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The risk-benefit paradox of exercise

While vigorous exercise can transiently increase the short-term risk for an adverse cardiac event, relatively small amounts of exercise can markedly reduce the long-term risk for chronic disease and premature mortality.

ABSTRACT: A risk-benefit paradox applies when considering how much exercise is needed for good health. Vigorous exercise can transiently increase the short-term risk for an adverse event (such as a myocardial infarction or sudden cardiac death); however, participation in routine exercise can also markedly reduce the long-term risk for premature mortality and is an effective primary and secondary preventive measure for more than 25 chronic medical conditions. Active individuals often exhibit risk reductions of 50% or more for mortality and morbidity. An exercise dose-response relationship exists; with the greatest benefits seen when previously inactive individuals become more active. There may, however, be an attenuation of benefit at the extreme end of the exercise continuum (e.g., for ultra-endurance events). Prolonged strenuous exercise training or events have been associated with various risks, including sudden cardiac death, atrial and ventricular arrhythmias, and pathological remodeling of the myocardium. The optimum and minimum amounts of physical activity/exercise needed to achieve health benefits are disputed. Inactive individuals may be discouraged by recommendations for an amount of activity that seems unachievable and is greater than what is required for clinically relevant health benefits, while endurance athletes often exercise at levels and intensities well beyond what is needed to achieve health benefits. Current physical activity guidelines have been widely criticized because they do not include varied types and amounts of activities to address the diverse needs of society. There is strong evidence to support the need for individualized exercise prescriptions for patients, including varied recommendations for improving health-related physical fitness and functional status. Despite the risk-benefit paradox, it is clear that the health benefits of physical activity far outweigh the risks, and virtually everyone can benefit from becoming more physically active.

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The health benefits of physical activity have been documented since ancient times, beginning more than 2000 years ago when Hippocrates highlighted the importance of active living.[1] Today irrefutable evidence indicates that habitual physical activity reduces premature mortality and is an effective primary and secondary prevention measure for more than 25 chronic medical conditions, including cardiovascular disease (CVD).[2-4] Moreover, various studies of former athletes have demonstrated reduced mortality rates and prevalence of chronic disease, including diabetes, cancer, and hypertension.[5-8] However,

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there is also evidence of sudden cardiac death (SCD) and advanced CVD occurring in athletes and former athletes, and risks are associated with both vigorous physical activity and prolonged strenuous activity.

In evaluating the literature, a risk-benefit paradox is revealed when the effects of physical activity on health are considered. Exercise appears to increase the short-term risk of CVD and SCD while simultaneously reducing the long-term risk for adverse events. This paradox can be better understood by examining the dose-response relationship between physical activity and health, by reviewing the risks associated with exercise, and by considering how physical activity guidelines might better reflect evidence-based best practice.

Health benefits of routine physical activity

Active adults have a 20% to 35% reduced risk of premature mortality and various other chronic medical conditions.[2-4] Even greater risk reductions for all-cause mortality and chronic disease (e.g., 50%) are often observed when objective measures of fitness are taken[9] (see **Table 1**). There is clear evidence that health-related physical fitness is a better predictor of the risk for chronic disease than physical activity level,[10-13] emphasizing the importance of assessing health-related physical fitness directly.[9]

At least 25 chronic medical conditions are thought to be related to physical inactivity.[2-4] The World Health Organization has estimated that physical inactivity is the fourth leading risk factor for global mortality, accounting for approximately 3.2 million deaths.[14] Virtually everyone can benefit from engaging in routine physical activity.[15,16] Awareness of this has led to marked changes in risk stratification strategies that reduce the barriers to physical activity participation, such as the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+)[17-19] and physical activity programming for a wide range of clientele, including those living with chronic medical conditions. Exercise is considered an essential medicine for the primary and secondary prevention of numerous chronic conditions. Ensuring that society members can benefit from routine physical activity is an important public health policy objective. However, as with prescribing any medicine, it is important to provide an appropriate and individualized dosage for each person.

The dose-response relationship

As already discussed in this theme issue, there is a clear dose-response relationship between physical activity and chronic disease and premature mortality,[4,9] with diminishing returns in health benefits seen at higher volumes of physical activity and the greatest changes in health status seen when physically inactive individuals become more physically active (see **Figure 1**). Importantly, relatively

Table 1. Relative risk reduction observed when comparing active/fit and inactive/unfit subjects.

All-cause mortality	• 31% risk reduction • 45% risk reduction when aerobic fitness is assessed
Cardiovascular disease	• 33% risk reduction • 50% or greater risk reduction when aerobic fitness is assessed
Stroke	• 31% risk reduction • 60% or greater risk reduction when aerobic fitness is assessed
Hypertension	• 32% risk reduction • 50% or greater risk reduction when aerobic fitness is assessed
Colon cancer	• 30% risk reduction
Breast cancer	• 20% risk reduction
Type 2 diabetes	• 40% risk reduction • 50% or greater risk reduction when aerobic fitness is assessed
Osteoporosis	• Bone adaptations to exercise are load dependent and site specific • Routine physical activity is associated with improved bone health

Sources: Warburton DE, Charlesworth S, Ivey A, et al.[4] and Warburton DER[9]

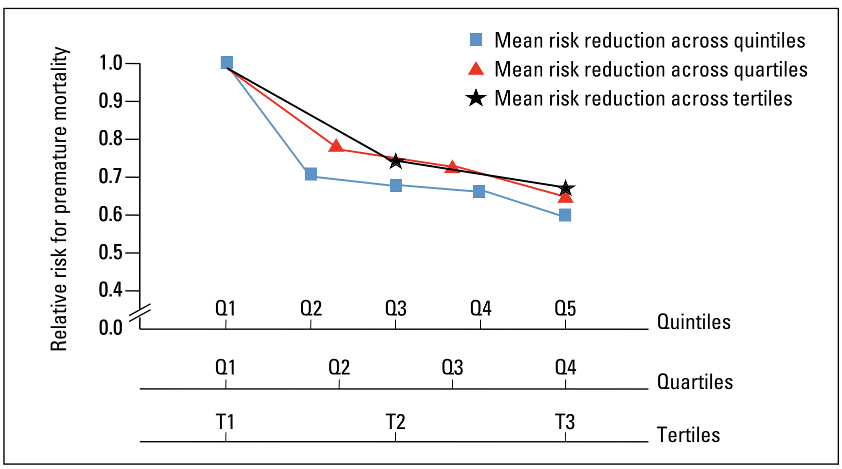

Figure 1. Mean relative risk reduction in all-cause mortality across physical fitness categories.

Data compiled from studies involving over 1.5 million participants.[4] Studies were grouped according to those that reported relative risk reductions in tertiles, quartiles, and quintiles.
Reproduced from Warburton DER[9] and used with permission.

minor increases in physical activity and fitness in previously inactive individuals will lead to marked reductions in the risk for chronic disease and premature mortality.[9] This appears to be particularly true for those living at the lower end of the fitness continuum, such as the frail elderly and those with chronic medical conditions. Unfortunately, this evidence-based information is frequently left out of physical activity messages, creating a barrier for the adoption and maintenance of routine physical activity for many individuals.[20] For instance, in Canada an unfortunate outcome of updates to physical activity guidelines has been the clear statement that you need 150 minutes of moderate-intensity weekly physical activity or 75 minutes of vigorous-intensity activity to achieve health benefits. This message has been promoted widely through various media campaigns, and findings from our research group, the Physical Activity Promotion and Chronic Disease Prevention Unit, are often cited to support this claim.[4,21] Unfortunately, this bold declaration is not evidence-based. Systematic reviews and randomized controlled trials from our research group demonstrate clearly that health benefits are achieved at much lower volumes and intensities of exercise.[4,22] This is also supported by a recent meta-analysis[23] that examined the effects of different exercise intensities on all-cause mortality and found a clear dose-response relationship, with previously inactive participants benefiting greatly from light to moderate exercise intensities. Importantly, there was only a minor additional mortality reduction with a further increase in the activity level and intensity. A recent study by Lee and colleagues[24] also demonstrated that running even once or twice a week for a total running time of less than 51 minutes and at a speed of less than 6 miles per hour led to a significant reduction in the risk of premature mortality.

Physical activity guidelines

Completing 150 minutes of moderate-intensity physical activity weekly can seem unachievable for many unaccustomed to exercise. Qualified exercise professionals are aware of this and seldom use generic physical activity guidelines when prescribing to their clients.[20,25] Evidence indicates that a volume of activity less than half of what is currently recommended by most international guidelines is sufficient for clinically relevant health benefits.[9] It is important for clinicians and practitioners to provide their patients and clients with individualized exercise prescriptions to increase the likelihood of adherence. The arbitrary application of generic physical activity guidelines is not effective evidence-based best practice.[20] In fact, criticism has recently been leveled at the generic nature of many current physical activity guidelines, which fail to include varied types of activities and amounts of exercise sufficient for marked health benefits.[26,27] It now appears that generic guidelines cannot address the diverse needs of society members, particularly those living with or at increased risk for developing chronic medical conditions. Accordingly, in our most recent development of clinical exercise prescriptions for prominent medical conditions such as atrial fibrillation,[28] we have ensured that the exercise prescriptions can be individualized for each client, and we have included diverse recommendations related to aerobic and musculoskeletal fitness and functional status.[29,30]

As well as taking an individualized approach, it is important to acknowledge that health status is multifaceted and not related to life expectancy alone. According to the pioneering work of Bouchard and Shephard,[31] at least five aspects need to be considered in the evaluation of health status:

- Genetics.
- Biochemical, physiological, and morphological conditions that determine the onset of illness, disease, impairment, and disability.
- Functional well-being.
- Psychological well-being associated with mood and cognitive processes.
- Health potential relating to longevity and functional potential.

When evaluated in isolation, life expectancy does not take into account the many components of health, including the number of years a person may live in a diseased or dependent state.[9,13] Various agencies have recognized the importance of quality of life and functional well-being by proposing new criteria to determine the number of years a person might live in a healthy state. For instance, the World Health Organization introduced the health-adjusted life expectancy (HALE) scale that takes into account the anticipated years of ill health to provide an estimate of years of healthy living.[9] Previously, we have used the term "healthy lifespan approach"[13] to highlight the importance of remaining healthy across the lifespan and focusing on quality of life.[9] It is clear that routine physical activity not only can prolong life,[32] it can also increase quality of life and delay the onset of chronic disease and disability. Ultimately, physical activity can effectively increase the number of years that a person lives in a healthy, nondependent state.[9,13] For active individuals, if disability occurs it often occurs for a short period of time near the end of life.[33] This is particularly important as we consider the impact of aging populations in developed nations.[9]

When discussing the health benefits of routine physical activity it is also prudent to recognize that multiple dose-response relationships exist, depending upon the endpoint.[9] This means the relationship between health status and physical activity can differ based on the endpoint being evaluated (e.g., blood pressure control, glucose homeostasis, functional status). This concept was originally proposed by Drs Norman Gledhill and Veronica Jamnik at York University and then subsequently incorporated into their landmark health-related physical fitness assessment battery (see Figure 2).[34] The pioneering theories of Drs Gledhill and Jamnik have since been supported by various studies demonstrating distinct, graded dose-response relationships for various clinical endpoints, for individual chronic medical conditions, and for premature mortality. Considerable research is still required to determine the optimal dosage for each medical condition and primary endpoint,[9] making it all the more important to avoid the arbitrary application of generic physical activity guidelines in clinical practice.

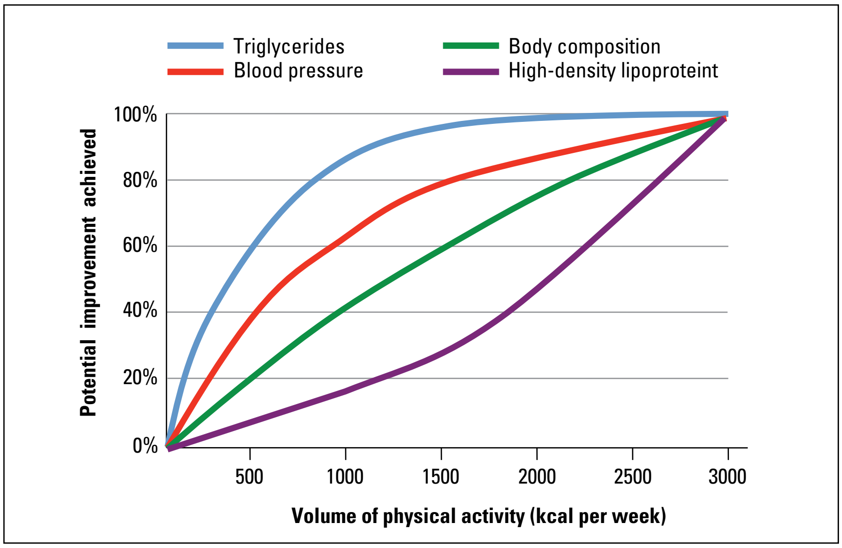

Figure 2. Theoretical relationship between physical activity and various determinants of health status as proposed by Drs Gledhill and Jamnik.

The temporal relationship between physical activity may vary according to the endpoint, meaning that some endpoints require significantly greater changes in physical activity before marked improvements are seen. Adapted from Gledhill N, Jamnik V[34] and used with permission.

Musculoskeletal fitness and health status

Most evidence for the effect of routine physical activity on health status is from studies of aerobic or endurance-type activities, and most current generic physical activity guidelines include only limited evidence-based advice regarding musculoskeletal fitness, even though musculoskeletal fitness is an important component of health-related physical fitness.[9]

There is a very strong body of evidence demonstrating the health benefits of physical activities that enhance musculoskeletal fitness, which encompasses muscular strength, muscular endurance, muscular power, flexibility, and back fitness.[3,35,36] Marked improvements in health status, particularly functional status in the elderly and in those living with chronic medical conditions, can occur with changes in musculoskeletal fitness in the absence of changes in aerobic fitness.[9] Leading experts in the exercise sciences and medicine have recognized a paradigm shift toward promoting the health benefits of physical activities that tax the musculoskeletal system.[3]

Canadian researchers are playing a leading role in establishing the close relationship between musculoskeletal fitness and health status.[35-40] A lack of musculoskeletal fitness is a significant predictor of weight gain over a 20-year period,[39] poor quality of life,[40] premature mortality,[38] and various other chronic medical conditions.[35,36] Enhanced musculoskeletal fitness is associated positively with functional status, glucose homeostasis, bone health, mobility, psychological well-being, and overall quality of life, and negatively associated with fall risk, morbidity, and premature mortality.[35,36] Moreover, exercise-training interventions that enhance musculoskeletal fitness have a positive effect on health status, especially in individuals with a low musculoskeletal fitness reserve.[3,4] High levels of musculoskeletal fitness appear to be very important for elderly or frail individuals particularly and contribute to the maintenance of functional independence.[3,35,36,41] Many activities of daily living do not require a significant aerobic output, but do require a level of musculoskeletal fitness.[35,36] Collectively, this research supports recommending daily activities that tax the musculoskeletal system to improve health status and reduce the risk for chronic disease, disability, and premature mortality.[4]

Change in physical fitness and health status

Changes in activity levels and physical fitness over the lifespan are highly predictive of risk for premature mortality and chronic disease.[3] Several studies have demonstrated that an increase in aerobic fitness will lead to a reduction in the risk, whereas a decrease in aerobic fitness will increase the risk.[3,42-45] The largest changes appear to be in the least active individuals who become more physically fit. For instance, Blair and colleagues reported that previously inactive individuals who improved enough over a 5-year period to move from the unfit to the fit category had a 44% reduction in risk for premature mortality compared with individuals who remained unfit.[44] Similarly, Erikssen and colleagues revealed a graded reduction in the risk for premature mortality with improvements in physical fitness (see **Figure 3**).[42,43] Individuals who had a high aerobic fitness level at baseline and maintained or improved their fitness levels were at the lowest risk.[43,44]

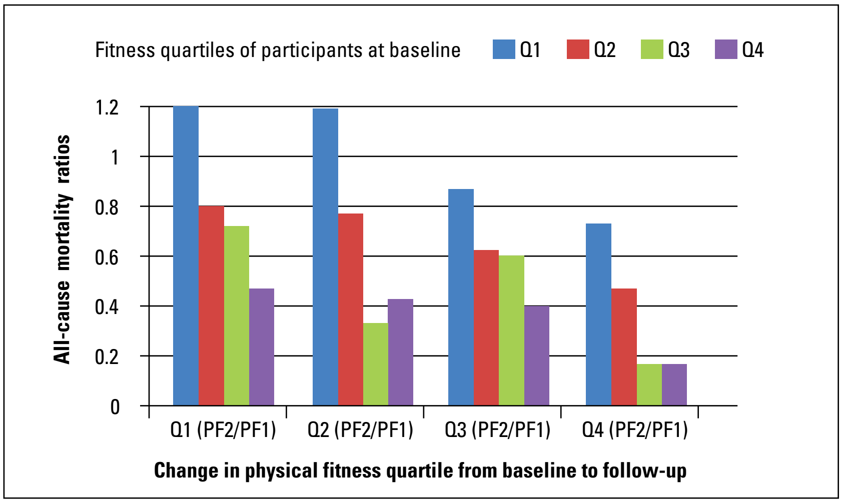

Figure 3. The relationship between changes in aerobic physical fitness (PF) and mortality over time.

Physical fitness of participants in a study by Erikssen G, Liestol K, Bjornholt J, et al.[43] were evaluated at baseline (PF1) and again 13 years later (PF2). The ratio of PF2/PF1 × 100 was calculated to evaluate changes in fitness over the study period compared with fitness level at baseline. Data for participants were then grouped according to fitness quartiles (Q1 = least fit, Q4 = most fit) for the baseline evaluation and again into quartiles for change in fitness from baseline to 13-year follow-up (Q1 PF2/PF1 = least change, Q4 PF2/PF1 = most change).
Reproduced from Warburton DER[9] and used with permission.

Table 2. Cases of sudden cardiac death in athletes.

- Pheidippides (age 40 years; 490 BC): Legendary runner
- Jim Fixx (age 52; 1984): Marathon runner
- Pete Maravich (age 40; 1988): Former professional basketball player
- Hank Gathers (age 23; 1990): College basketball player
- Reggie Lewis (age 27; 1993): Professional basketball player
- Sergei Grinkov (age 28; 1995): Olympic figure skater
- Jeron Lewis (age 21; 2010): College basketball player
- Micah True (age 58; 2012): Ultra-endurance runner
- Piermario Morosini (age 25; 2012): Soccer player
- Alexander Dale Oen (age 26; 2012): World champion swimmer
- Paul Reynolds (age 52; 2015): Triathlon competitor

Health risks of physical activity

The death of Pheidippides in 490 BC may be the first widely reported case of exercise-related sudden cardiac death (see **Table 2**). Legend holds that Pheidippides, a 40-year-old Athenian herald during the Greco-Persian War, ran 150 miles in 2 days to seek help from Sparta when the Persians landed at Marathon. The next day he ran 26 miles from Marathon to Athens to report that the Persians had been defeated, only to die suddenly after announcing the victory. The distance (42 km) and name of the modern-day Olympic endurance event were inspired by the story of Pheidippides, whether true or not.

A less legendary case of myocardial infarction during a marathon was presented in the *Annals of Internal Medicine* in 1976.[46] This case involved a 44-year-old male competing in the 1973 Boston Marathon. The autopsy revealed myocardial scarring with normal coronary vessels, leading the authors describing the case to state that "Advocates of long-distance running for prevention of, or rehabilitation from, ischemic heart disease should be aware of this possible complication."[46]

Sudden cardiac death incidence

Cases of sudden cardiac death in young and former athletes are tragic events that have a significant impact upon families and society as a whole. There have been several cases of SCD in highly trained athletes from diverse sporting disciplines. However, the actual risks associated with exercise participation are often poorly understood.

Despite the clear evidence regarding the long-term health benefits of physical activity, a compelling body of research also indicates that exercise transiently increases acute risk for myocardial infarction and SCD. As such, a risk-benefit paradox exists, whereby participation in physical activity increases the short-term risk for adverse events, while simultaneously reducing the long-term risk. Approximately 4% to 10% of myocardial infarction cases occur within 1 hour of vigorous exercise,[47] and approximately 6% to 17% of all SCD cases in men are associated with acute physical exertion.[48,49]

The absolute risk of an adverse exercise-related event appears to be quite low in men and even lower in women.[48,50] For instance, Albert and colleagues[48] revealed 1 excess sudden cardiac death per 1.51 million sudden cardiac death per 36.5 million hours of exertion in women. Collectively, this research indicates that the occurrence of life-threatening cardiovascular events is extremely rare in healthy individuals, including athletes. Traditional contemporary cardiac rehabilitation programs[51] also support these findings. Thompson and colleagues[51] estimated 1 cardiac arrest per 116 906 patient-hours, 1 myocardial infarction per 219 970 patient-hours, 1 fatality per 752 365 patient-hours, and 1 major complication per 81 670 patient-hours of participation in current exercise-based cardiac rehabilitation programs.

Risks associated with vigorous physical activity

According to Franklin and Billecke,[52] an estimated 7 million Americans receive medical attention for sports- and recreation-related injuries each year. The majority of these injuries are musculoskeletal in nature (e.g., strains, sprains, fractures);[52] however, of particular concern are the life-threatening events associated with vigorous exertion that can occur in susceptible individuals (e.g., sudden cardiac arrest, myocardial infarction).[51]

Vigorous exercise is classically defined as an absolute work rate of 6 METs (metabolic equivalent tasks) or more.[2,3,51] Vigorous aerobic exercise has been quantified as an oxygen uptake of approximately 21 mL per kg per minute,[51] and incudes activities such as jogging and swimming.[2,3] Most research in the field has evaluated the risks associated with vigorous aerobic exercise by considering a theoretical absolute exercise work rate of 6 METs or higher. However, the relative intensity of exercise is likely a better indicator of the risks associated with higher intensity exercise. As previously outlined,[2] 6 METs may be very easy, light-intensity exercise for an aerobically fit individual but above maximal for a deconditioned person or someone living with a chronic medical condition. In relative terms, vigorous effort can be quantified as 60% to 84% of heart rate reserve or 77% to 93% of heart rate maximum.[2,3] It is clear that the myocardial oxygen demands of exercise are more related to the relative intensity than to an arbitrary intensity such as 6 METs.[51] As such, the risks for exercise-related adverse events are likely to occur at much lower absolute work rates in unfit, elderly, or chronically ill individuals.

The transient risk for myocardial infarction and SCD with vigorous aerobic exercise participation has been demonstrated in several studies. This research has consistently shown that individuals are at greater risk for an adverse event during vigorous exercise than they are when engaged in less vigorous exercise or when not exerting themselves.[51] The risk for adverse exercise-related events is also markedly higher in individuals who are unaccustomed to vigorous physical exertion or who have underlying CVD.[51-53] Leading authorities have estimated that there is a 2-fold to 56-fold risk for exercise-related cardiac events in inactive individuals.[54] However, participation in habitual physical activity (particularly vigorous activities) decreases this risk markedly.[48-50,55-57] For instance, in a landmark study, Mittleman and colleagues[55] demonstrated that those not accustomed to vigorous exercise had a greater than 100-fold increased risk for a myocardial infarction. However, with higher levels of physical activity participation the risk decreased in a graded fashion to approximately 2.4-fold in individuals who exercised five or more times per week. Therefore, the likelihood of having an exercise-related myocardial infarction was 50 times higher in inactive individuals than it was in those who exercised five or more times per week. Simply exercising once or twice a week reduced the risk by more than 80%. A recent meta-analysis[58] supported this early work indicating that episodic physical activity was associated with an increased risk of SCD and myocardial infarction, with habitual physical activity attenuating this risk in a dose-dependent fashion. Importantly, the authors demonstrated that the relative risk for a myocardial infarction decreased by 45% and for SCD decreased by 30% for every additional time per week that a person engaged in physical activity, meaning that the most active had the lowest risk.

Risks associated with prolonged strenuous exercise

There appears to be an optimal amount of physical activity for health benefits, above which the law of diminishing returns applies.[3,4,13,23,59] Many current physical activity guidelines recommend 150 minutes of moderate-intensity to vigorous-intensity physical activity per week and state that "more is better." However, both messages are misleading and are no longer supported strongly by the literature. As outlined above and elsewhere in this theme issue,[9,18] a small change in physical activity and fitness can lead to a significant improvement in health status,[24] while there may be a potential attenuation of benefit (and even increased risk) at the higher end of the exercise range.

Highly trained elite endurance athletes are seldom included in large epidemiological studies comparing health outcomes to physical activity levels. However, research examining the upper end of the exercise range has demonstrated the attenuation in the health benefits and the possibility of increased risk in extremely active individuals. These individuals exercise at levels and intensities that are well beyond international recommendations for health. For instance, ultra-endurance athletes commonly engage in daily vigorous exercise ranging from 90 to 300 minutes (1.5 to 5 hours). This is equal to 630 to 2100 minutes of vigorous-intensity exercise a week, which is 5 to 10 times more than most recommendations for physical activity.

Highly trained endurance athletes exercising at this extreme may be at an increased risk for developing atrial and ventricular arrhythmias, pathological remodeling (particularly of the right side of the heart), CVD, and SCD.[60-63] Researchers have increasingly acknowledged the potential risks with exercising "too much" and with "too little recovery time." For instance, Patil and colleagues[64] argued that "Humans are not genetically adapted for protracted, sustained, and extreme aerobic exercise efforts." As a result, those engaging in chronic (and arguably excessive) endurance exercise may be susceptible to cardiovascular damage. Evidence from animal models also supports the potential for prolonged strenuous exercise training to lead to adverse cardiovascular complications. For instance, Benito and colleagues[65] exercised rats strenuously for 60 minutes a day for 16 weeks (equivalent to 10 years of daily running) and found a series of cardiovascular maladaptations such as right ventricular and left ventricular hypertrophy, diastolic dysfunction, bi-atrial dilatation, increased collagen deposition and fibrosis in the right ventricle and both atria, and increased susceptibility to atrial and ventricular arrhythmias. These changes appeared to be reversed after an 8-week rest period. Similar findings were reported recently in humans engaged in prolonged endurance events and training. For instance, La Gerche and colleagues[66] examined 40 athletes before and after endurance events lasting 3 to11 hours, including the marathon, endurance triathlon, alpine cycling, and ultra-endurance triathlon. The authors observed the greatest reduction in right ventricular function in athletes with the highest volume of activity. They also found delayed gadolinium enhancement (a marker of fibrosis) in the interventricular septum, particularly in those with the greater exercise volume. Collectively, this research indicates that individuals participating in repeat ultra-endurance events with little time for recovery appear to be at an increased risk for the development of fibrosis, arrhythmias, adverse ventricular remodeling, and CVD.

Conclusions

When considering the effects of exercise on health, a risk-benefit paradox applies. Exercise, particularly vigorous-intensity activity, transiently increases the short-term risk for an adverse event such as a myocardial infarction and SCD, while markedly reducing the long-term risk for premature mortality and chronic medical conditions. The evidence indicates that the health benefits of routine physical activity far outweigh the acute risks. In fact, the acute risk decreases with increasing levels of physical activity, such that the highly active individuals appear to have the lowest risk (2-fold to 5-fold). Those unaccustomed to vigorous activity or with underlying CVD appear to be at the greatest risk (50-fold to 100-fold). Moreover, there is a clear dose-response relationship between health and habitual physical activity, and more active individuals have a markedly lower risk (approximately 50%) for premature mortality and chronic disease. Very small changes in physical activity can lead to marked health benefits in inactive and deconditioned individuals.

Importantly, far less physical exercise than currently recommended in many physical activity guidelines can lead to clinically relevant changes in health status. The dose-response relationship between physical activity and health is similar to the relationship seen with other medicines, where an attenuation of benefit is found at the extreme end of the physical activity range. As such, the axiom that "more exercise is better" may not apply. In fact, individuals training for ultra-endurance events and leaving little time for recovery between events appear to be at an increased risk for the development of CVD and should be cautioned about the perils involved.

Competing interests

None declared.

References

1. Paffenbarger RS Jr, Blair SN, Lee IM. A history of physical activity, cardiovascular health and longevity: The scientific contributions of Jeremy N Morris, DSc, DPH, FRCP. Int J Epidemiol 2001;30:1184-1192.
2. Warburton DE, Nicol C, Bredin SS. Prescribing exercise as preventive therapy.

CMAJ 2006;174:961-974.

3. Warburton DE, Nicol C, Bredin SS. Health benefits of physical activity: The evidence. CMAJ 2006;174:801-809.
4. Warburton DE, Charlesworth S, Ivey A, et al. A systematic review of the evidence for Canada's Physical Activity Guidelines for Adults. Int J Behav Nutr Phys Act 2010;7:39.
5. Reimers CD, Knapp G, Reimers AK. Does physical activity increase life expectancy? A review of the literature. J Aging Res 2012;2012:243958.
6. Hernelahti M, Kujala UM, Kaprio J, et al. Long-term vigorous training in young adulthood and later physical activity as predictors of hypertension in middle-aged and older men. Int J Sports Med 2002; 23:178-182.
7. Sarna S, Kaprio J, Kujala UM, et al. Health status of former elite athletes. The Finnish experience. Aging (Milano) 1997;9:35-41.
8. Sanchis-Gomar F, Olaso-Gonzalez G, Corella D, et al. Increased average longevity among the "Tour de France" cyclists. Int J Sports Med 2011;32:644-647.
9. Warburton DER. The health benefits of physical activity: A brief review. In: Warburton DER (ed). Health-related exercise prescription for the qualified exercise professional. 5th ed. Vancouver: Health & Fitness Society of BC; 2015:1-17.
10. Blair SN, Cheng Y, Holder JS. Is physical activity or physical fitness more important in defining health benefits? Med Sci Sports Exerc 2001;33:S379-399; discussion S419-320.
11. Myers J, Kaykha A, George S, et al. Fitness versus physical activity patterns in predicting mortality in men. Am J Med 2004;117:912-918.
12. Williams PT. Physical fitness and activity as separate heart disease risk factors: A meta-analysis. Med Sci Sports Exerc 2001;33:754-761.
13. Warburton DER, Katzmarzyk PT, Rhodes RE, et al. Evidence-informed physical activity guidelines for Canadian adults. Can J Public Health 2007;98(suppl 2):S16-S68.
14. World Health Organization. Global recommendations on physical activity for health. Geneva: World Health Organization; 2010:58.
15. Warburton DER, Gledhill N, Jamnik VK, et al. Evidence-based risk assessment and recommendations for physical activity clearance: Consensus document 2011. Appl Physiol Nutr Metab 2011;36:S266-S298.
16. Warburton DER, Gledhill N, Jamnik VK, et al. The Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and electronic Physical Activity Readiness Medical Examination (ePARmed-X+): Summary of consensus panel recommendations. Health Fitness J Can 2011;4:26-37.
17. Warburton DER, Jamnik VK, Bredin SSD, et al. The Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and electronic Physical Activity Readiness Medical Examination (ePARmed-X+). Health Fitness J Can 2011;4:3-23.
18. Bredin SSD, Jamnik V, Gledhill N, et al. Effective pre-participation screening and risk stratification. In: Warburton DER (ed). Health-related exercise prescription for the qualified exercise professional. 5th ed. Vancouver: Health & Fitness Society of BC; 2015:1-30.
19. Warburton DER, Bredin SSD, Jamnik V, et al. Consensus on evidence-based preparticipation screening and risk stratification. Ann Rev Gerontol Geriatr 2016:53-102.
20. Bredin SS, Warburton DE. Physical activity line: Effective knowledge translation of evidence-based best practice in the real-world setting. Can Fam Physician 2013; 59:967-968.
21. Paterson DH, Warburton DE. Physical activity and functional limitations in older adults: A systematic review related to Canada's Physical Activity Guidelines. Int J Behav Nutr Phys Act 2010;7:38.
22. Foulds HJ, Bredin SS, Charlesworth SA, et al. Exercise volume and intensity: A dose-response relationship with health benefits. Eur J Appl Physiol 2014;114: 1563-1571.
23. Lollgen H, Bockenhoff A, Knapp G. Physical activity and all-cause mortality: An updated meta-analysis with different intensity categories. Int J Sports Med 2009; 30:213-224.
24. Lee DC, Pate RR, Lavie CJ, et al. Leisure-time running reduces all-cause and cardiovascular mortality risk. J Am Coll Cardiol 2014;64:472-481.
25. Bredin SS, Gledhill N, Jamnik VK, et al. PAR-Q+ and ePARmed-X+: New risk stratification and physical activity clearance strategy for physicians and patients alike. Can Fam Physician 2013;59:273-277.
26. Jung ME, Bourne JE, Little JP. Where does HIT fit? An examination of the affective response to high-intensity intervals in comparison to continuous moderate- and continuous vigorous-intensity exercise in the exercise intensity-affect continuum. PLoS One 2014;9:e114541.
27. Jung ME, Bourne JE, Beauchamp MR, et al. High-intensity interval training as an efficacious alternative to moderate-intensity continuous training for adults with prediabetes. J Diabetes Res 2015;2015: 191595.
28. Warburton DER, Bredin SSD, Giacomantonio N. Clinical exercise prescription for atrial fibrillation. Vancouver, BC: International Collaboration on Clinical Exercise Prescription; 2012.
29. Giacomantonio NB, Bredin SS, Foulds HJ, et al. A systematic review of the health benefits of exercise rehabilitation in persons living with atrial fibrillation. Can J Cardiol 2013;29:483-491.
30. Bredin SSD, Warburton DER, Lang DJ. The health benefits and challenges of exercise training in persons living with schizophrenia: A pilot study. Brain Sci 2013;3:821-848.
31. Bouchard C, Shephard RJ. Physical activity fitness and health: The model and key concepts. In: Bouchard C, Shephard RJ, Stephens T (eds). Physical activity fitness and health: International proceedings and consensus statement. Champaign, IL: Human Kinetics; 1994:77-88.
32. Lee IM, Paffenbarger RS Jr, Hennekens CH. Physical activity, physical fitness and

longevity. Aging (Milano) 1997;9:2-11.
33. Powell KE, Blair SN. The public health burdens of sedentary living habits: Theoretical but realistic estimates. Med Sci Sports Exerc 1994;26:851-856.
34. Gledhill N, Jamnik V. Canadian physical activity, fitness and lifestyle approach 3rd ed. Ottawa: Canadian Society for Exercise Physiology; 2003.
35. Warburton DE, Gledhill N, Quinney A. Musculoskeletal fitness and health. Can J Appl Physiol 2001;26:217-237.
36. Warburton DE, Gledhill N, Quinney A. The effects of changes in musculoskeletal fitness on health. Can J Appl Physiol 2001;26:161-216.
37. Katzmarzyk PT, Craig CL, Gauvin L. Adiposity, physical fitness and incident diabetes: The physical activity longitudinal study. Diabetologia 2007;50:538-544.
38. Katzmarzyk PT, Craig CL. Musculoskeletal fitness and risk of mortality. Med Sci Sports Exerc 2002;34:740-744.
39. Mason C, Brien SE, Craig CL, et al. Musculoskeletal fitness and weight gain in Canada. Med Sci Sports Exerc 2007;39: 38-43.
40. Payne N, Gledhill N, Katzmarzyk PT, et al. Health implications of musculoskeletal fitness. Can J Appl Physiol 2000;25:114-126.
41. American College of Sports Medicine. Position stand: Exercise and physical activity for older adults. Med Sci Sports Exerc 1998;30:992-1008.
42. Erikssen G. Physical fitness and changes in mortality: The survival of the fittest. Sports Med 2001;31:571-576.
43. Erikssen G, Liestol K, Bjornholt J, et al. Changes in physical fitness and changes in mortality. Lancet 1998;352(9130):759-762.
44. Blair SN, Kohl HW, 3rd, Barlow CE, et al. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. JAMA 1995;273: 1093-1098.
45. Bijnen FC, Feskens EJ, Caspersen CJ, et al. Baseline and previous physical activity in relation to mortality in elderly men: The Zutphen Elderly Study. Am J Epidemiol 1999;150:1289-1296.
46. Green LH, Cohen SI, Kurland G. Fatal myocardial infarction in marathon racing. Ann Intern Med 1976;84:704-706.
47. Corrado D, Basso C, Schiavon M, et al. Does sports activity enhance the risk of sudden cardiac death? J Cardiovasc Med (Hagerstown) 2006;7:228-233.
48. Albert CM, Mittleman MA, Chae CU, et al. Triggering of sudden death from cardiac causes by vigorous exertion. N Engl J Med 2000;343:1355-1361.
49. Siscovick DS, Weiss NS, Fletcher RH, Lasky T. The incidence of primary cardiac arrest during vigorous exercise. N Engl J Med 1984;311:874-877.
50. Whang W, Manson JE, Hu FB, et al. Physical exertion, exercise, and sudden cardiac death in women. JAMA 2006;295:1399-1403.
51. Thompson PD, Franklin BA, Balady GJ, et al. Exercise and acute cardiovascular events: Placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. Circulation 2007;115:2358-2368.
52. Franklin BA, Billecke S. Putting the benefits and risks of aerobic exercise in perspective. Curr Sports Med Rep 2012;11: 201-208.
53. Franklin BA. Preventing exercise-related cardiovascular events: Is a medical examination more urgent for physical activity or inactivity? Circulation 2014;129:1081-1084.
54. Mittleman MA. Triggers of acute cardiac events: New insights. Am J Med Sports 2002;4:99-102.
55. Mittleman MA, Maclure M, Tofler GH, et al. Triggering of acute myocardial infarction by heavy physical exertion. Protection against triggering by regular exertion. Determinants of Myocardial Infarction Onset Study Investigators. N Engl J Med 1993; 329:1677-1683.
56. Willich SN, Lewis M, Lowel H, et al. Physical exertion as a trigger of acute myocardial infarction. Triggers and Mechanisms of Myocardial Infarction Study Group. N Engl J Med 1993;329:1684-1690.
57. Hallqvist J, Moller J, Ahlbom A, et al. Does heavy physical exertion trigger myocardial infarction? A case-crossover analysis nested in a population-based case-referent study. Am J Epidemiol 2000;151:459-467.
58. Dahabreh IJ, Paulus JK. Association of episodic physical and sexual activity with triggering of acute cardiac events: Systematic review and meta-analysis. JAMA 2011;305:1225-1233.
59. Warburton DER. The physical activity and exercise continuum. In: Bouchard C, Katzmarzyk PT (eds). Advances in physical activity and obesity. Champaign, IL: Human Kinetics Publishing; 2009:7-17.
60. La Gerche A, Prior DL. Exercise—Is it possible to have too much of a good thing? Heart Lung Circ 2007;16(suppl 3):S102-104.
61. La Gerche A, Heidbuchel H. Can intensive exercise harm the heart? You can get too much of a good thing. Circulation 2014;130:992-1002.
62. Scott JM, Warburton DE. Mechanisms underpinning exercise-induced changes in left ventricular function. Med Sci Sports Exerc 2008;40:1400-1407.
63. Trivax JE, McCullough PA. Phidippides cardiomyopathy: A review and case illustration. Clin Cardiol 2012;35:69-73.
64. Patil HR, O'Keefe JH, Lavie CJ, et al. Cardiovascular damage resulting from chronic excessive endurance exercise. Mo Med 2012;109:312-321.
65. Benito B, Gay-Jordi G, Serrano-Mollar A, et al. Cardiac arrhythmogenic remodeling in a rat model of long-term intensive exercise training. Circulation 2011;123:13-22.
66. La Gerche A, Burns AT, Mooney DJ, et al. Exercise-induced right ventricular dysfunction and structural remodelling in endurance athletes. Eur Heart J 2012; 33:998-1006. BCMJ