitting[11]. These observations were confirmed later in the 1970s by two studies by Paffenbarger and colleagues who recorded the occupational activities of San Francisco longshoremen[12,13]. In the first study, occupational activities were quantified in terms of kilocalorie expenditure and it was noted that the longshoremen who expended 925 kcals more per working day than other longshoremen sustained a coronary death rate 20% lower than their less active counterparts[12]. In the second study, the longshoremen's occupational activities were categorised as light, moderate or heavy based on their kilocalorie expenditure. Overall, longshoremen that engaged in light or moderate work were twice as likely to die from CHD when compared to those whose work was classified as heavy[13].

Following these earlier studies, research turned its focus to the 'dose-response' relationship between the volume expressed in kilocalorie expenditure of LTPA and the risk of CHD. Morris et al[14] observed the LTPA habits of middle-aged male civil servant executive office workers who recorded their activities over a 2-day period (Friday and Saturday). The office workers' LTPA was classified as vigorous (energy output of 7.5

kcal/min) or non-vigorous. After an average follow-up period of 8.5 years, the rate of CHD death was more than twice as high in the non-vigorous group (2.9%) when compared to the vigorous group (1.1%), giving a relative risk (RR) of 2.6. In support of the benefits of LTPA, Paffenbarger and colleagues were among the first to publish a comprehensive dataset that clearly described an inverse relationship between moderate and vigorous amounts of LTPA and the reduction in CHD risk in male Harvard University alumni[15]. In this dataset, men who reported that they expended more than 2000 kcal per week through walking, stair climbing and recreational sports were at a 56% lower risk of CHD than their peers who reported expending less than 2000 kcals each week[15]. In addition, CHD risk decreased by a further 10% when the energy expenditure occurred in vigorous sports rather than in walking or climbing stairs[15].

Throughout the 1980s, substantial evidence started to emerge on the benefits of PA in the reduction of CHD risk. Berlin and Golditz[16] were one of the first to publish a meta-analysis, which included studies on active occupations and LTPA. In summary, the meta-analyses revealed that the RR of CHD was 1.4 for sedentary vs active occupations and 1.6 for low vs high LTPA[16]. Further, the RR for CHD death was 1.9 for sedentary vs active occupations and also for low vs high LTPA[16]. Since this publication, two large systematic reviews were published in 2008 and 2010, which supported the US and Canadian PA guidelines listed in Table 1[4,6]. The first review, by the American PA guidelines committee[4], included 30 prospective cohort studies with more than 141,000 men and 263,000 women in gender-specific analyses and more than 50,000 subjects in analyses of both genders combined. It concluded that the most active men and women had a medium risk reduction for developing CHD of 30 to 35% when compared to the least active subjects[4]. In addition, the findings in this review on CHD risk reduction are not too dissimilar for the medium risk reduction in CVD[4]. The second systematic review, which underlies the Canadian guidelines[6], included 49 studies with a total of over 726,000 participants (average 12,313 participants per study) among which the medium risk reduction in developing CVD was 36% for those participating in regular PA.

EVIDENCE FOR PHYSICAL ACTIVITY IN THE SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE

The benefits of PA in patients with CVD are well established with sufficient evidence coming from both epidemiological studies and randomised controlled trials (RCT). In an 18-year follow-up prospective study that included just over 3500 men and women with established CHD, men showed a 21% lower risk in CVD mortality with low-intensity exercise and a 39% lower CVD mortality with moderate- to high-intensity exercise, whereas women with low and moderate- to high-intensity exercise had 26% and 36% lower risk of CVD mortality, respectively[17]. These findings are supported by a wealth of evidence from RCTs in exercise-based cardiac rehabilitation (CR)[9,18-22]. Over the last 3 decades, several large meta-analyses have reported a significant reduction in hospital admissions, all-cause and cardiac mortality and improvements in quality of life in patients receiving structured exercise training compared to those receiving usual medical care[9,18-22]. In two recent meta-analyses[9,18], Heran et al[9] pooled the results of 47 studies randomising over 10,500 patients to exercise-based CR or usual care. In 12 or more months follow up, exercise-based CR reduced overall and cardiac mortality by 13% and 26%, respectively, and hospital readmissions by 31% in the shorter term (<12 months follow

Table 2	
Frequency	*1-7 supervised sessions and/or home exercise*
Intensity	*50-85% HR max or 60-70% VO_2 max*
Time	*20-90 minutes (15 min warm up 10 min cool-down)*
Type	*Jogging/walking/cycling/circuit interval training*

Table 2: Exercise training interventions[9]. HRmax=heart rate max, VO2 max=maximal amount of oxygen uptake.

up)[9]. However, in this meta-analysis CR did not reduce the risk of total myocardial infarction, coronary artery bypass graft surgery or coronary angioplasty[9]. Nevertheless, Lawler et al[18] pooled the results of 34 randomised controlled trials, which included over 6000 patients and overall, patients randomised to exercise-based CR had a 47% lower risk of reinfarction and a 26% and 36% lower all-cause and cardiac mortality, respectively. Moreover, in a stratified analysis, the treatment effects were consistent regardless of study periods, duration of CR or time beyond the active intervention[18]. Table 2 provides an overview of the exercise interventions used in Heran et al's meta-analysis[9].

EVIDENCE FOR CARDIORESPIRATORY FITNESS IN THE REDUCTION OF CARDIOVASCULAR DISEASE

There is sufficient evidence to suggest that CRF is a useful measure to estimate CVD risk in individuals free from disease and in those with traditional CVD risk factors or in patients with established CVD[23-25]. CRF is defined as a physiological attribute and is related to the body's ability to uptake and use oxygen to perform dynamic, moderate- to high-intensity exercise for prolonged periods of time. Cross-sectional, observational and exercise training studies suggest that high levels of PA are associated with an increase in CRF levels in a dose-response manner in both primary and secondary prevention[26-28]. The relative reduction in the incidence of CVD averages 47 to 70% in studies that have used an objective measure of CRF, whereas studies reporting subjective measures of PA have shown an average risk reduction of only 30 to 36%[6,24,29]. CRF is normally measured by direct expired gas analysis but it can be estimated by using regression equations based on the time and workload performed on a given exercise test. The majority of the larger epidemiological studies have used the latter method to estimate maximal oxygen uptake, which is expressed in metabolic equivalents (METs). METs define the peak levels of PA as multiples of the energy cost above that required to maintain a seated position at rest[30]. One MET is defined as the energy expended in a sitting position at rest, which is equivalent to an oxygen consumption of approximately 3.5 ml per kilogram of body weight per minute for an average adult[30]. Walking one mile in 15 minutes is equivalent to 5 METs or five times the energy cost of sitting, whereas jogging one mile in 10 minutes is equivalent to 10 METs.

At present there is no clinical consensus on the optimal level of CRF in the prevention of CVD; however, evidence from a meta-analysis by Kodama et al[24] on 33 studies suggests that a minimal CRF of 7.9 METs is significant in CVD risk reduction. Further, evidence from Myers et al[23] shows that subjects (including patients with established CVD) with an exercise capacity lower than 4.9 METs have a RR of death 4.1 times greater compared to those with an exercise capacity above 10.7 METs. In both these studies a 1-MET improvement in CRF was associated with a 12 to 13% reduction in all-cause mortality and 15% reduction in CHD or CVD events[23,24].

THE CAUSAL RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND THE REDUCTION OF CARDIOVASCULAR DISEASE RISK

The causal relationship between aerobic PA and the reduction of CVD risk has been attributed to multiple biological changes, which favourably alter the function and structure of the coronary endothelia and myocardial function and a number of established atherosclerotic risk factors[31,32]. Risk factors which benefit from PA include a reduction in hypertension[33,34], dyslipidaemia[35], insulin resistance[36], inflammatory markers[37] and psychological factors[38]. Further, PA has been shown to halt the progression, and cause regression, of atheromatous plaques within the coronary arteries after 12 months of aerobic exercise training[39] and has also proved to be more

> **sitting for extended periods is a significant risk factor for CVD, irrespective of the amount of PA that is performed**

medically effective than angioplasty with a significantly greater 'event-free' survival rate[40].

Resistance training complements aerobic PA and is associated with the enhancement and maintenance of lean muscle mass, strength and power[41], which leads to an improvement in functional ability to perform everyday living activities[42]. Further, regular resistance training has been shown to improve glucose metabolism[43,44] and body composition and it also reduces the cardiac demands of muscular work during daily living activities[41].

In relation to improving CRF, Kodama et al's[24] meta-analysis highlighted that a 1-MET higher level of CRF is comparable to a 7-cm, 5-mmHg, 1-mmol/L (88-mg/dL) and 1-mmol/L (18-mg/dL) decrement in waist circumference, systolic blood pressure, triglyceride level (in men) and fasting plasma glucose, respectively, and a 0.2-mmol/L (8-mg/dL) increment in high-density lipoprotein cholesterol.

PHYSICAL ACTIVITY IN A PREVENTIVE CARDIOLOGY SETTING

PA is one of the essential components in preventive cardiology programmes along with smoking cessation, healthy eating, stress management and cardio-protective medication[8]. Each of these interventions is delivered by a multidisciplinary team that includes a cardiologist, cardiac specialist nurse, dietician, psychologist and PA specialist or physiotherapist. In the context of the PA specialist or physiotherapist's role, PA should be prescribed and tailored to the clinical profile of the individual taking into account their risk stratification and screening for any contra-indications[45,46]. In general, patients at high CVD risk should be advised to reduce the amount of time spent in prolonged static sedentary activities and to participate in the PA guidelines presented in Table 1. However, for patients that are unable to maintain a normal weight and for adults with increased risk of CVD or type 2 diabetes, additional benefits will be gained from gradually progressing towards 300 minutes or more of moderate-intensity aerobic activity per week, 150 minutes or more of vigorous-intensity aerobic activity each week or equivalent combinations of moderate- and vigorous-intensity aerobic activities[7].

In order to achieve these recommendations, most preventive cardiology programmes offer structured exercise training sessions set at a moderate intensity, which can be performed three times per week for 30 to 40 minutes each time[30]. The exercise programme should include a 15-minute warm up and a 10-minute cool down, which is additional to the time spent during the conditioning component. The exercise intensity should be guided by using heart rate monitoring within the range of 60 to 80% of maximum or an age-predicted maximum heart rate formula[30]. In addition, ratings of perceived exertion should be used in conjunction with heart rating monitoring and the patient

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should exercise at a 'moderate to hard' (but not strenuous level) intensity[30]. The mode of exercise should be aerobic in nature and be performed continuously or in intervals. Continuous training involves uninterrupted aerobic exercise performed at a sub-maximal level, whereas interval training entails bouts of relatively intense work separated by periods of rest or lower intensity exercise. This style of training has several advantages as it allows deconditioned individuals to achieve a greater volume of work at a higher intensity when compared to continuous training and therefore the stimulus to physiological change is greater. Typical modalities include walking, cycling, jogging or circuit-based exercise and resistance training. In addition, all apparently-healthy adults and medically-stable patients should perform muscle-strengthening activities using a variety of modalities including weight training, resistance training and circuit training[7,41]. Resistance training is an important complement to aerobic exercise and it is recommended that one set of 8 to 12 repetitions are performed on 8 to 10 different exercises that work the larger muscle groups (chest , back, shoulders, legs, arms and trunk) of the body on 2 or more days each week[7]. The weight or resistance chosen for each muscle group should elicit volitional local muscular fatigue at the end of each set; guidelines for patients with established CVD can be found in a statement update on the topic by Williams et al[41].

FUTURE DIRECTIONS IN PHYSICAL ACTIVITY RESEARCH

Evidence is now emerging that 'one size does not fit all' and there appears to be two ends to the PA spectrum between low-level PA and high-intensity interval training (HIIT). Recent evidence shows that people who stand for most of their day have a 16 to 32% lower risk of premature CVD mortality, compared with those who sit for most of the day[47]. These findings suggest that sitting for extended periods is a significant risk factor for CVD, irrespective of the amount of PA that is performed each week. However, on the other hand, evidence is starting to emerge on the benefits of HIIT in patients with CVD[48]. According to recent research, HIIT results in superior improvements in peak oxygen uptake, ventricular and endothelial function, as well as improvements in CVD and metabolic risk factors when compared to moderate continuous training[48-51]. At present, there are no set standards for an optimal HIIT programme, although most studies have used a protocol that includes a 1:1 ratio of work to recovery lasting between 30 seconds and 4 minutes set at intensities equal to 50 to 120% of VO_2 peak (oxygen consumption) for the work intervals and 0 to 50% VO_2 peak for the rest intervals[48-51]. The modes of exercise involve uphill walking and stationary cycling performed two to five times per week. However, it should be noted that further research is required to assess the long-term safety and efficiency of HIIT programmes on a wide range of patients with CVD.

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