

Run for your life ... at a comfortable speed and not too far

James H O'Keefe,^{1,2} Carl J Lavie^{3,4}

During the Greco-Persian War in 490 BCE, Phidippides, a 40-year-old herald messenger (professional running-courier) ran the 26 miles from a battlefield near Marathon, Greece, into Athens carrying momentous news of Greek victory. Upon arriving at the Acropolis, he proclaimed: 'Joy, we have won!' and then immediately collapsed and died.¹ Fast-forward about 2500 years to an era when the baby-boomer's came of age and long-distance running boomed. The prevailing logic held that aerobic exercise is clearly good for one's health and that, if some is good, more must be better. In 1975, Dr Thomas Bassler, a physician/runner, boldly proclaimed that, if you could run a marathon, you were immune to death from coronary heart disease (CHD).² This urban myth has long since been disproven; indeed an emerging body of evidence suggests the opposite: extreme endurance exercise may exact a toll on cardiovascular (CV) health.

'SHOW ME THE BODIES'

After our recent articles on this topic,^{1 3-5} Amby Burfoot, winner of the 1968 Boston Marathon and Editor-at-Large for *Runner's World Magazine*, challenged our assertions about the dangers of extreme endurance efforts by demanding, 'Show me the bodies'. Amby has a good point: the risk of dropping dead in a marathon is remote, about 0.5 to 1 in 100,000 participants.⁶ But the occasional marathoner or triathlete who dies while strenuously exercising is the 'canary in the coal mine'. Chronic extreme exercise appears to cause excessive 'wear-and-tear' on the heart, inducing adverse structural and electrical remodelling, which offsets some of the CV benefits and

longevity improvements conferred by moderate physical activity. Thus, even though chronic extreme exercise may not kill you, it may erase many of the health advantages of regular moderate exercise.

Indeed, regular vigorous exercise is probably the single best step a person can take to ensure robust CV health. In a study of 416 000 adults followed for a mean of 8 years, 40–50 min per day of vigorous exercise reduced risk of death by about 40% (figure 1).⁷ In that study, at about 45 min, a point of diminishing returns is reached whereby longer exercise efforts do not appear to translate into lower death risk. Light to moderate physical activity reduced death rates too, albeit not as strongly, but in this case more physical activity appeared to be better, with no plateau out to 110 min daily. Indeed, if we had a pill that confers all the benefits of exercise, many physicians might be looking for work. Approximately 30–45 min of daily vigorous exercise significantly reduces risks for many maladies including early death, Alzheimer's disease, CHD, diabetes, osteoporosis and depression.^{4 5} Yet, as can be expected with any potent drug, an insufficient dose will not confer the optimal benefits, while an excessive dose can cause harm, and even death in extreme overdoses.

The 'survival of the fittest' concept does not fully apply to the modern world, where it appears that even the moderately fit have an excellent CV prognosis and superb longevity. Studies of CV fitness, as

measured by peak performance on a treadmill, show a curvilinear relationship whereby improvements from unfit to moderately fit confer dramatic reductions in morbidity and mortality (figure 2).⁸ However, fitness levels above 12 metabolic equivalents do not seem to translate into additional gains in CV health and longevity. Thus, if one is training to be able to run at speeds above 7.5 miles per hour, this is being done for some reason other than further improvements in life expectancy.

CV DAMAGE FROM EXCESSIVE EXERCISE

High-intensity exercise sessions lasting beyond 1–2 h cause acute volume overload of the atria and right ventricle (RV), which can bring about overstretching and micro-tears in the myocardium, as evidenced by a transient rise in cardiac biomarkers, including troponin and B-natriuretic peptide and a fall in the RV ejection fraction.⁹ Although within 1 week, these transitory abnormalities usually return to baseline,⁹ after years to decades of excessive exercise and repetitive injury, this pattern can lead to patchy myocardial fibrosis, particularly in the pliable walls of the heart such as the atria and RV, creating a substrate for atrial and potentially malignant ventricular arrhythmias.^{1 3-5} In addition, long-term excessive exercise may accelerate aging in the heart, as evidenced by increased coronary artery calcification, diastolic ventricular dysfunction, and large-artery wall stiffening.^{1 3-5}

At rest, the heart pumps about 5 litres/min; with strenuous aerobic exercise, the cardiac output can rise 5–7-fold, pumping up to 25–35 litres/min. This massive increase in cardiac work is what the heart is designed to do for short bursts, or even for up to as long as 30 or 50 min

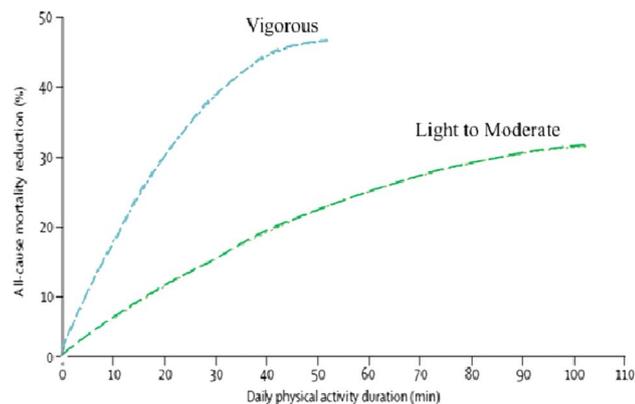


Figure 1 Duration of daily exercise and reduction in long-term all-cause mortality.⁷

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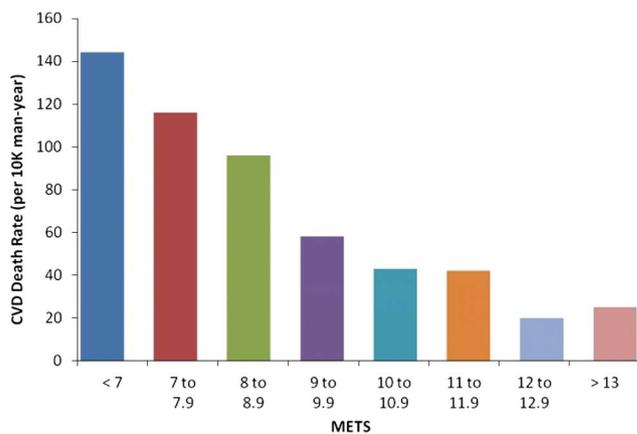


Figure 2 Death rates as a function of cardiovascular fitness as measured by metabolic equivalents achieved on maximal exercise treadmill testing.⁸ CVD, cardiovascular disease.

continuously. However, with protracted efforts, these high volumes can overstretch the chambers, eventually disrupting cardiac muscle fibres and causing micro-tears in the myocardium.¹⁰ The presence of sustained exercise-induced elevations in catecholamines and pro-oxidant free radicals worsen the situation by adding inflammation to the injury, leading eventually to scarring and stiffening of the CV structures.¹⁰

A trial randomised 60 male patients with CHD to vigorous exercise sessions of either 30 or 60 min.¹¹ The 30 min exercise workouts improved arterial elasticity and produced minimal oxidant stress. In contrast, the 60 min sessions increased oxidant stress and worsened vascular stiffness as measured by pulse wave velocity, particularly in those over the age of 50. MRI scans of runners who have been participating in marathons for decades show a threefold increased incidence of scattered fibrosis and scarring in the walls of the atria, interventricular

septum and RV (figure 3).¹² Cardiologists from Minnesota evaluated a group of runners who had completed at least 25 marathons over 25 years and found a 60% increase in coronary plaque burden compared with sedentary age-matched controls.¹ These findings were replicated by a group from Germany, who showed increased coronary plaque in 108 chronic marathoners compared with sedentary controls.¹³ This scarring can set the stage for dangerous heart rhythms, such as atrial fibrillation, which is increased approximately fivefold in veteran endurance athletes.¹⁰ Ventricular tachycardia and sudden cardiac arrest can also be seen in endurance athletes even in the absence of CHD and hypertrophic cardiomyopathy.¹⁵

An enlightening study by Benito *et al* reinforced the concept of cardiac damage from chronic excessive exercise. Mice after being forced to run to exhaustion every day for 4 months showed the same cardiac enlargement, scarring and

predisposition to dangerous ventricular dysrhythmias that have been documented in some veteran extreme endurance athletes.¹⁴ Encouragingly, when the mice were withdrawn from the 'Iron-Mouse' training regimen and allowed to resume normal mouse physical activity levels, their cardiac abnormalities showed marked improvements, even showing regression of myocardial fibrosis and resolution of the tendency toward serious ventricular dysrhythmias.¹⁴

PHIDIPIDES CARDIOMYOPATHY

Born to Run is a non-fiction bestseller book published in 2009 that glamorises ultra-endurance running. The story's hero is Micah True, an American who dropped out of modern civilisation to live and run with the Tarahumara Indians in Mexico. Nicknamed Caballo Blanco, or white horse, for his legendary running endurance, he routinely ran daily distances of 25–100 miles. This March on a 12-mile training run in New Mexico, Micah True dropped dead at age 58. On autopsy, his heart was enlarged and thickened with 'focal areas of interstitial chronic inflammatory infiltrate' in the myocardium; the coronary arteries were 'focally thickened with mild coronary arteriosclerosis'. Chief Medical Investigator Ross Zumwalt, MD summarised the findings as, 'Unclassified cardiomyopathy, which resulted in a cardiac dysrhythmia during exertion'.¹⁵ When considered in the context of True's decades-long lifestyle of daily ultra-marathon running, we suspect that the autopsy findings were an example of 'Phidippides cardiomyopathy'—the constellation of cardiac pathology that has been observed in the hearts of some veteran extreme endurance athletes.¹

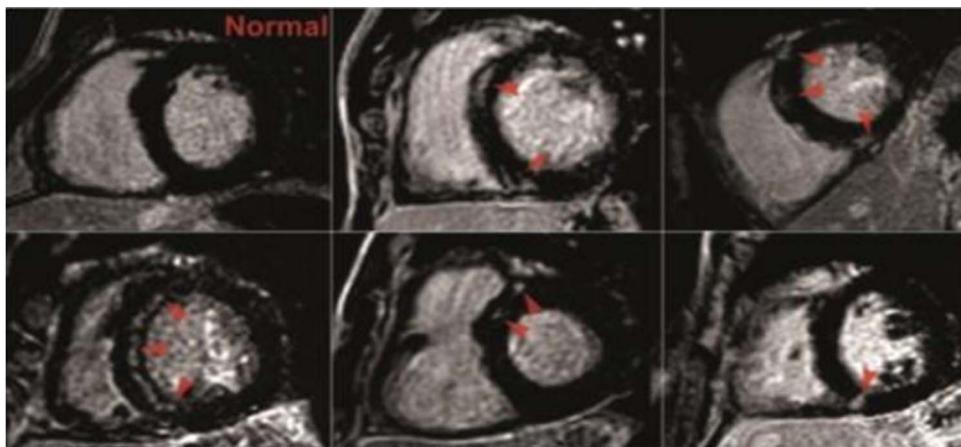


Figure 3 MRI scans showing scattered scarring (red arrows) in the heart, especially in the interventricular septum.¹⁴

MODERATE EXERCISE: THE SWEET-SPOT FOR LONGEVITY

Two very recent studies presented in abstract form at major national meetings may revolutionise our thinking about running and its health effects.^{16 17} One is a prospective observational study that followed 52 600 people for up to three decades.¹⁷ The 14 000 runners in that study had a 19% lower risk of death compared with the 42 000 non-runners. Yet, when they sub-grouped the runners by weekly mileage, those who ran over 20 or 25 miles per week seemed to lose their survival advantage over the non-runners (figure 4). On the other hand, those who ran between 5 and 20 miles total per week enjoyed a 25% decrease in risk of death during follow-up. The same pattern emerged for speed of running: the fast runners, those running typically over 8 miles an hour, appeared to get no mortality benefit compared with the non-runners, whereas those who fared best usually ran about 6–7 miles per hour—a comfortable jog for most people. In addition, the individuals who ran 6 or 7 days per week appeared to lose the mortality benefits, whereas the survival advantages accrued best for those who ran 2–5 days per week.¹⁶

The Copenhagen City Heart Study showed remarkably similar results. After following 20 000 Danes since 1976, they found that the joggers lived about 6 years longer than the non-runners, with a 44% lower risk of death during the study.¹⁷ Intriguingly, those who did best were the people who jogged at a slow to average pace, for one to 2.5 h per week total, accumulated during two or three sessions. According to Dr Peter Schnohr, the study's director, 'The relationship appears much like alcohol intakes—mortality is lower in people reporting moderate jogging than in non-joggers or those undertaking extreme levels of exercise'.¹⁷

THE U-CURVE

Hippocrates, the father of medicine and a contemporary of Phidippides in ancient Greece, taught, 'The right amount of nourishment and exercise, not too much, not too little, is the safest way to health'.¹ If you listen to your body, this is just common sense. Yet, nothing we have published previously has stirred so much controversy, especially among the general public. Increasingly our culture is one of extremes: during the past 30 years, obesity has tripled in the USA and has increased in much of the Western World, while during the same time the number of people completing a marathon has risen 20-fold. On one side of the U-curve, the couch loungers/channel surfers embrace this message as justification for continuing their sedentary lifestyle. And, on the far end of the U-curve, the extreme exercise aficionados want to ignore the message and instead kill the messenger. As with many things in life, the safe and comfortable zone at the bottom of the U curve—moderate exercise—is the 'sweet spot' for which most should try to aim.

Sitting is the new smoking; a sedentary lifestyle will cause disability and disease, and will shorten life expectancy. We are not so much born to run as born to walk. Ethnographic research indicates that, in the environment of human evolution, our ancient ancestors walked 4–10 miles a day.⁴ Walking is superior to running for mechanical efficiency and musculoskeletal durability. Indeed, we advise our patients that they can walk or garden hours a day without concern about CV overuse injury.

So while it is true that exercise confers powerful health benefits, the common belief that more is better is clearly not true. The unique and potent benefits of exercise are best bestowed by moderate exercise and physical activity. The exercise patterns for maximising CV fitness/

peak aerobic capacity are very different from those that best confer CV health, durability and overall longevity. So, if one's goal in life is to compete in the marathon or triathlon of the Rio Olympics in 2016, this will certainly require high-intensity exercise for hours a day. But, for those whose goal is to be alive and well while watching the 2052 Olympics from the stands, then exercise and physical activity at lower intensities and durations would be more ideal.

CONCLUSION

The take home message for most is to limit one's vigorous exercise to 30–50 min/day. If one really wants to do a marathon or full-distance triathlon etc, it may be best to do just one or a few and then proceed to safer and healthier exercise patterns. On the other hand, light or moderate intensity exercise does not present the dose-dependent risks associated with excessive endurance exercise. A routine of moderate physical activity will add life to your years, as well as years to your life. In contrast, running too fast, too far, and for too many years may speed one's progress towards the finish line of life.

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Competing interests None.

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Author note A video presentation on this topic is available on the internet: You Tube, TEDx Talk, James O'Keefe, Run for your life... at a comfortable pace and not too far.

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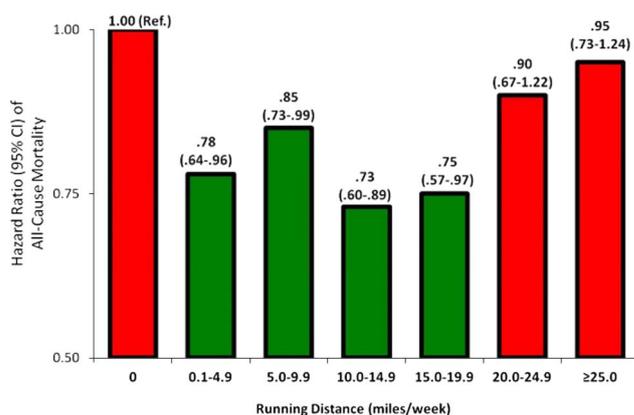


Figure 4 All-cause mortality by running distance per week.¹⁶

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