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Exercise and the heart: A review of the early studies, in memory of Dr R.S. Paffenbarger

The role of activity in lowering the risk of death from heart disease was clarified by the work of public health pioneer Ralph Paffenbarger, who died in July 2007

ABSTRACT: Studies completed by Ralph Paffenbarger and others have made a significant contribution to our understanding of the relationship between exercise and coronary artery disease. In the 1950s there was a skeptical response when researchers first hypothesized that men in middle age who are engaged in physically active work experience less coronary artery disease than men who are not engaged in active work. This skepticism began to change when Jeremy Morris and colleagues studied London transport workers and British civil servants to explore the incidence of coronary artery disease in men according to activity level. In the 1970s Paffenbarger built on the results of Morris's studies by analyzing data collected from longshoremen and college alumni. Today the notion that exercise promotes cardiovascular health is accepted by the medical profession, by governments, and by the public at large—an acceptance made possible by the work of Paffenbarger and other 20th-century visionaries.

Those who think they have not time for bodily exercise will sooner or later have to find time for illness.

—Edward Stanley, Earl of Derby, in an address at Liverpool College, 20 December 1873

On 9 July 2007, Dr Ralph S. Paffenbarger Jr. died of heart failure at age 84. Over the course of his career, this renowned physician-epidemiologist published more than 150 articles, many of which focused on the development of cardiovascular disease and the relationship between exercise and longevity. Through his scientific work, Dr Paffenbarger has shaped the current culture of exercise and how that relates to the practice of medicine across all levels of care. In recognition of his passing, we have reviewed the early seminal studies of Dr Paffenbarger and others, and tried to put in context the profound effects this research has had on the modern fitness for health movement.

Biography

Dr Ralph Seal Paffenbarger Jr. was born on 21 October 1922 in Columbus, Ohio. He received a bachelor's degree from Ohio State University in 1944, and subsequently graduated from Northwestern University's medical school in 1947. He followed his medical education with a master's degree (1952) and then a doctorate (1954) in public health from Johns Hopkins University. Throughout his career he held positions as a researcher and physician at the University of California at Berkeley, and as a professor of epidemiology at the Stanford Uni-

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versity School of Medicine and the Harvard University School of Public Health. He was president of the American Epidemiological Society from 1987–1988 and in 1996 was a recipient of the first International Olympic Committee prize for sport science along with Dr Jeremy N. Morris.

His research interests focused on preventive medicine and public health. Initially he examined the transmission and pathogenesis of poliomyelitis. In the mid-1950s he began focusing on physical activity as it relates to the development of cardiovascular-hypertensive-metabolic diseases. Like Dr Morris before him he looked into the epidemiological associations between populations and their habit patterns and compared them with longevity outcomes. Morris's studies of London bus drivers and Paffenbarger's studies of longshoremen and college alumni were the first to link physical activity and exercise to a lower risk of heart disease. The medical and scientific community initially met these results with skepticism, but by the 1970s it became an accepted notion that men who exercised regularly had a lower risk of death from heart disease and stroke, independent of obesity, diet, and blood pressure.

The results of these studies had a profound effect on the modern fitness movement and public policy, influencing the 1996 Surgeon General's Report on Physical Activity and Health and shaping numerous international guidelines (including those produced by CDC, CDA, CHS, CCS, ACC, AHA, ESC, JNC 7, American College of Sports Medicine, Canadian Association of Cardiac Rehabilitation, American Association of Pulmonary and Cardiac Rehabilitation, and Health Canada). The results also influenced Paffenbarger himself. His finding that men who take up exercise later in life receive similar benefits to those enjoyed by lifelong exercisers moved Dr Paffenbarger, a previously sedentary man with a strong family history of premature coronary disease, to start running in the fall of 1967 at the age of 45. By 1993, when he was forced to retire from running at age 71, he had competed in 151 marathons and ultramarathons, including 22 Boston Marathons and 5 gruelling Western States 100 Endurance Runs—completing the first 100-mile race through the Sierra Nevada in less than 29 hours at the age of 54.

It is worth noting that information we now take for granted, such as the incidence and prevalence of coronary artery disease (CAD) and the pathogenesis of CAD were far from established in Dr Paffenbarger's day. His early reports were some of the first to describe the association of CAD with age, suggest multifactorial causes, and draw the link between CAD and smoking, hypertension, and dyslipidemia.

Early studies linking exercise and heart disease

Bus drivers and conductors

In 1953 Dr Jeremy (Jerry) Morris and colleagues examined the onset of coronary artery disease in 31 000 male transport workers aged 35 to 65 years between 1949 and 1950.[1] Initially, they described an association of CAD with age ("the disease is uncommon until 45 years of age"), general presentation ("angina pectoris, coronary thrombosis, and coronary thrombosis causing death"), and mortality pattern ("far more deaths occurred in the first 3 days than within 3 months").[1] Their main objective, however, was to "seek for relations between the kind of work men do and the incidence among them of CAD."[1] They chose to examine the bus, tram, and trolleybus conductors, who climbed 500 to 750 steps per working day on average, and the drivers, who sat for over 90% of their shift. They found that conductors had less CAD than the drivers (overall annual incidence 2.7/1000 versus 1.9/1000). If the conductors did develop disease it was of later onset, manifested differently ("presenting first as angina pectoris and other benign forms"),[1] and was less likely to be fatal (early case fatality 30% compared with 50% in drivers). They postulated that "physically active work"[1] offered a protective effect, predominantly related to sudden cardiac death as a first manifestation of disease.

In the same paper, Morris and colleagues described similar findings in a group of 110 000 postal workers and civil servants.[1] They demonstrated that postmen who cycled or walked to deliver mail had fewer CAD events when compared with workers engaged in less intermediate physical activity (counter-hands, postal supervisors, and higher grade postmen) and their more sedentary counterparts (telephonists, civil service executives, and clerks): 1.8/1000/year versus 2.0/1000/year versus 2.4/1000/year. The active postmen also had a lower rate of early case fatality (0.6/1000/year versus 0.9/1000/year versus 1.2/1000/year) but a higher rate of angina pectoris (0.7/1000/year versus 0.4/1000/year versus 0.5/1000/year).

As a further test of their hypothesis the researchers examined coronary mortality by work activity in disparate social classes.[2] Using the occupational mortality volume of the Registrar-General's Decennial Supplement for 1930–1932 they replicated the finding of lower coronary mortality in the most active occupations in three separate social classes—III (skilled workers), IV (semi-skilled workers), and V (unskilled workers).[2]

This early hypothesis that "men doing physically active work have a lower mortality from coronary heart disease in middle age than men in less active work"[2] was met with "considerable skepticism by medical scientists and practitioners."[3]

As a result Morris went on to complete further examinations of the London transport workers in an attempt to address these concerns. In a 1956 publication he and his colleagues described how they studied uniform sizes from two central bus garages and one central trolleybus garage.[4] In comparing the waist measurement (trouser size) and breast measurement (jacket size) of 1276 drivers and 994 conductors between the ages of 25 and 65 years, they found that when adjusted for height and weight, drivers "measure more round the chest and… waist."[4] This difference was found even in the youngest age group, suggesting that the difference was present at the time drivers joined the service and were not the result of the occupation. At 10-year follow-up, however, they showed that the rates of sudden death as a first manifestation of CAD were more than twice as high among drivers regardless of their physique.[3]

In 1966 Morris and colleagues published a follow-up paper examining "many factors known, or suspected, to be related to the incidence of ischemic heart disease."[5] Between 1956 and 1960 they undertook thorough clinical and laboratory examinations in a sample of 667 drivers and conductors working on London's central buses and followed them up 5 years later. The initial examination included a familial, personal, and clinical history; measurements of blood lipids, blood pressure, physique, and skin-fold thickness; urinalysis; and 12-lead ECG results. Over the course of the 5 years of observation, 47 patients developed CAD, an incidence of 7%. These patients were then subdivided into four groups: sudden cardiac death less than 24 hours after symptom onset (7 patients), myocardial infarction not suddenly fatal (27 patients), angina (7 patients), and Q/QS changes on ECG (6 patients).

This early hypothesis that men doing physically active work have a lower mortality from coronary heart disease in middle age than men in less active work was met with considerable skepticism by medical scientists and practitioners.

Through univariate and multivariate analysis the researchers concluded that CAD incidence is higher in later age, in men with a family history of CAD, in cigarette smokers, in shorter men, and in obese men.[5] However, they concluded that levels of systolic blood pressure and plasma cholesterol were the predominant predictors of the incidence of CAD, accounting for 75% of new cases. The interaction with work-related activity level was significant: not only were there lower levels of elevated blood pressure and lipids in the middle-aged conductors, but for the same level of blood pressure, drivers had a higher incidence than conductors (overall 8.5/100 men/5 years versus 4.7/100 men/5 years).[5]

British civil servants

Realizing that in many occupations physical activity would have to be undertaken outside of the work environment, Morris and colleagues then completed a prospective study of middle-aged male civil servants who held sedentary desk jobs. The first analysis published in 1973 evaluated 16 882 civil servants employed between 1968 and 1970.[6] The researchers concentrated on "executive-grade" men between the ages of 40 and 64 years in six government departments across Britain, using questionnaires to collect data on leisure activities, social circumstances, relevant aspects of behavior, and medical and personal history. Over the 3-year follow-up period they recorded 232 first clinical CAD events. These affected individuals were then matched to two nonaffected individuals with subsequent finding that men who recorded vigorous activities (peak energy output of 7.5 kcal/minute) had a 33% relative risk of developing CAD, a protection against "rapidly fatal heart disease and other first clinical attacks."[6] Unfortunately, lighter activity did not have this effect, driving the researchers' hypothesis that "vigorous activity promotes cardiovascular health."[6]

An 8.5-year follow-up of 17 944 male civil servants confirmed and elaborated on the earlier findings.[7] Using the same methodology for data collection, Morris and colleagues relied on over 150 000 man-years of observation to demonstrate a lower rate of fatal clinical attack (early—0.65% versus 1.6%; late—1.1% versus 2.9%), as well as nonfatal first clinical attack (age-adjusted rate of 3.1% versus 6.9%) in those who undertook vigorous physical activity during leisure time. These findings were "more striking in middle age and early old age"[7] and present in all subgroups (men with a family history of CAD, obese men, short men, cigarette smokers, and men with hypertension). As a result, they extended their hypothesis to claim "vigorous exercise is a natural defence of the body, with a protective effect on the aging heart against ischemia and its consequences."[7]

Studies by Paffenbarger

San Francisco longshoremen

In 1951 a group of San Francisco longshoremen underwent multiple screening examinations as part of their employment. In 1970 Paffenbarger and colleagues reported on their 16-year follow-up of 3263 men who were 35 to 64 years old at study onset.[8] In the follow-up time of 44 585 man-years, there were 888 deaths, including 291 fatal coronary events and 67 fatal strokes. The researchers found that the most active group of cargo handlers, who expended over 1000 kilocalories (kcal) more than other longshoremen, had CAD death rates significantly lower than their sedentary colleagues (59 versus 80 incidents per 10 000 man-years of work). They noted that differences related to work activity persisted when smoking patterns, weight for height, and blood pressure were taken into account.

In 1975 Paffenbarger and colleagues looked specifically at the effects of "repeated bursts of work activity" in 6351 longshoremen.[9] When analyzed as work-years according to energy output over an 8-hour shift (high—1876 kcal, medium—1473 kcal, light—865 kcal) they found that there was a lower age-adjusted CAD death rate in heavier workers (26.9 versus 46.3 versus 49 deaths per 10 000 man-years of work). This finding was seen especially in terms of the "sudden-death syndrome" (5.6 versus 19.9 versus 15.7 deaths per 10 000 man-years of work). They postulated that there was a protective effect inherent in repeated bursts of high-energy output in terms of CAD mortality.

In 1979 Paffenbarger and colleagues further characterized the benefits of greater exertion in the 22-year follow-up of this cohort.[10] In a sample of 3975 longshoremen who were followed for 57 632 man-years there were 410 fatal MIs. After adjusting for age, race, systolic blood pressure, smoking, body mass index, glucose intolerance, and ECG status the authors found that men with a high-energy work activity (7 kcal/min) had half the rate of fatal MI when compared with men in the lowest energy work activity group (1 kcal/min). The authors also looked at rate of change for work activity over the preceding 4-year interval and found that workers "had a higher risk if they were on a downward trend"—that is, undertaking progressively less strenuous activity.

College alumni

In 1960 Paffenbarger was involved in the creation of one of the most widely cited studies on the topic of CAD and exercise, the college alumni study. Its original design was to "explore causes, pathways, and preventabilities of chronic degenerative disorders that remain largely unknown . . . through the sociomedical science of epidemiology."[11] Male and female alumni from the University of Pennsylvania and Harvard College who were born between 1896 and 1934 and enrolled between 1916 and 1950 were included in the study population. Although well known for its focus on CAD, the study also looked into hypertension, stroke, peptic ulcer disease, diabetes, accidental death, suicide, cancer, and "other distresses of middle and later ages."[11] Since the study's inception, more than 80 papers have been published on topics as diverse as diabetes, Parkinson disease, lymphoma, and prostate cancer.

The Harvard cohort yielded some of the most influential findings from this study. This cohort included 36 500 male alumni who entered college from 1916 to 1950. At time of enrollment it was customary to have a routine physical examination, thus providing an

An energy expenditure of 2000 kcal per week was associated with a 28% decrease in all-cause mortality, but was strongest and most significant in relation to cardiovascular and respiratory causes.

Table. 2007 ACSM/AHA Joint Recommendation on Physical Activity and Public Health.[20,21]

Adults 18–65 years of age

- Moderate-intensity aerobic physical activity (i.e., brisk walking, dancing, golf, doubles tennis) should be performed for a minimum 30 minutes per day at least 5 days per week (Class I) OR
- Vigorous-intensity aerobic physical activity (i.e., jogging, cross-country skiing, volleyball, competitive basketball) should be performed for a minimum 20 minutes per day at least 3 days per week (Class I)
- Combinations of moderate and vigorous physical activity can be performed to meet this recommendation (Class IIa)
- Moderate-intensity activity can be divided into sessions lasting >10 minutes each in order to meet total daily requirement (Class I)
- Activities that maintain or increase muscle strength (i.e., weight-lifting or resistance exercises, 8–12 repetitions for a total of 8–10 exercises) should be performed a minimum 2 non-consecutive days per week (Class IIa)

Adults >65 years of age

- Aerobic physical activity as above except activity is relative to an individual's level of fitness
  - Moderate—perceived exertion of 5–6 out of 10 (0 represents sitting and 10 all-out effort)
  - Vigorous-intensity activity—perceived exertion of 7–8 out of 10
- Muscle-strengthening activity as above except repetitions should be increased to 10–15 for a total of 8–10 exercises at a moderate-intensity (5–6/10) or high-intensity (7–8/10) effort
- Activities that maintain or increase flexibility should be performed for 10 minutes per day at least 2 days per week (Class IIb)
- Community-dwelling adults with significant fall risk should perform exercises that maintain or improve balance (Class IIa)
- Older adults with one or more medical conditions for which physical activity is therapeutic should perform physical activity in the manner that effectively and safely treats the condition (Class IIa)
- Older adults should have a plan for obtaining sufficient physical activity in the manner that addresses each recommended type of activity (Class IIa)

Evidence used to support recommendations

- Class I: Evidence and/or agreement that a given treatment/procedure is useful and effective
- Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy
- Class IIb: Usefulness/efficacy is less well established by evidence/opinion

For an in-depth explanation of policies used to prepare these guidelines, see the *Methodology Manual for ACC/AHA Guideline Writing Committees,* from American College of Cardiology Foundation and American Heart Association, Inc. 2006.

extensive baseline record. The study subjects were then followed periodically with questionnaires and surveys regarding adult exercise and doctor-diagnosed diseases. Alumni and college records provided information with respect to student athleticism and personal background. Weekly updates of the death lists by the alumni office were followed by examination of the death certificates for circumstances and cause of death.

In 1978 Paffenbarger and colleagues reported a follow-up of 117 680 person-years of observation.[12] The authors quantified physical activity using standardized measures and attributed kilocalorie-per-minute expenditures to these activities. For example, one flight of stairs per day (10 steps) accounted for 28 kcal/week energy expenditure. They created a physical activity index and then divided the groups into low-energy (less than 2000 kcal/week) and high-energy categories (more than 2000 kcal/week). In the 6-year to 10-year follow-up period between 1962 or 1966 and 1972, there were 572 first MIs, of which 215 were fatal. There was an inverse relationship between physical activity and risk of CAD, and alumni in the low-energy category on the physical activity index had a 64% increased risk of MI. This finding persisted across all age groups for both fatal and nonfatal MI and angina pectoris, regardless of traditional risk factors and previous activity level. Overall, the average MI rate was 50% to 70% higher in sedentary alumni. In contrast to their earlier reports,[13,14] they found that "only a physically active adulthood is associated with lower heart attack rates" and student athleticism is "unrelated to heart attack risk later in life."[12] They also noted that at any given level of energy expenditure the risk of heart attack, angina, and delayed cardiac death was lower for alumni who undertook strenuous activity. When combined with the other independent risk factors of smoking or hypertension, they found that the presence of all three conferred a relative risk of 7.70, as opposed to 2.78 for the presence of any two factors and 1.50 for any one factor.

In 1986 Paffenbarger and colleagues elaborated on these findings in a 12-year to 16-year follow-up of this cohort, accounting for 213 716 person-years of observation.[15] In this expanded analysis, physical activity was divided into tertiles and energy expenditure was divided into 500-kcal increments. The researchers showed that an energy expenditure of 2000 kcal/week was associated with a 28% decrease in all-cause mortality, but was strongest and most significant in relation to cardiovascular and respiratory causes. To compare the interrelationship between risk factors, stereograms were created comparing tertiles of energy expenditure (less than 500 kcal/week, 500 to 1999 kcal/week, 2000 or more kcal/week) with tertiles of established risk factors (blood pressure, smoking status, body mass index, family history of early death, and college sports activity). For almost every category the risk was independent and additive, with higher energy expenditures being increasingly protective. These findings were confirmed on multivariate analysis, which showed a 31% higher risk of death in sedentary individuals. Based on these results an estimated added longevity emerged, indicating potential benefit up to age 80 with an energy expenditure of 2000 or more kcal/week. For example, men aged 45 to 54 years of age who began to exercise could expect to live, on average, 10 months longer than their sedentary peers.

To address concerns regarding the fluctuant nature of energy expenditures over time, Paffenbarger examined characteristics that predicted a consistent energy expenditure of less than 1000 kcal/week versus those predicting an expenditure of 2500 or more kcal/week. He found that lack of varsity athletic status, less leisure time spent playing sports, older age, obesity, and cigarette smoking predicted a more sedentary existence.[16]

During 166 410 person-years of follow-up in 2000, there were 2135 CAD events (512 angina pectoris, 576 MI, 207 revascularization, 840 cardiac deaths).[17] An L-shaped curve was noted with decreased risk of CAD with increasing energy expenditure up to 2000 kcal/week, after which the benefit plateaued at 20% lower than baseline. However, for vigorous activity, there was an additional 10% to 20% benefit above 2000 kcal/week. Even for lower energy expenditures (1000 kcal/week) there was benefit in terms of CAD risk; men who expended this level of activity had a lower incremental risk in terms of additional cardiac risk factors.

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Legacy

It is difficult to remember a time when regular exercise was not considered essential to an individual's well-being. The teaching that "some exercise is better than none, while more is better than some"[18] may seem simplistic and obvious today, but it took over 30 years of research before it was accepted. Even today, research continues based on these early principles. For example, this past May marked the publication of the DREW[19] trial, a study of 464 sedentary, postmenopausal, overweight or obese women randomly assigned to one of four different levels of exercise. The researchers demonstrated a dose-response change in fitness across levels of exercise training (0, 4, 8, and 12 kcal/kg per week of energy expenditure as measured by peak absolute oxygen consumption—a finding that confirms and expands upon the early epidemiological associations noted by Paffenbarger and colleagues in the 1970s.

As the current epidemic of obesity, diabetes, and CAD reach staggering proportions, and concerns rise about the health of our children, the focus is again returning to the benefits of exercise. The simple concept of regular aerobic and resistance exercise, as advocated by the newly published 2007 American College of Sports Medicine/American Heart Association (ACSM/AHA) joint recommendation[20,21] (see Table), can have dramatic and cost-effective benefits over a wide range of conditions. For example, regular exercise results in a reduced rate and severity of CAD, a reduction in systolic and diastolic pressure, a decreased risk of stroke, improved lipid profiles, improved insulin sensitivity and glucose handling, a reduction in weight, and lower colon cancer and breast cancer risks as well as beneficial effects on bone mineral density, balance, mood, sleep, and job performance.[22]

While Paffenbarger's early studies showed benefits across all risk groups, including the obese and those with traditional cardiac risk factors, the key finding is that benefit can be derived regardless of age. While the benefits may be more dramatic when a sedentary 45-year-old takes up exercise, like Dr Paffenbarger himself did, benefit can be seen even in 80-year-olds who can improve the quantity and quality of their lives significantly.

If not for the work of Paffenbarger and other early visionaries such as Morris we would not have been able to extol the many benefits of exercise. These early studies shaped governmental regulations, public policy and, even more remarkably, the attitudes of millions of people. Dr Paffenbarger's influence will be felt for years to come.

Competing interests

None declared.

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