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Physical Activity and its Effect on Reducing Disease: A Literature Review of The National Runner's Health Study

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Introduction

In 1996, Dr. Paul Williams began The National Runner's Health Study. The study had over one hundred thousand respondents who were questioned about their physical activity habits (walking or running), diet, weight, height, and use or previous use of tobacco and alcohol. Some of the participants were involved in case studies of several years. Primarily, the study tested the effects of vigorous physical activity and its ability to reduce disease. For close to twenty years, Dr. Williams has continued an impressive amount of research on various topics in the health and exercise field. The study is one of the most informative resources of knowledge of the benefits of physical activity available. Primarily, it looks at the effects of physical activity on coronary heart disease, hypertension, cholesterolemia, and diabetes. However, the range of topics the study covers is immense.

Heart Disease

Coronary Heart Disease: One of the most covered topics during the study was the effect of physical activity on heart disease. Obtaining physical activity above the national guidelines (30 mins/day, 5 days/week) resulted in significant coronary heart disease incidence reduction. For each kilometer run per day over the guidelines, a 5% incidence reduction was observed in coronary heart disease, a 7% reduction in myocardial infarction, and a 10% reduction in angina. When measured against those who ran less than 3 km/day, participants who exceeded a 9km/day run observed a 65%, 29%, and 26% reduced incidence for angina, nonfatal CHD, and

fatal CHD respectively (1). A kg/m^2 decrease in BMI correlated to an 11.2% decrease in CHD. The optimal BMI for lowest risk of CHD lies somewhere below 22.5kg/m^2, even though a normal BMI is considered to be 18.5 – 24.9kg/m^2(2). High-density lipoprotein (HDL cholesterol) aides in preventing coronary heart disease. In woman who partook in physical activity higher than current guidelines, they (on average) increased their HDL levels by .1333(+/- .02mg) per deciliter. Those who ran >64km/wk saw much higher HDL levels(3). When measured against those who ran <16km/wk, participants who ran >80km/wk showed an 85% lower prevalence of HDL levels considered clinically low, 2.5 times greater prevalence of high levels of HDL, 50% less participants responded positive for hypertension, and more than 50% less responded positive for blood pressure and cholesterol medications(4).

Interestingly, while overall fitness level and amount of physical activity are often closely associated, they were shown to be separate factors in determining heart disease risk. Independent of physical activity, having a low fitness level remains a risk factor. In one study, along with the relationship of physical activity and risk reduction level, a significant drop in risk was observed at the 25th percentile of the fitness distribution(5). Fitness can be a heritable trait. In a 2010 study, rats were bred for running endurance on a treadmill. Their offspring showed higher baseline fitness levels and lower incidence of CHD. Inherited fitness was studied in 29,721 men for 7.7 years in m/s increments. For each increase in fitness level showed at baseline fitness level, study participants observed decreased CHD incidence(6). Furthermore, exercise intensity has a major effect on preventing

coronary heart disease. While causality was unknown, men and women who ran faster during the study observed reduced blood pressure levels, triglycerides, improved HDL/LDL ratios, and decreased BMI and circumference measurements (wasit, hips, chest)(7).

Cardiac Arrhythmias and Stroke: The National Runner's Health Study observed various heart conditions. A dose response is seen between increasing exercise levels and decreased number of cardiac arrhythmias. Larger decreases in number of incidents were observed in walkers. However, Dr. Williams attributes this to the fact that inadequately active walkers skewed the size of % reductions seen. Incidence reduction in runners was significant but less than walkers. Williams attributes this to the observation that most of the runners had been running for over 10 years. Overall, incident cardiac arrhythmias decreased 4.4% per METhr/d(8). For each km/day run, men and women observed an 11% decrease risk of stroke. Even when adjusted for hypertension, diabetes, hypercholesterolemia, and body weight, risk of stroke was reduced in individuals who exceeded The Physical Activity Guidelines(9).

Hypertension, Hypercholesterolemia, and Diabetes mellitus

Studies on Hypertension, Cholesterolemia, and Diabetes: A major benefit of increased physical activity is lowering risk of hypertension, cholesterolemia, and diabetes. Williams tested walking and running (moderate versus vigorous) to see if they provided different risk reductions of these conditions. At equal energy expenditures, comparable reduced incidence of hypertension,

hypercholesterolemia, and diabetes mellitus was observed in walkers and runners studied (vigorous provided slightly more). A dose-response relationship was shown between energy expenditure and risk reduction(10). Measurements of total physical activity were indicators of reduced risk for hypertension, diabetes, and cholesterolemia as well. Weekly walking distance, longest walk, and walking intensity were shown to be inversely related to medication use (for previous mentioned conditions). Those who walked >2.1m/s had 48 and 52% decreased use in antihypertensive medication, 68 and 59% decreased antidiabetic medication, and 53 and 40% decreased use of LDL lowering medications for men and women respectively (when compared to men and women who walked <1.2m/s)(11). Similarly, vigorous physical activity and increased cardiorespiratory fitness were inversely related to prevalence of diabetic, hypertensive, and hypercholesterolemia medication use. When compared with participants who ran <16km/wk, those who ran >64km/wk saw 69 and 55% reduced use of diabetic medication, 48 and 52% reduced use of hypertension medication, and 64 and 51% usage of LDL lowering medications for men and women respectively(12).

In marathon runners, incidence of hypertension, hypercholesterolemia, and diabetes was reduced. Men who averaged between 0.2 and 0.8 marathons a year saw reductions of 13% for hypertension, a 22% reduction in cholesterolemia, and a 67% reduction for diabetes, based off of reduced use of medications(13). It was observed that even in normal weight males and females, higher BMI's and body circumference measurements were positively correlated with increased risk for

hypertension, hypercholesterolemia, and diabetes even though risks were still less than for those who were overweight or obese(14).

Fitness had a clear effect on reductions in incident hypertension, high cholesterol, and diabetes. An increased cardiorespiratory fitness level was related to a decreased risk of hypertension, hypercholesterolemia, and diabetes, independent of physical activity. During the same physical activity regimen, the fittest men (men who ran at a faster m/s rate during equal distances) had 62%, 67%, and 86% lower chances of developing hypertension, hypercholesterolemia, and diabetes respectively(15). Results of another study also showed that increasing exercise intensity reduces risk of developing hypertension, hypercholesterolemia, and diabetes (independent of exercise volume and fitness level). For each increase in m/s rate (adjusted for km/day), men and women (respective values) showed a 54 and 46% reduced incidence of hypertension, 55 and 48% reduced incidence of hypercholesterolemia, and 50 and 75% reduced incidence of diabetes(16).

<u>Hypertension (isolated):</u> There is evidence that current guidelines provide insufficient risk reduction for hypertension. Major reductions in hypertension were achieved at levels between 1.8 and 3.6 METh/d. Williams cautions to be aware of ventricular atrophy when working with a hypertensive individual(17). Even amongst more active, fit, individuals, weight gain was correlated with increased risk of hypertension in a dose-dependent response. No advantage was noted to previously lean individuals. Those whose weight increased >2.4kg/m^2 had a 1.68 odds ratio for males and 1.42 odds ratio for females for becoming hypertensive (at a 95% confidence interval)(18). Risk of becoming hypertensive with age was reduced

in those who remained vigorously active and depends on dose. Individuals who ran 40km/wk compared to those who ran 8km/wk experienced an 80% reduced risk for 34-44 y/olds, a 66% reduced risk for 45-54 y/olds, 69% reduced risk for 55-64 y/olds, and a 57% reduced risk for hypertension for those older than 65 y/olds(19).

Diabetes mellitus (isolated): Vigorous physical activity has shown considerable effects on reducing risk of developing diabetes mellitus. Risk of developing diabetes seemed to be associated to total distance run. Its sizable effect is especially due to the prevention of age-related weight gain. Men who ran >8km/wk had a 95% reduced incidence of diabetes between the ages of 35-44, 92% lower for those aged 45-54, 87% lower for those ages 55-64, and 46% lower for those ages 65-75(20).

Hypercholesterolemia (isolated): Cardiorespiratory exercise has been shown to decrease risk of cholesterolemia. Risk of hypercholesterolemia was reduced with increasing run mileage and greater amounts of vigorous exercise. When compared to participants who ran the same or decreasing distance, men and women showed a .8 odds ratio (95% confidence interval) for hypercholesterolemia. When adjusted for changes in BMI, the significance of this ratio was reduced, but still present (21). Weight gain changes in total and regional adiposity were shown to increase incidence of hypercholesterolemia. An increase >2.4kg/m^2 greatly increased prevalence of hypercholesterolemia of 94% for men and 129% for women(22). HDL levels observed in 6847 men suggested that concentrations were highest with those experiencing their most significant weight loss since lifetime maximum. These

results also revealed decreased triglycerides, LDL levels, and total cholesterol to HDL level ratios(23).

Genetics and diet strongly influence LDL levels even when comparing active and sedentary physical activity levels. Upon switching from high fat/low carb to low fat/high carb diets, HDL levels decreased and some LDL levels increased in identical twins with divergent exercise levels(24). Vigorous physical activity (behavior) does have the ability to decrease risk of genetic influences on BMI. In identical twins with discordant running distances, significantly lower BMI was associated with higher HDL levels. Similarly to the previous study mentioned, low HDL levels may be greatly predetermined by heredity. High HDL concentrations were associated with decreasing BMI(25).

Weight Loss, BMI, Genetics, Aging, and Diet

BMI and Weight Loss: Triglyceride levels observed were highly associated with waist and hip circumferences and BMI even in active participants. When compared to the 5th percentile, men at the 95th percentile (per unit triglyceride/adiposity) showed a 14 times greater BMI, 7.8 greater waist circumference, and 3.6 greater hip circumference. Increased triglycerides were seen in whites than blacks and men than women. LDL concentrations mirrored these triglyceride levels(26). With physical activity, it was observed that participants with low HDL levels remained around the same HDL measurements while those with high HDL levels saw an increase in HDL. This suggests that medication is a more appropriate method for those with low HDL concentrations. HDL-C levels appeared

to increase with alcohol intake. Williams suggests these results may have been skewed by the diets of those at the 95th percentile (HDL-C levels), and that runners may have different diets and drinking habits than sedentary individuals(27).

It is widely known knowledge that obesity contributes to several negative health conditions. However, in 2011, Williams found that obesity is actually a risk factor for weight gain via a sedentary lifestyle. It was observed that risk factors that aren't a major cause in weight gain increase with increased adiposity. In laymen's terms, someone being obese is actually a major component to easily gaining more weight. A study showed that participants at the highest percentiles of BMI saw much larger risk of increasing body weight from a sedentary lifestyle than those with the smallest BMIs(28). Of opposite effects observed, a previous study of 27,596 women suggested that the obese population obtain the greatest benefits from walking(29).

A much higher loss of weight was noted in runners over walkers. While a decrease in BMI was seen in both runners and walkers, the decrease in BMI was significantly more so for runners. This was due to higher energy expenditure in METh/d in runners than walkers(30). Similar to what was mentioned in the previous paragraph, Williams concluded that those with higher benefits experienced greater weight loss from running. Per km/wk increase, decrease in BMI observed was 3 times greater at the 95th % than the 5th % for men and 6 times greater at the 95th % than the 5th % for women(31) It is important to note that as well as superficial body fat, visceral body fat decreases in relation to increasing vigorous physical activity level (especially when beginning a vigorous routine)(32).

Interestingly, research has shown that running exercise is not exchangeable with non-running. Assumptions made by The Physical Activity Guidelines that 1 minute of running is the same as 2 minutes of walking are incorrect. Distance-based running provided increased health benefits compared to other types of exercises even with equal energy expenditure. When measured, decline in BMI were much greater for runners than non-runners at .12kg/m^2 greater declines observed in male runners and .11kg/m^2 for female runners(33). Another misconception explored by Williams was if weight gains cost the same energy expenditure as weight loss. It was found that weight gained due to reduction in exercise per week (below 30kcal/kg for men and 15kcal/kg for women) is not always reversed by starting back up at previous activity level(34).

<u>Aging and Weight Gain:</u> As people grow older, weight gain is almost inevitable. However, it has been observed that with increasing age, men and women gained less weight correlated to an increase in vigorous exercise. Acute weight loss correlated with increased activity as well. Generally, men of modest (0-23km/wk), intermediate (24-47km/wk), and prolonged (>48km/wk) gained weight through age 64. But, the prolonged group (>48km/wk) saw only half of the annual weight gain compared to the modest (0-23km/wk) group. On average, men age 35-44 and women age 30-39y/o gained 2.1-2.9kg per decade for those who ran <24km/wk compared to those who ran >48km/wk(35). Age-related weight gain does still happen even amongst individuals who led highly active lives. In order to prevent age-related weight gain, vigorous physical activity would have to increase with age. Williams predicted that vigorous physical activity may need to increase 4.4km/wk

annually for men and 6.2km/wk annually for women(36). Again, weight maintenance is not likely with increasing age <50y/o if activity levels and diet remain similar. Males would have to annually increase distance by 2.24km/wk to make up for age related weight gain. Williams attributes some of this causation to decreasing plasma testosterone and HGH levels with age(37).

As stated previously, exercise clearly can have an effect in attenuating age-related weight gain. It was observed that age affected the relationship between adiposity and vigorous physical activity. As expected, Williams notes that declines were greater with younger participants out of 41,582 women(38). Results were similar in 60,617 males who ran. Age and vigorous physical activity clearly affected the male population's adiposity level. Vigorous physical activity is required to maintain weight with age(39).

<u>Inherited Weight and Genetics:</u> Results have also shown physical activity has a role in mitigating inherited weight and BMI. In monozygotic twins, Williams found that the twin who ran more (km/d) experienced a lower BMI. Females saw a 14.3% decrease in BMI and males saw a 7.4% decrease(40). It was observed that runner's BMI was also highly related to their parents. Those who exceeded the base level physical activity dose for general health have the chance to significantly decrease their risk of becoming obese. These results found similarities with other studies that physical activity to prevent weight gain is higher than those for general health benefits. Relationship to parent's BMI decreased immensely with increased run distance. When measured against those who ran <3km/d, those who ran >9km/d saw a 48% and 58%reduction of mirroring parental BMI for males and females

respectively(41). Genetic inheritance is responsible for 40-70% of variation of BMI. Moderate physical activity had a direct inverse relationship with total and regional adiposity due to inheritance(42).

Diet: It's clear that exercise and diet share a role in weight gains and reductions. In 2012, Williams studied the effect of moderate physical activity on participants weight when consuming a high meat, low fruit diet. A diet of this type generally leads to an increase in BMI. This correlation was weakened with physical activity. For men and women who walked >1.5km/d, BMI decreased 21% and 31% for women and men respectively(43). Williams also studied if a sedentary lifestyle can actually increase risk of weight gain due to diet. The answer seemed clear – it was observed in 106,737 runners that vigorous exercise has the ability to attenuate diet related weight-gain. Specifically, running >8km/d compared to running <2km/d decreased the rise in BMI for men by 43% per serving of meat and 55% per serving of meat in men and women respectively(44). In 1997, Williams studied the combined effects of diet, alcohol, and exercise on coronary artery disease. Specifically, it was observed that an increase of 1.55mmol/L in HDL occurred for men running a distance greater than 72km who drank 6oz of alcohol each week than nondrinkers who ran less than 24km/wk. It was also shown that alcohol and running distance were independent factors in increasing HDL cholesterol, and that alcohol continued to increase hypertension regardless of physical activity level(45).

Distance and its Metric Use: Williams is convinced that distance may be the best method of measuring physical activity. In a study of 17,201 male and 16,173 runners, Williams found that measurements based on distance (METhr/d) run or

walked appeared to show more accurate scaling for epidemiological tests(46). Similar results were observed when comparing distance vs. time estimates for estimating adiposity. After testing exercise dose and BMI, distance appeared to be a preferred method for epidemiological obesity. Total distance presents a higher correlation with predicted health benefits(47).

It seems clear that increasing distance correlates with a greater reduction in BMI. However, decreasing BMI and waist circumference measurements were greater for those at the 90^{th} percentile of BMI's by .076km/m^2 per week when compared to a decline of .015kg/m^2 per week of men at the 10^{th} percentile of BMIs. Interestingly, greatest decline in BMI was observed in men older than 74 y/o(48). Finally, Williams found that even though leanness experienced a relationship with intensity and distance of exercise, distance was more heavily related. He encourages distance as a metric for weight loss(49).

There are important distinctions to make involved with physical activity and body weight. While physical activity has several benefits on preventing hypertension, diabetes, etc., Williams suggests that increasing HDL concentration is correlated with loss of body fat. He acknowledges the positive effects of physical activity, but notes the relationship of fat and HDL levels (in addition to the inverse response between adiposity and physical activity levels)(50). Also, in a study of 44,370 and 25,252 respective male and female participants, starting BMI was found to determine current BMI and fitness level(51).

Physical Activity and its Effect on Assorted Conditions

Ocular Conditions: In a study of 32,610 runners and 14,917 walkers, exercise highly correlated to a decreased risk of cataracts. In fact, up until 9METhr/d energy expenditure and reduced risk of cataracts exhibited a dose response(52). Another study on cataracts done by Williams 4 years earlier exhibited a 35% reduced incidence of cataracts for men who ran >64km/wk. It was noted also that men with a higher cardiorespiratory fitness level were at a much lower risk for development of cataracts than the least fit men. Decreased BMI also attributed to a lower chance of cataracts(53).

Increased vigorous physical activity was associated with decreased risk of macular degeneration. The risk of macular degeneration decreased 10% per km/d increase. A 42-54% decreased incidence observed of macular degeneration was observed with participants who ran >4km/d(54). The number of incidences of glaucoma observed also decreased 5% per km/d. This suggests an inverse relationship between increasing vigorous physical activity and incidence of glaucoma as well(55).

Assorted Diseases: A recent study (2013) by Williams suggested that attaining the Physical Activity Guidelines significantly reduces the risk of kidney cancer. An often-repeating theme of William's studies, slightly higher reduction in incidence of kidney cancer was observed in runners vs. walkers(56). Incidence of gallbladder disease saw a sharp increase when participants reached a BMI >27.5kg/m^2. Compared to unfit participants, men who ran >4.75m/s observed an

83% decreased incidence observed of gallbladder disease(57). Age adjusted, the fastest men also observed a 32% decrease in incidence of prostatic hyperplasia when measured against the slowest. A dose response relationship was observed between decreased risk of benign prostatic hyperplasia and increased exercise intensity(58). During a 2009 study, Williams completed a 7.7 year follow up dealing with diverticular disease. It was observed that for each km/d ran, incidence of diverticular disease decreased by 6.2%. Participants who ran >8km/d showed results of a 48% reduced incidence. There was a clear inverse association(59).

A study in 2013 observed that running decreased incidence of osteoarthritis and hip replacement. Williams attributes this to lower BMI's of runners. Surprisingly, no evidence was found to suggest an increased risk of osteoarthritis in runners(60). Male participants who ran more than 8 km/d observed a 50% reduced incidence of gout. Williams's findings suggest that risk of gout is inverse associated with increasing physical activity level(61). Finally, physical activity was seen to have an effect on respiratory disease. For every METhr/d, risk of aspiration pneumonia decreased by 19.9% and respiratory disease decreased by 7.9% for walkers and runners. A larger dose of physical activity was associated with an inverse, dose response relationship with respiratory disease, pneumonia, and aspiration pneumonia mortality(62)

Conclusion

The positive effects of physical activity, especially vigorous, cannot be ignored. Its role in preventing risk factors for heart disease, weight gain, and a

massive number of other negative health conditions is immense. In leading a functional lifestyle as an individual ages, physical activity is an invaluable tool that attenuates age related weight gain. Interestingly, we observe that even diseases that don't seem to be related to cardiorespiratory systems are positively affected (such as conditions involved with the renal system and vision). It should be noted that Williams measured physical activity most often by km/wk, km/day, or METhr/d. He defines fitness in these studies as m/s that participants completed a certain kilometer distance in (VO2 max was not measured). Weight was primarily measured in BMI via kg/m^2 or observed in circumference measurements. Data was self-reported via a survey or recorded from medical records, with over 100,000 participants who contributed to The National Runner's Health Study.

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