Pre-Marathon Evaluations: Is there a role for runner pre-race medical screening and education to reduce the risk of medical complications?

M P Schwellnus, MBBCh, MSc (Med), MD, FACSM [a]

[a] Professor of Sport and Exercise Medicine, Faculty of Health Sciences, Sport, Exercise Medicine and Lifestyle Institute (SEMLI) and Section Sports Medicine, University of Pretoria, South Africa, Sports Campus, Burnett Street, Hatfield, Pretoria 0020, South Africa South Africa

Corresponding author for proof and reprints:
[a] Martin P. Schwellnus, Director: Sport, Exercise Medicine and Lifestyle Institute (SEMLI), Faculty of Health Sciences, University of Pretoria, South Africa, Sports Campus, Burnett Street, Hatfield, Pretoria 0020, South Africa
Telephone: -27-12-420 6057 Fax number: -27-12-362 3369
Email: mschwell@iafrica.com

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Abstract

There is irrefutable evidence that regular participation in physical activity has substantial health benefits, and as such participation in mass community-based sports events should be supported. However, with the promotion of physical activity comes the potential risk of medical complications during an acute exercise session, with this risk varying according to the risk factor profile of an individual and the nature of the event. The demographics of marathon race entrants changed over the past 2-3 decades, and currently about 50% of runners are older than 40 years. A consolidated view of previously published research shows that in a marathon with a field of 50 000 runners for example, the medical staff will, on average, encounter a sudden death every 2-3 years, a sudden cardiac arrest every year, 25 runners that present with a serious medical complication

requiring specialized management or hospitalization, and 1000 runners that require medical attention.

Runners may have several intrinsic risk factors that can predispose them to serious acute cardiovascular or other serious non-cardiac medical complications on race day. This intrinsic risk can be exacerbated by several extrinsic risk factors as well. As healthcare professionals we are obliged to give the best medical advice to individuals who wish to participate in moderate- and high-intensity endurance activities, and at the same time reduce their risk of a medical complication during exercise. Preliminary data indicate that an online pre-race medical screening and targeted educational intervention program can be successfully implemented and is effective in reducing the risk of acute medical complications during a race.

Introduction – health benefits of regular exercise

There is irrefutable evidence that regular participation in physical activity has substantial and wide-ranging health benefits, and therefore regular physical activity is an important lifestyle component in the prevention and management of non-communicable diseases (NCDs). (1-5) Specifically, regular moderate- to vigorous physical activity is associated with a reduction in all cause premature mortality, cardiovascular mortality and morbidity, stroke, various cancers, metabolic disease, including diabetes mellitus, and chronic diseases in a number of other organ systems (1, 2, 6).

Very strong evidence that a weekly healthy "dose" of exercise for most individuals is 150 minutes of moderate to vigorous physical activity (6) and this is now universally recommended by influential international organizations including the World Health Organization (WHO) (7), European Association on Cardiovascular Prevention and Rehabilitation (EACPR) (8), American College of Sports Medicine (ACSM) and American Heart Association (AHA)(3) and others such as the Centers for Disease Control and Prevention (CDC) in the USA (https://www.cdc.gov/physicalactivity/basics/adults/ - accessed on 1 March 2017).

Recreational brisk walking, jogging, distance running, cycling and swimming as forms of regular physical activity are frequently recommended and routinely prescribed.

Marathon running - increased popularity and growth worldwide

Given the public awareness and focus on regular exercise as an important component of a healthy lifestyle, it is not surprising that participation in mass community-based sports events such as distance running events has, over the last 2-3 decades, resulted in substantial growth in participant numbers (9). More specifically, annual reports from Running USA (http://www.runningusa.org/annual-reports - accessed on 1 March 2017) show an increase of > 12 fold in overall participation in marathon runners since 1976, with a notable increase in participation in the older age groups (> 40 years). In 2015, 49% of all runners completing marathons in the USA were master (>40 years old) athletes (http://www.runningusa.org/annual-reports). Apart from age, the gender composition of race finishers has also changed dramatically, from 10% female finishers in 1980, to 44% of race finishers being female in 2015 (http://www.runningusa.org/annual-reports). Participation rates in other distance running events, including park runs, 5km and 10km races, the half-marathon (21.1km), the standard marathon (42.2km), and ultra-marathons have also increased. Therefore, currently more individuals participate in mass community-based sports events such as distance running (marathons), and the demographics of the marathon participant shifted to older runners and female runners (9).

The exercise benefit-risk paradox

Although moderate- to high-intensity regular physical activity, including distance running, is widely recommended (6), there is also equally strong evidence that moderate-to high-intensity exercise acutely, and transiently, increases the risk of a range of acute medical complications (10, 11), including acute myocardial infarction and sudden cardiac death (12-16).

Therefore, the first exercise benefit-risk paradox is that although regular moderate-to

high-intensity physical activity is both associated with substantial long-term health benefits, there are also potential negative health consequences during an acute exercise session (12-16). Recently there has also been a growing awareness and interest in the potential deleterious effects of chronic endurance exercise, particularly on the cardiovascular system. A detailed discussion of these potential long-term deleterious effects of endurance exercise is beyond the scope of this manuscript, but has recently been reviewed (13, 17).

A second, observation is that the greatest health benefits of regular exercise are frequently observed in two groups: 1) sedentary individuals that transition to becoming physically active, and 2) patients with known chronic disease (18). However, sedentary individuals that become active (9, 14, 19, 20) as well as patients with risk factors for, or known chronic disease (12, 21) also have a higher risk of potential acute adverse events during an exercise session. Therefore, a second benefit-risk paradox is that two groups of individuals, who will benefit from regular physical activity the most, also have the highest the risk of an acute medical complication during an exercise session.

These paradoxical observations need to be placed in perspective. Data from > 30 meta-analyses unequivocally support the recommendation that, from a population perspective, the participation in regular physical activity in these two groups of individuals still far outweighs the potential negative health consequences of an acute exercise session (13, 14, 20) (12, 19).

However, this does not imply that the risk during an acute exercise session should be ignored. We need to make every effort to ensure that an increased risk of an acute medical complication during an exercise session is reduced. Therefore, as much as we as health professionals must lead the drive to promote regular moderate-to high-intensity physical activity, including participation of our patients in mass community-based sports events such as distance running events, the safety of our patients is also our responsibility. We are obliged to give the best medical advice to individuals who wish to participate in moderate- and high-intensity endurance exercise, and at the same time

reduce their risk of a medical complication during an exercise session. In the context of distance running events, there is also a responsibility of race medical directors to reduce the risk of medical complications at these mass community-based sports events. In this manuscript I would like to suggest three steps are important to reduce this risk: 1) quantify the risk of acute medical complications during exercise, 2) identify causes, risk factors and "at-risk" individuals for medical complications, and 3) design and implement measures to reduce the risk of acute medical complications during an exercise session.

Quantifying the risk of acute medical complications during exercise

The risk of physical exercise as a trigger of acute cardiovascular events has been reviewed extensively for both younger and older athletic populations (12, 16, 22-24) (25) (9) (26)(27). There is a wide range in the relative risk of an acute cardiovascular event during an exercise session, compared with sedentary activity, and this can vary from 2 times in young athletes (16) to as much as 56 times in older individuals who are at risk for cardiovascular disease or who have existing cardiovascular disease (12, 16, 21). However, the absolute risk of acute cardiovascular events during an exercise session is consistently reported as being very low (1 in 50 000 to 1 in 200 000 annually) (16, 20) (14) (13) (12, 19).

The risk of sudden death during distance running events such as the half-marathon (21km) and the marathon (42km) is also well described (28) (29) (22) (30) (31) (32) (33) (16) (11). However, these data also show a considerable variation in the reported absolute risk of sudden death during marathons and similar races (between 1 in 30 000 to 1 in 250 000 race entrants)(Table 1), but generally this risk is 1 in 114 000 race entrants (calculated cumulative risk) (16) and therefore also reported as being very low. To date, there has been little attention to reduce this risk in marathon runners by prevention programs, probably because of the reported low absolute risk and the societal perspective that deaths at marathons are less of a public health threat (16). To date, most race organizers and medical staff focus on providing acute care to deal with acute cardiovascular events on race day.

However, sudden death during marathon running is only the “tip of the iceberg”, where the iceberg represents the risk of all medical complications during marathon running, including sudden cardiac arrest (including non-fatal cardiac arrest) and other serious medical complications. In Table 1, the absolute risk of medical complications during distance running by severity (sudden death, sudden cardiac arrest, serious medical complications, and any medical complication) is summarized from studies where this has been documented. The first observation from these data is that the absolute risk of sudden cardiac arrest is generally about 1 in 50 000 race entrants (ranging from 1 in 21 000 to 1 in 200 000). In comparison to sudden death, the risk of sudden cardiac arrest during a marathon race is 2-3 times higher (16).

The second observation from the data in Table 1 is that there is a risk of other cardiac (not resulting in cardiac arrest or death) and serious non-cardiac medical complications during marathon running. Most race medical directors of larger races are well aware of the risk of these serious (life threatening) medical complications presenting on race day. Whilst there is no consensus on the precise definition of a “serious life threatening” medical complication on race day, there are data on the incidence of runners that require transfer for further investigation and/or management to hospitals or similar facilities (Medical Transfer Rate - MTR) (34). The absolute risk of a serious medical complication, using this definition, also varies but is about 1 in 2000 race entrants (varies between 1 in 645 to 1 in 6000 race entrants)(Table 1). Therefore, in comparison to sudden death the relative risk of a serious medical complication at a distance running event, such as the marathon 50-100 times higher than sudden death.

The final observation from Table 1 is the risk of any medical complication during a marathon race. This is generally defined as the number of athletes that are assessed and treated by the on-site medical team (Patient Presentation Rate - PPR) (34). The absolute risk of any medical complication during a marathon race also varies between 1 in 22 to 1 in 121 entrants, but generally is about 1 in 50 runners.

Table 1: The absolute risk of medical complications during distance running by severity (sudden death, sudden cardiac arrest, serious medical complications, any medical complication) - rates are expressed per 100 000 race entrants and number of entrants per single incident

Severity of medical complications	Event/s	Absolute risk (per 100 000 race entrants)	Absolute risk (number of race entrants per 1 incident)
Sudden cardiac death (SCD)	US Marathons (1976-1994) (35)	1.8	55 556
	US Marathons (1995-2004) (36)	0.5	200 000
	US marathons (1976-2009) (29)	0.58	171 005
	UK marathons (1981-2006) (37)	1.5	66 667
	RACER registry - US marathons and half-marathons (2000-2010) (31)	0.4	250 000
	Two Oceans races (SA)(2008-2011) (11)	3.4	29 412
	French marathons and half marathons (RACE)(2006-2012) (38)	0.4	250 000
	Tel Aviv races (2007-2013) (39)	1.4	69 000
Sudden cardiac arrest (SCA)	US Marathons (1976-1994) (35)	2.3	43 478
	US Marathons (1995-2004) (36)	1.8	55 556
	US marathons (1976-2009) (29)	1.75	57 002
	Two popular US marathons (1982-2009) (28)	2.6	38 461
	UK marathons (1981-2006) (37)	2.5	40 000
	RACER registry - US marathons and half-marathons (2000-2010) (31)	0.5	200 000
	Two Oceans races (SA)(2008-2011) (11)	4.6	21 739
	French marathons and half marathons (RACE)(2006-2012) (38)	1.8	55 556
Serious medical condition *	Vancouver International Marathon (2006-2011) (34)	53	1887
	Baltimore Marathon (2002-2005) (34)	47	2128
	Baltimore Marathon (2001) (34)	155	645
	Twin Cities Marathon (1983-1994) (34)	35	2857
	Two Oceans races (SA)(2008-2011) (11)	56	1786
	Tel Aviv races (2007-2013) (39)	16.7	5988
Any medical condition **	Vancouver International Marathon (2006-2011) (34)	4449	22

	Baltimore Marathon (2002-2005) (34)	3395	29
	Baltimore Marathon (2001) (34)	2282	44
	Twin Cities Marathon (1983-1994) (34)	1908	52
	Two Oceans races (SA)(2008-2011) (11)	827	121

*: Variable definitions: Generally the Number of patients transferred by any means by the medical team for further investigation and/or management (Medical Transfer Rate - MTR) (34)
**: Variable definition: Generally the number of athletes that are attended to on site by the medical team (Patient Presentation Rate - PPR) (34)

The clinical relevance of these data are that in a marathon with a large field of 50 000 runners, the medical staff will, on average, encounter a sudden death every 2-3 years, a sudden cardiac arrest every year, 25 runners that present with a serious medical complication requiring specialized management or hospitalization, and 1000 runners that require medical attention. This risk continuum is an important consideration to determine the relative severity of complications and the need for screening to reduce the risk (Figure 1).

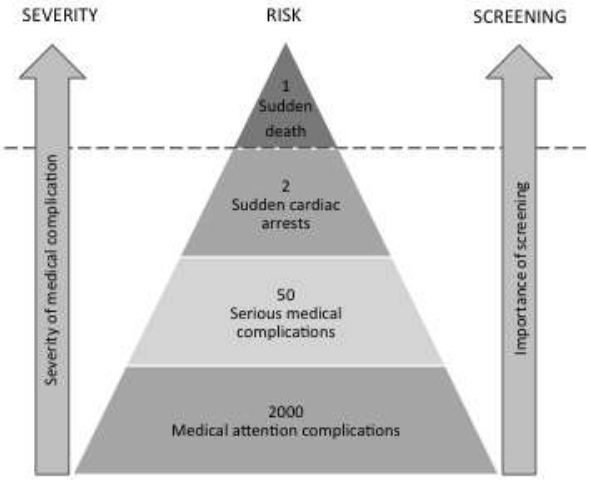

Figure 1: Risk of Medical Complications, Severity and Screening Continuum – Estimated absolute risk (per 100 000 race entrants) of medical complications in distance running events (summary from Table 1)

This risk continuum is an important consideration in planning medical coverage at large mass community based sports events. Providing this coverage is a considerable undertaking and requires careful planning long in advance of the event, recruitment of a large team of specialized medical staff (34), the establishment of considerable infrastructure, and securing sophisticated equipment at race medical facilities to ensure race safety. Many factors such as environmental conditions on race day, the course and

race distance and the "risk" demographics of the running population (runner experience, runner education, and runners with risk factors for acute medical complications during exercise) may influence the incidence of these complications at a specific race (34). Finally, although I am not aware of any reports detailing this, the provision of medical care at these races also translates to considerable cost to race organizers and event managers.

Causes, risk factors and "at risk" individuals for medical complications during marathon running

The second consideration in reducing the risk of medical complications is identifying causes, risk factors and "at-risk" individuals for medical complications. A detailed discussion of the causes of cardiac and non-cardiac medical complications during exercise is beyond the scope of this manuscript. The most common causes of sudden cardiac arrest/death are well documented for both younger and older (> 35 years) athletes (40) (15) (26). The distance running population demographics changed over the past 2-3 decades, with almost 50% of current marathon entrants being older than 40 years. A recent survey among Masters athletes (mean age 50 $\pm$ 9 years) showed that 10% of these athletes have existing cardiovascular disease, and 64% have at least one risk factor for cardiovascular disease (41). Therefore, it is not surprising that most common cause of sudden death or cardiac arrest in older marathon runners is coronary artery disease. There is good evidence that the risk of an acute cardiovascular complication during an exercise session is related to specific risk factors (Table 2).

Table 2: Risk factors associated with an increased relative risk of acute cardiovascular complications during moderate- to high-intensity exercise

Risk factor	Sub-category with increased relative risk
Sex (9, 14, 19)	• Males
Age (9, 14)	• Older age (> 35 years)
Habitual exercise status (9, 14, 19, 20, 34)	• Sedentary (no exercise sessions per week)(novice runner)
Exercise duration (34)	• Unaccustomed prolonged exercise
Exercise intensity (20)	• Unaccustomed high-intensity exercise (> 80% maximum capacity)
Underlying chronic disease (known or unknown)(9, 14, 20)	• Cardiovascular disease, metabolic disease including diabetes mellitus, renal disease, other chronic disease
Presence of risk factors for chronic disease (9)	• Family history of premature CVD, dyslipidemia, increased BMI, smoking status, hypertension
Symptoms of cardiovascular disease (14, 20, 42)	• Chest pain including discomfort in the chest, neck, jaw, arms or other areas, shortness of breath at rest or with mild exertion, dizziness or syncope, orthopnea or paroxysmal nocturnal dyspnea, ankle edema, palpitations or tachycardia, intermittent claudication, know heart murmur, unusual fatigue or shortness of breath with usual activities
Acute illness and inflammation (43) (23)	• Inflammation and increased risk of plaque rupture • Infective illness associated with myo-pericarditis • Infective illness associated with exertional heatstroke • Infective illness associated with exertional rhabdomyolysis
Drugs and medication use (44-46)	• Arrhythmogenic drugs (including performance enhancing drugs, social drugs, prescribed medication) • Drugs associated with rhabdomyolysis • Drugs increasing the risk of severe electrolyte abnormalities resulting in arrhythmias (e.g. hyponatremia, hypokalemia)
Education (34)	• Poor runner education

However, it is important to point out that there are other causes of sudden death and serious medical complications during marathon running that are not related to coronary artery disease. These causes include, but are not limited to severe fluid and electrolyte abnormalities (mainly hyponatraemia), acute renal failure, and exertional heat stroke. The risk factors for these other non-cardiac causes (Table 3) should also be considered in an intervention strategy to reduce the risk of acute medical complications during exercise.

Table 3: Risk factors associated with an increased relative risk of other serious medical complications during moderate- to high-intensity exercise

Medical complication	Risk factors
Hyponatremia (47-49)	• Overdrinking (water, sports drinks and other hypotonic beverages) • Exercise duration >4 hours • Event inexperience or inadequate training • Slow running or performance pace • High or low body mass index • Readily available fluids • Drugs and medication • Skeletal muscle damage (rhabdomyolysis)
Acute kidney injury and renal failure (50-53)	• Underlying chronic renal disease • Renal hypouricemia, • Sickle cell disease • Latent myopathy • Rhabomyolysis • Acute illness (viral, bacterial) • Drugs and medication (NSAIDs, analgesics) • Dehydration
Exertional heatstroke (54-58)	• History of heatstroke • Fever • Acute infective illness (upper respiratory, gastrointestinal) • Diarrhea, vomiting • Sweat gland dysfunction • Sunburn • Dehydration • Medications (diuretics, anti-depressants) • Sleep loss • Advanced age • Excessive alcohol use • Lack of heat acclimatization • Sedentary lifestyle (low physical fitness) • Overweight/obesity • Cardiovascular dysfunction • Hypokalemia

In summary, runners may have several intrinsic risk factors that can predispose them to serious acute cardiovascular (Table 2) or other serious non-cardiac medical complications (Table 3) on race day. It is important to note that some of these risk factors are transient such as acute illness or medication use on race day. Finally, the risk of a medical complication on race day in the "at risk" runner is also influenced by other extrinsic factors such as exposure to adverse environmental conditions (heat and humidity, altitude, pollution), the race distance, and course characteristics.

Measures to reduce the risk of acute medical complications during marathon running – is there a role for pre-race medical screening and targeted education?

International guidelines to reduce the risk of acute cardiovascular risk during exercise have been developed and implemented. To date, many sports federations (15, 59) and international bodies including the International Olympic Committee (IOC) (60) and the International Paralympic Committee (IPC) either mandate or recommend pre-participation screening (15). However, currently these screening programs focus mostly on screening younger elite athletes (26, 61, 62), and concentrate almost exclusively on pre-participation *cardiac* screening (including a resting ECG) to reduce the risk of acute cardiovascular complications. We are not aware of any pre-screening programs that also target other non-cardiac risk factors for serious life-threatening medical complications.

The concept of pre-exercise screening for the older (masters) and leisure (recreational, amateur) athlete has not received the same attention (63). This is rather surprising as the incidence of acute medical complications, including acute cardiovascular events, is significantly higher in the older exercising population than in younger elite athletes (64). In Canada, the Physical Activity Readiness Questionnaire (PAR-Q+) and the Physical Activity Readiness Medical Examination (ePARMed-X+) were developed as primary front-line pre-participation tools for physical activity (65), and are based on a systematic review of evidence (66) (67). Similarly, the American Heart Association (AHA) (68) and the American College of Sports Medicine (ACSM) (20) have recommendations for pre-participation screening. The European Society of Cardiology together with the European

Association of Cardiovascular Prevention and Rehabilitation (69) specifically developed recommendations, by consensus, for the pre-participation screening of masters and leisure athletes. These recommendations include the pre-participation screening of both novice and already active middle-aged/senior individuals prior to engaging in sports activities of moderate to high intensity (42) and were developed to "provide a pragmatic and practical approach to identifying high-risk individuals to minimize the risk of sudden cardiac death (SCD)".

The first step in the recommended screening process is a "self-assessment of risk", and this is based on the American Heart Association (AHA)/American College of Sports Medicine (ACSM) pre-participation screening questionnaire for individuals at Health/Fitness facilities (70) and the PAR-Q (42). The European guidelines recommend that this initial "self-assessment of risk" can be conducted by the individual and consists of health information related to: a) any history of known cardiovascular disease, cardiovascular symptoms, medication use, and other health issues (section 1), and b) known risk factors for cardiovascular disease including male gender, older age, hypertension, smoking, hypercholesterolemia, diabetes or hyperglycemia, and obesity (section 2). Based on the responses to questions in section 1 (any one positive response to a question) and section 2 (presence of $\geq$2 risk factors), it is then recommended that individuals undergo a thorough medical assessment by a qualified physician before participating in moderate- to high-intensity exercise, such as distance running (42).

However, despite these recommendations for pre-participation screening, we are not aware of any International Sports Federations, sports organizations or event managers or mass community-based endurance sports events that routinely mandate or recommend a pre-participation process for entrants, based on these international guidelines. We are aware of only one study to date, where the ESC/EACPR screening guidelines have been applied to adult participants > 40 years of age, who participated in the National Health and Nutrition Examination Survey (2001 to 2004) (71). Based on "self assessment of risk", approximately 95% of women and 93.5% were advised to consult a physician before embarking on exercise (20). In two other studies, full pre-participation screening

incorporating medical histories, physical examination and special investigations (electrocardiography, echocardiography and blood tests) effectively identified middle-aged athletes with risk factors of cardiovascular disease (CVD) (64) (72). However, neither study identified the links between the "risk self assessment" and the outcome of the full screening. Although ideal, full screening of every leisure athlete older than 45 years who participate in large community events would not be cost-effective or logistically feasible.

In 2008, we initiated a series of studies that formed the basis of a long-term strategy to reduce the risk of an adverse medical event in endurance exercisers: the **SAFER** (**S**trategies to reduce **A**dverse medical events **F**or the **E**xercise**R**) studies (73) (11) (74) (75). In the first studies that we conducted at the Two Oceans Marathon races in South Africa in the time period from 2008 to 2011, we recorded a very high incidence of sudden death of 1 in 20 000 in the 21km race entrants (11) and also showed a high incidence (1 in 1786 all entrants) of other serious medical complications in these runners. These high rates of medical complications and deaths in runners, particularly 21km runners were of great concern, and we identified the need to plan strategies to prevent deaths and serious medical complications in these races (SAFER studies) (73).

In the first of these follow-up SAFER studies, an online "self assessment screening" and runner targeted educational intervention (based on risk and risk profile) system was designed and implemented in 2012. The "self assessment screening" questionnaire was based, in part, on the PAR-Q+, the American Heart Association (AHA) (68), and the European Society of Cardiology together with the European Association of Cardiovascular Prevention and Rehabilitation (69) pre-participation screening recommendations. In addition, we included screening questions to identify other risk factors associated with serious non-cardiac medical complications (Table 3), and also conducted two studies focusing on acute illness screening and education in the few days before the races (76) (77). Novel algorithms were developed for a risk stratification process and these were applied, in an automated fashion, following the screening process.

This was followed by a targeted educational intervention in the form of an email notification of participants in the high and intermediate risk categories. Race entrants were given advice on the risks of a medical complication, practical advice to reduce this risk during training and competitions, and a recommendation to consult with their doctor to obtain clearance for safe participation in the event (as per the international guidelines). The main aim of the general educational component was to inform runners about the risks of medical complications during running as listed in Tables 2 and 3.

In the period 2012 to 2015, we undertook a series of follow-up SAFER studies to explore the effect of the online pre-participation screening and educational intervention program. The preliminary data from this study were presented recently, and show the incidence of any medical complication during the race was reduced by 29%, and the incidence of serious life-threatening medical complication during the race was reduced by 64% (78). These data show that an online "self assessment of risk" screening program with a targeted educational program can be implemented successfully in a pre-race setting for large community based events, and that such a program can result in substantial reductions in medical complications, specifically serious medical complications.

Summary and future perspectives

The health benefits of regular physical activity (150 min per week, moderate- to high-intensity) are undisputed and should be recommended for all. Participation in large community-based sports events must be encouraged and supported. However, the same "dose" of the exercise "medicine" is also associated with a higher risk of triggering acute medical complications (including sudden death) during the exercise session such as a marathon race, and this risk varies according to the risk factor profile of an individual and extrinsic factors such as environmental conditions. Although the concept of pre-exercise screening to reduce the risk of acute medical complications is widely debated, it is generally supported. Currently pre-participation screening is mandated or supported but mostly to younger elite athletes, who are in fact at lower risk for cardiovascular complications during exercise than older leisure athletes.

We argue that pre-exercise screening is at least as important, if not more important, in the older leisure athlete. Preliminary data show that an online pre-race screening and targeted educational intervention program can be successfully implemented and is effective in reducing the risk of acute medical complications during a race.

Further studies are suggested to 1) determine the effects of implementing such a program in other race populations and settings, 2) determine if the application of current screening guidelines actually predict medical complications (risk) and so that current guidelines can be refined, 3) consider a centralized annual self-screening process (participation passport) to avoid a repetitive process for runners that race regularly (weekly or monthly), 4) determine the ethical and legal issues resulting from screening (or not screening), and 4) determine the cost-benefit of the reduction in complications for health care providers on race days.

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