

**Longer distance races and slower running pace are associated with Exercise associated collapse – SAFER XXV study in 153208 distance runners**

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## **ABSTRACT**

**BACKGROUND:** Exercise associated collapse (EAC) is a common medical encounter at distance running events. Risk factors associated with EAC are not well documented. The objective is to determine the overall incidence of EAC and identify risk factors associated with EAC in 21.1km and 56km runners.

**METHODS:** A cross-sectional analysis of 153208 race starters from the Two Oceans Marathon races (2008-2015). All EACs on race day were documented by medical staff. Risk factors associated with EAC investigated included demographics, race distance (21.1km vs. 56km), running speed, race experience and race day environmental data (wet-bulb globe temperature [WBGT], humidity, wind speed). Incidence (per 1000 starters; 95% CIs) and incidence ratios (95% CIs) were calculated.

**RESULTS:** The overall incidence of EAC was 1.50 (95% CI 1.31-1.71). Longer race distance (IR: 2.1; 1.6-2.7;  $p < 0.0001$ ) and slower running speed (IR: 1.3; 1.1-1.5;  $p = 0.0017$ ) were significant risk factors associated with EAC. The incidence of EAC was higher in female vs. male 21.1km race starters (IR=2.25; 1.47-3.46;  $p = 0.0229$ ). Age and environmental conditions were not associated with EAC ( $p > 0.05$ ) in a cool and temperate environment.

**CONCLUSIONS:** About 1 in 667 race starters (21.1km and 56km) develop EAC. Longer race distance, slower running speed and female sex (in 21.1km starters) are significant risk factors associated with EAC. Race medical directors can identify race entrants that may be at risk of developing EAC, develop prevention strategies and better prepare medical care at these events.

### **Keywords:**

Running, postural hypotension, collapse, marathon, risk factors.

## **Introduction**

Non-communicable diseases (NCDs) are a leading cause of mortality worldwide <sup>1</sup>. The beneficial effects of a healthy lifestyle, including regular exercise, on the treatment and prevention of NCDs have been well researched and proven <sup>2-4</sup>. Distance running is a practical, accessible and popular way to maintain a healthy lifestyle. Running has seen an increase in the number of participants in mass community-based participation running events over the past ten years <sup>5 6</sup>. These running events range in distance from 5km to ultra-marathon events.

Distance running can also be associated with an increased risk of medical complications (exercise paradox) <sup>7-9</sup>. There has been an increase in minor, moderate and serious medical encounters reported at mass community-based participation running events <sup>10 11</sup>. Serious or life-threatening encounters are relatively rare, occurring at an incidence of 0.6-1.9 per 100 000 race starters and include death and sudden cardiac arrest <sup>12</sup>.

A common moderate medical encounter in distance running events is Exercise associated collapse (EAC) <sup>11,13-15</sup>. EAC is a clinical syndrome characterised by an inability to stand or walk unaided because of dizziness, light-headedness, syncope or presyncope after the cessation of intense exercise <sup>14,16</sup>. The aetiology of EAC is multifactorial but the main pathophysiological mechanism is thought to be an abrupt decrease in venous return when the lower limb muscles (muscle pump) cease rhythmic contraction <sup>17</sup>. This transient postural hypotension is associated with impaired baroreflexes immediately following cessation of exercise <sup>14-15,18</sup>. EAC is a clinical diagnosis and has been adopted as the term to describe all cases of collapse, even those with no identifiable cause <sup>17,19</sup>. The reported incidence of EAC in distance running races varies from 1.5 per 1000 starting runners in half marathons to a

higher rate of 11 per 1000 in marathon runners<sup>13,15</sup>. Whilst the populations and environments (one in Europe and the other in the USA) differed greatly<sup>13,15</sup>, these two studies illustrate the large discrepancies in the reported incidence of EAC in distance running events.

Risk factors associated with EAC have also not been well documented. Previous studies have found that race duration and increased environmental temperature<sup>20</sup> is associated with an increased risk of developing EAC<sup>17</sup>. Other risk factors such as runner experience, and faster running pace have also been reported in the literature<sup>16</sup>.

The aim of this study was to determine the incidence of EAC in 21.1km and 56km runners and to explore risk factors that may be associated with EAC in distance runners. This information would assist race day medical teams and race organisers to predict runners that would be at risk of developing EAC.

## **Materials and methods**

### ***Study Design***

This study was a cross-sectional analysis of data collected over 8 years, from 2008-2015.

### ***Setting***

The Two Oceans Marathon races are a 21.1km and a 56km race held in Cape-Town, South Africa. The 21.1km race is open to all runners 16 years and older on the day of the event, and entry does not require a qualifying time. The 56km race requires entrants to complete a pre-qualifying 42km race in under 5 hours and be 20 years or older on the day of the event.

### ***Participants and Data Collection***

This study is part of the ongoing SAFER (Strategies to reduce Adverse medical events For the ExerciseR) series <sup>21</sup>. Study participants were race starters for either the 21.1km or the 56km race across 8 annual races from 2008–2015. The data for this study were obtained from: 1) race entrant data, 2) race day medical encounter data, and 3) race day data including environmental data on the day of the event.

Race entrant data included demographic details of the athlete (sex, age group, race distance entered, running experience). Running experience was reported as previous running experience in the Two Oceans (<1, 2–4, >5 previous medals). Medical encounter data were collected by the medical team working at the event. The race day medical team consisted of physicians and physical therapists. Medical team members were present on the race route and at a medical and physical therapy facility at the finish line. Athletes who presented for medical care during the event or at the finish line were triaged and either admitted to the onsite facility for further management or transferred to the closest hospital. A medical encounter was defined as "*any runner who required medical care on race day that was severe enough to warrant a medical assessment by a doctor, either in the medical facility at the end of the race, on the route at the medical stations or one of the referral hospitals*" <sup>22</sup>. Further details regarding the collection of medical encounter data on race day have been described <sup>23</sup>. For this study, only encounters diagnosed by the medical team as EACs were analysed. The inclusion criteria for an EAC was a confirmed clinical diagnosis made by the attending physician, and defined as the "inability to stand or walk unaided because of dizziness, light-headedness, syncope or presyncope after the cessation of intense exercise". Other causes of serious life-threatening medical encounters with a confirmed diagnosis were not included

(e.g. cardiac arrests, exertional heatstroke and hyponatemia). EAC encounters were recorded, coded, and entered into a database.

Race day data were obtained from the race organisers and included starting and finishing times to calculate the average running speed for each runner. Data regarding the environmental conditions from 6:00 until 12:00 on race day of each year, including the temperature, humidity, rainfall, cloud cover and wind speed, were obtained from one weather station from the South African Weather Services database. The Wet-Bulb Globe Temperature (WBGT) index was also included in this dataset. For analysis, the weather data were classified as either “high” (H) or “low” (L) based on the following criteria: WBGT: H>15.2, L<15.2, Wind speed: H>7, L<7 and Relative Humidity: H>80%, L<80%.

Ethical clearance for the ongoing data collection and subsequent analysis was received from the Research Ethics Committee of the University of Pretoria (REC 433/2015) and the Research Ethics Committee of the University of Cape Town (REC 009/2011).

### ***Outcome Measures and Risk Factors***

The incidence of EAC was reported as an incidence per 1000 race starters over the 8 years.

Risk factors associated with EAC that were explored included:

- Race distance (21km and 56km)
- Individual runner characteristics (sex, age group, running speed, running experience)
- Environmental conditions (WBGT, wind speed, humidity)

### *Statistical Analysis*

Data collected during the study period from 2008 to 2015 were entered into an Excel spreadsheet (Microsoft 2010) and then analyzed using the SAS 9.3 statistical program (SAS Institute Inc, Cary, North Carolina, USA). Statistical analyses included a Poisson regression model with a robust error estimator (log link function). During the 8-year period runners could participate in the races more than once, resulting in correlated data. An unstructured correlation matrix was used to account for the correlated structure of the data. Incidence, incidence rate (IR) and 95% confidence intervals are reported throughout, and the statistical significance level was 5% throughout.

**Table 1: The demographics of all race starters (n=153208) over the 8-year period (by sex, age group and year of participation) (n; %)**

Sex	Age group (years)	2008	2009	2010	2011	2012	2013	2014	2015	Total
Males	All	10142 (100)	10596 (100)	10708 (100)	9580 (100)	12612 (100)	13204 (100)	12403 (100)	12793 (100)	92038 (100)
	≤ 30	2600 (25.6)	2850 (26.9)	2560 (23.9)	2397 (25.0)	3194 (25.3)	3361 (25.5)	2600 (21.0)	2584 (20.2)	22146 (24.1)
	31-40	3059 (30.2)	3124 (29.5)	3275 (30.6)	3006 (31.4)	3938 (31.2)	4186 (31.7)	3958 (31.9)	4167 (32.6)	28713 (31.2)
	41-50	2754 (27.2)	2727 (25.7)	2896 (27.0)	2455 (25.6)	3215 (25.5)	3283 (24.9)	3406 (27.5)	3534 (27.6)	24271 (26.4)
	> 50	1729 (17.0)	1895 (17.9)	1977 (18.5)	1722 (18.0)	2265 (18.0)	2373 (18.0)	2439 (19.7)	2508 (19.6)	16908 (18.4)
Females	All	5600 (100)	6248 (100)	6650 (100)	6341 (100)	8628 (100)	9151 (100)	8857 (100)	9695 (100)	61170 (100)
	≤ 30	1691 (30.2)	2105 (33.7)	2192 (33.0)	2166 (34.2)	2932 (34.0)	2957 (32.3)	2529 (28.6)	2579 (26.6)	19151 (31.3)
	31-40	1803 (32.2)	1909 (30.6)	2063 (31.0)	1992 (31.4)	2693 (31.2)	2944 (32.2)	2922 (33.0)	3315 (34.2)	19641 (32.1)
	41-50	1453 (25.9)	1574 (25.2)	1657 (24.9)	1488 (23.4)	2034 (23.6)	2147 (23.5)	2160 (24.4)	2460 (25.4)	14973 (24.5)
	> 50	653 (11.7)	660 (10.6)	783 (11.8)	695 (11.0)	969 (11.2)	1103 (12.1)	1246 (14.1)	1341 (13.8)	7405 (12.1)

## Results

### *Demographics*

The demographics of all the race starters by sex, age group and year of participation in the 8-year period are shown in Table 1.

Over the 8-year period, there were 153 208 race starters. Of all the starters, 60% were male, and 40% were female. The majority of the female race starters were in the 31–40-year age group (32.1%), which was also the largest age group in males (31.2%).

### *Environmental conditions on race day*

The average measure for the day for each environmental condition over the eight years are shown in Table 2.

**Table 2: Environmental conditions on each race day (mean; SD)**

Year	Wet-bulb globe temperature (WBGT)	Wind speed (km/hr)	Relative humidity (%)
2008	16.5 (2.4) (H)	9.6 (2.4) (H)	77 (8) (L)
2009	15.4 (1.6) (H)	7.8 (1.0) (H)	83 (7) (H)
2010	15.2 (1.4) (H)	3.5 (0.6) (L)	93 (3) (H)
2011	13.5 (2.9) (L)	1.5 (1.3) (L)	87 (2) (H)
2012	12.1 (0.7) (L)	6.9 (3.1) (L)	92 (4) (H)
2013	18.4 (2.0) (H)	13.1 (0.7) (H)	78 (6) (L)
2014	15.1 (1.6) (L)	9.6 (2.4) (H)	77 (8) (L)
2015	13.4 (0.5) (L)	6.6 (0.9) (L)	83 (7) (H)

H: Data on these years were included in “High” sub-group for the analysis

L: Data on these years were included in “Low” sub-group for the analysis

WBGT: H>15.2, L<15.2

Wind speed: H>7, L<7

Relative Humidity: H>80%, L<80%

Environmental conditions varied over the years however had a very narrow range. The WBGT was highest in 2013 at 18.4 and lowest in 2012 at 12.1. The highest wind speeds were recorded in 2013 at 13.1km/hr, and relative humidity was highest in 2010 at 93%. The lowest wind speeds were recorded at 1.5km/hr in 2011 and the lowest relative humidity was 77% which was recorded in both 2008 and 2014.

### ***Incidence of EAC and factors associated with EAC***

The overall incidence of EAC over the 8 years was 1.50 (95% CI 1.31-1.71) per 1000 race starters. The incidence of EAC in the race starters by race distance, sex, age group, running speed and experience is shown in Table 3.

**Table 3: The incidence (per 1000 race starters; 95%CI) of exercise associated collapse (EAC) in race starters by race distance, sex, age group, running speed and experience**

<b>Runner characteristics</b>	<b>Category</b>	<b>n</b>	<b>Incidence per 1000 race starters (95%CI)</b>	<b>IR (95%CI)</b>	<b>p-value</b>
<b>Race Distance</b>	21.1km	98	1.06 (0.86-1.29)		<0.0001
	56km	132	2.19 (1.83-2.61)	2.07(1.59-2.70)	
<b>Sex</b>	Female	105	1.73 (1.42-2.10)		0.073
	Male	125	1.35 (1.12-1.61)	0.78 (0.60-1.02)	
<b>Age group (years)</b>	≤30	54	1.30 (1.00-1.70)		0.2875
	31-40	67	1.39 (1.09-1.77)	1.07 (0.75-1.52)	
	41-50	62	1.58 (1.23-2.03)	1.22 (0.84-1.75)	
	>50	47	1.92 (1.42-2.61)	1.48 (0.99-2.21)	
<b>Running speed (km/h) *</b>	8.2	-	1.61 (1.36-1.92)	1 unit increase: 0.89 (0.79-1.01)	0.0417
	9.2	-	1.46 (1.27-1.67)		
	10.4	-	1.28 (1.05-1.55)		
<b>Experience</b>	1	148	1.35 (1.14-1.58)		0.0612
	2	34	1.73 (1.24-2.42)	1.29 (0.89-1.86)	
	3	48	2.07 (1.54-2.79)	1.54 (1.10-2.16)	

IR: Incidence Ratio

\*Running speed is a continuous variable; the points represent the 1<sup>st</sup> quartile, median, 3<sup>rd</sup> quartile

The incidence of EAC incidence was higher in the 56km compared to the 21.1km race starters (IR=2.1; p<0.0001). For all race starters, sex was not a significant risk factor associated with EAC. However, there was a significant interaction between race distance and sex (p=0.023); in 21.1km race starters there was a higher incidence of EAC in female race starters compared to males (IR=2.3; 95%CI 1.47-3.46, p=0.0002) which did not hold for the 56km race (IR=1.2; 95%CI: 0.8-1.7, p=0.391). There was also a significant interaction between running speed and age, (p=0.012), which showed that older athletes (>50years) had a lower incidence at higher speeds (9.2km/hr vs 8.2km/hr, IR=0.5; 10.4km/hr vs 8.2km/hr,

IR=0.3; p=0.001). There was no significant interaction between race distance and running speed (p=0.5532).

The association between selected environmental factors and the incidence of EAC is shown in Table 4.

**Table 4: The incidence (per 1000 race starters; 95% CIs) of exercise associated collapse (EAC) by categories of selected environmental factors (wet bulb globe temperature, wind speed and humidity)**

Environmental factors	Category	Incidence per 1000 race starters (95% CIs)	p-value
<b>WBGT</b>	High	1.44 (1.18-1.75)	0.548
	Low	1.55 (1.30-1.85)	
<b>Wind speed (knots)</b>	High	1.63 (1.36-1.94)	0.193
	Low	1.37 (1.13-1.66)	
<b>Humidity (%)</b>	High	1.38 (1.16-1.64)	0.140
	Low	1.68 (1.38-2.05)	

WBGT: Wet bulb globe temperature

There was no significant difference in the incidence of EAC in race starters when exposed to high and low values for selected environmental conditions, although it must be noted that there was a very small range for these conditions.

## Discussion

The aim of the study was to determine the incidence of EAC in 21.km and 56km runners and to explore risk factors that may be associated with EAC in distance runners. The overall incidence of EAC was 1.5 per 1000 starters and longer race distance and slower running speed were significant risk factors associated with EAC. In the 21.1km race distance, female sex was a significant risk factor associated with EAC. Environmental conditions were not significantly associated with a risk of EAC in our study.

The overall incidence of 1.06 per 1000 starters in the half marathon (21.1km) race is lower compared to that documented in the Gothenburg half marathon (1.53 per 1000 starters) <sup>15</sup>.

The difference between these two incidences could be attributed to differences in the inclusion criteria between these two studies. In the Gothenburg event, any medical collapse requiring admittance to the medical tent or picked up by the ambulance and not due to any specific cause was included and therefore more cases of EAC could have been included. The incidence of EAC in our 56km race starters (2.19 per 1000 starters) was significantly higher than in our 21.1km race starters, but lower than the incidence reported in a previous study on 42.2km race entrants (11.5 per 1000 entrants, defined as collapses without an immediately identifiable medical condition)<sup>13</sup>. Roberts et al.<sup>13</sup> included the following diagnoses within the EAC classification “problems of dehydration, vasovagal syncope, orthostatic syncope, exhaustion, hyperthermia, and hypothermia”, this again differs from the definition in our study and would attribute to the differences between the findings. Our findings are in keeping with recent data showing that longer race distances are associated with a higher incidence of medical encounters, including EAC<sup>17,24-25</sup>. Rhythmic skeletal muscle contraction in the lower limb ("second heart") is an increasingly important mechanism during more prolonged exercise (56km vs. 21.1km) to maintain central blood volume, facilitate cardiac output and maintain blood pressure<sup>26</sup>. Therefore, EAC is more likely to occur on cessation of prolonged exercise when the inactive muscle pump results in diminished venous return and reduced cardiac output leading to symptomatic reduction in arterial pressure. In races of longer duration, this response can also be worsened by dehydration and exercise in the heat<sup>27-29</sup>.

Although sex was not associated with increased risk of EAC or PEH in previous studies<sup>15,30-31</sup>, we show that there was a significant interaction between race distance and sex. Female compared to male 21.1km race starters had a 2X higher incidence of EAC. This differs from the results reported in other 21.1km races where the incidence of EAC was similar in male and female runners<sup>15,32</sup>, except for one study where females had almost a 3X higher

incidence compared to males ( $p=0.0394$ )<sup>33</sup>. This may be explained by the differing hemodynamic mechanisms responsible for blood pressure reduction after exercise between the sexes and that females may be more vulnerable to orthostatic hypotension which can be exacerbated with cessation of exercise<sup>30 34</sup>. However female sex as a possible risk factor for EAC in shorter race distances requires further investigation.

Our finding that there is a higher incidence of EAC in slower runners is in contrast to previous reports that a slower running pace/speed is associated with a lower incidence of EAC<sup>16,18,35</sup>. A slower running pace may indicate a poor level of fitness or less experience, and both these factors were previously reported as risk factors for EAC in endurance athletes<sup>25</sup>. In our study, less running experience was not significantly associated with a higher incidence of EAC but we noted a tendency ( $p=0.0612$ ). In general, a slower running pace is also associated with longer race duration (56km vs. 21.1km distance) and more prolonged exercise is a risk factor for EAC<sup>26</sup>. Previous literature has found that more experienced runners in both shorter and longer distances are less likely to present with medical encounters than runners with less experience<sup>36-38</sup>. Although speculative, these data indicate that EAC may be associated with a combination of the following combination of internal risk factors in a distance runner: less running experience, slower running speeds, age and longer race distances. This hypothesis requires exploration in future studies where a multiple model can be applied in studies with a larger sample size of EAC.

In previous studies, environmental risk factors (external risk factors) were associated with increased risk of EAC. Warmer weather was found to be a risk factor for EAC<sup>17-18,24-25</sup>. In one study when temperatures ranged between 15–29°C, an increase of 1°C was associated with an increase in collapses requiring ambulance services<sup>39</sup>. In a study at the Twin Cities

Marathon, warmer conditions and humidity contributed to 72% of the risk for moderate to severe EAC in runners. Additionally, the medical team is likely to care for a greater number of EAC runners in hotter weather<sup>13</sup>. A possible explanation for the increased incidence of EAC in hotter weather is that a reduction in peripheral vascular resistance is worsened as vasodilation increases in response to heat<sup>26,40</sup>. In our study, environmental conditions were not associated with increased risk of EAC. We suggest that the main reasons for our finding are a relatively narrow range of environmental conditions and the fact that the range for WBGT was consistently in the “low risk” category (cooler temperatures)<sup>41</sup>.

### ***Strengths and Limitations***

To our knowledge, this is one of the first studies to identify risk factors of EAC in both a 21.1km and an ultra-marathon race (56km). Other studies have focused on shorter (10km or 21.1km) distances. All EACs were diagnosed by members of the race day medical team, and data were collected over several years, which allowed for a large sample size. The main limitation of the study is that it is a cross-sectional study and therefore causal relationships could not be identified. Additional limitations were that the diagnosis of EAC was a clinical diagnosis although we used a standardized definition of EAC and races did not take place in a range of environmental conditions (cooler to warmer), which limited our ability to relate environmental conditions to the risk of EAC. We also could not explore risk factors in a multiple model because of a small sample size and did not consider other internal runner-related risk EAC factors such as chronic diseases, previous history of collapse and medication use. Future studies, using information from a comprehensive medical screening questionnaire, could assist with identifying these internal risk factors.

## **Conclusions**

EAC is a common cause of medical encounters in distance running events but there are little data on the risk factors associated with EAC. We showed that the incidence of EAC was 1.06 per 1000 race starters (1 in 943) in 21.1km and 2.19 per 1000 race starters (1 in 457) in 56km, i.e. >2 times higher in the longer distance. A slower running speed and female sex (in 21.1km race starters) were associated with a higher risk of EAC. There was a tendency for less running experience to be associated with EAC risk. Environmental conditions in a narrow band within the “low risk” range were not associated with EAC. These data allow race medical directors to identify race entrants that may be at risk of developing EAC and implement prevention programs such as pre-race educational material that may reduce the incidence of EAC. Future studies should further investigate other internal and external risk factors that may be associated with EAC, using a multiple model in larger sample sizes of EAC.

## **Data sharing statement:**

No additional data are available.

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### **Author contributorship:**

All authors read and approved the final version of the manuscript

DN: study planning, data interpretation, manuscript (first draft), manuscript editing

NS: study planning, data interpretation, manuscript (first draft), manuscript editing

MS: responsible for the overall content as guarantor, study concept, study planning, data collection, data interpretation, manuscript (first draft), manuscript review & editing, facilitating funding

DCJVR: study planning, data interpretation, manuscript editing

EJ: study planning, data cleaning, data analysis including statistical analysis, data interpretation, manuscript editing

### **References**

1. Organization WH. Global health risks : Mortality and burden of disease attributable to selected major risks. 2009.
2. Slentz CA, Houmard JA, Kraus WE. Modest exercise prevents the progressive disease associated with physical inactivity. *Exer Sport Sci Rev.* 2007; 35(1):18-23.
3. Anderson RJ, Brice S. The mood-enhancing benefits of exercise: Memory biases augment the effect. *Psychol Sport Exer.* 2011; 12(2):79-82.
4. Warburton DER, Crystal Whitney N, Bredin SSD. Health benefits of physical activity: The evidence: Cmaj. *Canad Med Assoc J.* 2006; 174(6):801-809.
5. @runnersworldza [Internet] South africa has the fastest ultra runners in the world, study finds. @runnersworldza; 2020 [updated 2020-01-17; cited 2021 20 May]. Available from: <https://www.runnersworld.co.za/race-news/south-africa-fastest-ultra-runners/>.
6. [Internet] History - two oceans marathon. 2021 [cited 2021 20 May]. Available from: <https://www.twooceansmarathon.org.za/about-two-oceans/history/>.

7. Warburton DE, Taunton J, Bredin SS, Isserow S. The risk-benefit paradox of exercise. *BC Medical Association Journal*. 2016; 58:210-218.
8. Parto P, O'Keefe JH, Lavie CJ. The exercise rehabilitation paradox: Less may be more? *Ochsner J*. 2016; 16(3):297-303.
9. Franklin BA. Cardiovascular events associated with exercise: The risk-protection paradox. *J Cardiopul Rehabil Prev*. 2005; 25(4):189-195.
10. Sewry N, Schwellnus M, Boulter J, Seocharan I, Jordaan E. Medical encounters in a 90-km ultramarathon running event: A 6-year study in 103 131 race starters-safer xvii. *Clin J Sport Med*. 2021.
11. Breslow RG, Giberson-Chen CC, Roberts WO. Burden of injury and illness in the road race medical tent: A narrative review. *Clin J Sport Med*. 2020.
12. Waite O, Smith A, Madge L, Spring H, Noret N. Sudden cardiac death in marathons: A systematic review. *Physician Sportsmed*. 2016; 44(1):79-84.
13. Roberts WO. A 12-yr profile of medical injury and illness for the twin cities marathon. *Med Sci Sports Exer*. 2000; 32(9):1549-1555.
14. Asplund CA, O'Connor FG, Noakes TD. Exercise-associated collapse: An evidence-based review and primer for clinicians. *Br J Sports Med*. 2011; 45(14).
15. Lünig.H, Mangelus.C, Carlström.E, Nilson.F, Börjesson.M. Incidence and characteristics of severe exercise-associated collapse at the world's largest half-marathon. *Plos one*. 2019; 14(6).
16. Worley DM, Renier CM, Woehrle TA, Stovitz SD, Nelson BD. Preventing exercise-associated collapse using online runner education: A randomized, controlled trial. *Clin J Sport Med*. 2020; 30(3).

17. Childress MA, O'Connor FG, Levine BD. Exertional collapse in the runner: Evaluation and management in fieldside and office-based settings. *Clin Sports Med.* 2010; 29(3):459-476.
18. Khorram-Manesh A, Löf T, Börjesson M, Nilson F, Thorsson S, Lindberg F, et al. Profiling collapsing half marathon runners-emerging risk factors: Results from gothenburg half marathon. *Sports.* 2019; 8(1).
19. Roberts WO. Exercise-associated collapse care matrix in the marathon. *Sports Med.* 2007; 37(4-5).
20. Thorsson S, Rayner D, Palm G, Lindberg F, Carlström E, Börjesson M, et al. Is physiological equivalent temperature (pet) a superior screening tool for heat stress risk than wet-bulb globe temperature (wbgt) index? Eight years of data from the gothenburg half marathon. *Br J Sports Med* 2021; 55(15).
21. Schwellnus M, Derman W. The quest to reduce the risk of adverse medical events in exercising individuals: Introducing the safer (strategies to reduce adverse medical events for the exerciser) studies. *Br J Sports Med* 2014; 48(11):869-870.
22. Schwabe K, Schwellnus M, Derman W, Swanevelder S, Jordaan E. Medical complications and deaths in 21 and 56 km road race runners: A 4-year prospective study in 65 865 runners—safer study i. *Br J Sports Med.* 2014; 48(11):912-918.
23. Schwellnus M, Swanevelder S, Derman W, Borjesson M, Schwabe K, Jordaan E. Prerace medical screening and education reduce medical encounters in distance road races: Safer viii study in 153 208 race starters. *Br J Sports Med* 2019; 53(10).
24. Krabak BJ, Parker KM, DiGirolamo A. Exercise-associated collapse: Is hyponatremia in our head? *PMR J Inj Funct Rehabil.* 2016; 8(3 Suppl).
25. Schwellnus M, Derman W. The collapsed endurance athlete - causes and management : Sports medicine. *J Mod Pharm.* 2004; 11(7):14-16.

26. Noakes TD. Reduced peripheral resistance and other factors in marathon collapse. *Sports Med.* 2007; 37(4-5).
27. Halliwill JR, Sieck DC, Romero SA, Buck TM, Ely MR. Blood pressure regulation x: What happens when the muscle pump is lost? Post-exercise hypotension and syncope. *Euro J Appl Physiol.* 2014; 114(3).
28. Halliwill J, Buck T, Lacewell A, Romero S. Postexercise hypotension and sustained postexercise vasodilatation: What happens after we exercise? *Experi Physiol.* 2013; 98(1).
29. Anley C, Noakes T, Collins M, Schwellnus M. A comparison of two treatment protocols in the management of exercise-associated postural hypotension: A randomised clinical trial. *Br J Sports Med.* 2011; 45(14).
30. Queiroz A, Rezk C, Teixeira L, Tinucci T, Mion D, Forjaz C. Gender influence on post-resistance exercise hypotension and hemodynamics. *Int J Sports Med.* 2013; 34(11):939-944.
31. Kenney MJ, Seals DR. Postexercise hypotension. Key features, mechanisms, and clinical significance. *Hypertension.* 1993; 22(5).
32. Mourot L, Fornasiero A, Rakobowchuk M, Isacco L, Brighenti A, Stella F, et al. Post-exercise hypotension and reduced cardiac baroreflex after half-marathon run: In men, but not in women. *Int J Environ Res Pub Health.* 2020; 17(17):6337.
33. Schwabe K, Schwellnus MP, Derman W, Swanevelder S, Jordaan E. Older females are at higher risk for medical complications during 21 km road race running: A prospective study in 39 511 race starters—safer study iii. *Br J Sports Med.* 2014.
34. VH H. Sex and the cardiovascular system: The intriguing tale of how women and men regulate cardiovascular function differently. *Advan Physiol Edu.* 2007; 31(1).
35. St Clair Gibson A, De Koning J, Thompson K, Roberts W, Micklewright D, Raglin J, et al. Crawling to the finish line: Why do endurance runners collapse? Implications for understanding of mechanisms underlying pacing and fatigue. *Sports Med.* 2013; 43(6).

36. Buist I, Bredeweg SW, Bessem B, Van Mechelen W, Lemmink KA, Diercks RL. Incidence and risk factors of running-related injuries during preparation for a 4-mile recreational running event. *Br J Sports Med.* 2010; 44(8):598-604.
37. Damsted C, Parner ET, Sørensen H, Malisoux L, Nielsen RO. Projectrun21: Do running experience and running pace influence the risk of running injury—a 14-week prospective cohort study. *J Sci Med Sport.* 2019; 22(3):281-287.
38. Schwabe K, Schwellnus MP, Derman W, Swanevelder S, Jordaan E. Less experience and running pace are potential risk factors for medical complications during a 56 km road running race: A prospective study in 26 354 race starters—safer study ii. *Br J Sports Med.* 2014; 48(11):905-911.
39. Carlström E, Borjesson M, Palm G, Khorram-Manesh A, Lindberg F, Holmer B, et al. Medical emergencies during a half marathon race – the influence of weather. *Int J Sports Med.* 2019; 40:312-316.
40. Wendt D, van Loon L, Lichtenbelt W. Thermoregulation during exercise in the heat: Strategies for maintaining health and performance. *Sports Med.* 2007; 37(8).
41. Mears S, Watson P. Iirm medical care manual. International Institute for Race Medicine Web site. Available at: <http://www.racemedicine.org/en-us/Admin/Medical-Manual-Preview>. Published. 2015.