AUSTRALASIAN COLLEGE OF SPORT AND EXERCISE PHYSICIANS

IOC Research Centre

ACSEP ANNUAL SCIENTIFIC CONFERENCE 2017

Surfers Paradise Marriott Hotel, Gold Coast, QLD

Exercise Associated Muscle Cramping (EAMC) – Risk, Causes, Diagnosis and Management

Prof Martin Schwellnus

Professor of Sport and Exercise Medicine

Section Sports Medicine, Department of Orthopedics, Faculty of Health Sciences, University of Pretoria

Director: Institute of Sport, Exercise Medicine and Lifestyle Research, University of Pretoria

Director: IOC Research Centre, University of Pretoria, South Africa

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Disclosure

ACSEP Conference

February 2017, Gold Coast, Australia

Neither I, Martin Schwellnus, nor any family member(s), have any relevant financial relationships to be discussed, directly or indirectly, referred to, or illustrated with or without recognition within this presentation

Prof Martin Schwellnus

Acknowledgments

- My colleagues that I have had the privilege to work with over many years
- My students that have contributed to the work in this field
- All the athletes that have participated in many research studies

Outline

- Definition
- Classification of EAMC
- Epidemiology
- Etiology and risk factors
- Clinical approach
  - Diagnostic approach
  - Prevention
  - Acute treatment
- Summary

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Definition:

Exercise Associated Skeletal Muscle Cramp (EAMC)

Painful, spasmodic, involuntary contractions of skeletal muscle that occur during, immediately after, or within 24 (6) hours after muscular exercise

Schwellnus M et al: J Sports Science, 1997, 15(3); 277-285
Edouard, P: Science & Sports, 2014, 29; 299-305

Definition vs. Diagnosis

Exercise Associated Skeletal Muscle Cramp (EAMC)

- **EAMC - collection of symptoms and clinical signs**
- **EAMC - is a syndrome and <u>not a diagnosis</u>**

Causes of Skeletal Muscle Cramps

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Idiopathic

Motor neuron disease

Autosomal cramping disease, familial nocturnal cramps, Continuous muscle fibers activity syndrome

Continuous muscle fibers activity syndrome, Syndrome of progressive muscle spasm, alopecia and diarrhea (Satayashi's syndrome), nocturnal cramps, generalized myokymia, myokymia-hyperhidrosis syndrome

Symptomatic

Others	Muscle cramps in cancer patients
CNS disease	Motorneuron disease, occupational dystonias, Parkinson's disease, Tetanus, multiple sclerosis, radiculopathies, plexopathies, peripheral neuropathies, others
Muscular disease	Metabolic myopathies, mitochondrial myopathy, endocrine myopathy, dystrophinopathies, myotonia, inflammatory myopathies, others
CVS disease	Venous disease, arterial disease, heart disease, hypertension
Endocrine-metabolic	Thyroid disease, parathyroid disease, cirrhosis, isolated ACTH deficiency, Conn's, Addisons. Ureamia and dialysis
Hydro-electrolyte	Generalized dehydration (diarrhea, vomiting), sodium, potassium, magnesium, "heat"
Toxic/pharmacological	Drugs, pesticides, black widow bite, malignant hyperthermia
Psychiatric	

Paraphysiological

Occasional cramps

Pregnancy

Sporting activity

Parisi L, et al, Acta Neurol Scand 2003, 107: 176-186

Lecture dedicated to Joost Van Der Westhuizen

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Joost van der Westhuizen dies

SOUTH AFRICA Monday 6 February 2017 - 2:15pm

Lecture dedicated to Joost Van Der Westhuizen

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- Died Monday 6 February from Motor Neuron Disease at the age of 45 years
- South African Rugby Player
- 89 Test matches
- Prolific tri-scorer
- Member of the 2005 Rugby World Cup winning team

Causes of Skeletal Muscle Cramps

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Idiopathic	**Familial**	Autosomal cramping disease, familial nocturnal cramps, Continuous muscle fibers activity syndrome
	Sporadic	Continuous muscle fibers activity syndrome, Syndrome of progressive muscle spasm, alopecia and diarrhea (Satayashi's syndrome), nocturnal cramps, generalized myokymia, myokymia-hyperhidrosis syndrome
	Others	Muscle cramps in cancer patients
Symptomatic	**CNS disease**	Motorneuron disease, occupational dystonias, Parkinson's disease, Tetanus, multiple sclerosis, radiculopathies, plexopathies, peripheral neuropathies, others
	Muscular disease	Metabolic myopathies, mitochondrial myopathy, endocrine myopathy, dystrophinopathies, myotonia, inflammatory myopathies, others
	CVS disease	Venous disease, arterial disease, heart disease, hypertension
	Endocrine-metabolic	Thyroid disease, parathyroid disease, cirrhosis, isolated ACTH deficiency, Conn's, Addisons. Ureamia and dialysis
	Hydro-electrolyte	Generali… …sodium, potassium, ma…
	Toxic/pharmacological	…ermia
	Psychiatric	
Paraphysiological	**Occasional cramps**	
	Pregnancy	
	Sporting activity	

Exercise Associated Muscle Cramps (EAMC)

Parisi L, et al, Acta Neurol Scand 2003, 107: 176-186

Diagnostic Classification of EAMC

1. **Primary (Exercise as only apparent cause or precipitant)**
   - Intensity related, training related, fatigue, non-recurrent
   - Episodic (often isolated, single or irregular episode)

2. **Secondary (Exercise "unmasking" secondary factor/s)**
   - Cramping during exercise as a result of injury
   - Cramping during exercise "unmasking" underlying other chronic systemic disease
   - Drug associated (skeletal muscle or neurological)
   - Recurrent cramping
   - Other

Severity Classification of EAMC

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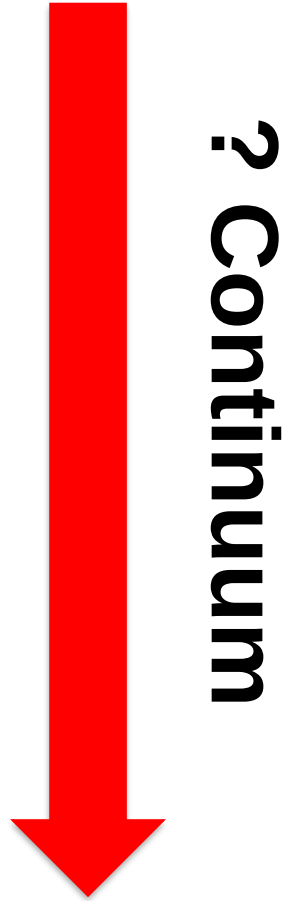
1. Cramp “prone state” / “Near cramping”
   - Onset of heightened neuromuscular excitability (“cramp prone state”) preceding EAMC (increased EMG activity, muscle fasciculation)
2. Less severe (“benign”) EAMC
   - Localized
   - Self limiting if activity stops
   - No systemic or CNS symptoms
3. Severe EAMC
   - Localized EAMC together with associated systemic symptoms / signs:
     - Confusion
     - Dizziness
     - Collapse
     - Nausea/vomiting
     - Dark urine
   - Diffuse (generalized) cramping (with or witout associated systemic symptoms / signs)



? Continuum

Schwellnus M, BJSM, 2009;43;401-408
Schwabe, K, Schwellnus M; et al: BJSM 2014
Hoffman, MD, Stuempfle KJ: Sports Medicine Open 2: 8; 2016

Epidemiology of EAMC

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1. Lifetime prevalence:

21km distance runners:	14%
42km marathon runners:	39%
56km ultra-marathon runners:	30%
Tri-athletes:	78%
Cyclists:	60%
Elite football players	46%

2. Incidence

Marathon runners (42km):	18% of runners in a marathon (1 in 4 runners)
161-km running race:	Cramping (14%), Near cramping (27%) (1 in 3 runners)
21km running race:	Serious EAMC (1 in 4000)
56km running race:	Serious EAMC (1 in 526)
Club Rugby (seasonal):	52%

3. Prevalence (% admissions) after an event:

Marathon:	10-22% of admissions
Ultra-marathon:	29% of admissions
Ironman:	55% of admissions

Manjra S, Schwellnus M, 1991; Grundling C, Schwellnus M, 1994; Sulzer N, Schwellnus M, 2001; Tindall R, Schwellnus M, 2003; Schwellnus M et al, 2012; Sumemrs K, et al, 2013; Schwabe, K, et al: 2014; Hoffman M D, et al (2016), Schwellnus, et al, 2016 (in preparation)

Etiology and risk factors - EAMC

Debate over the past 20 years

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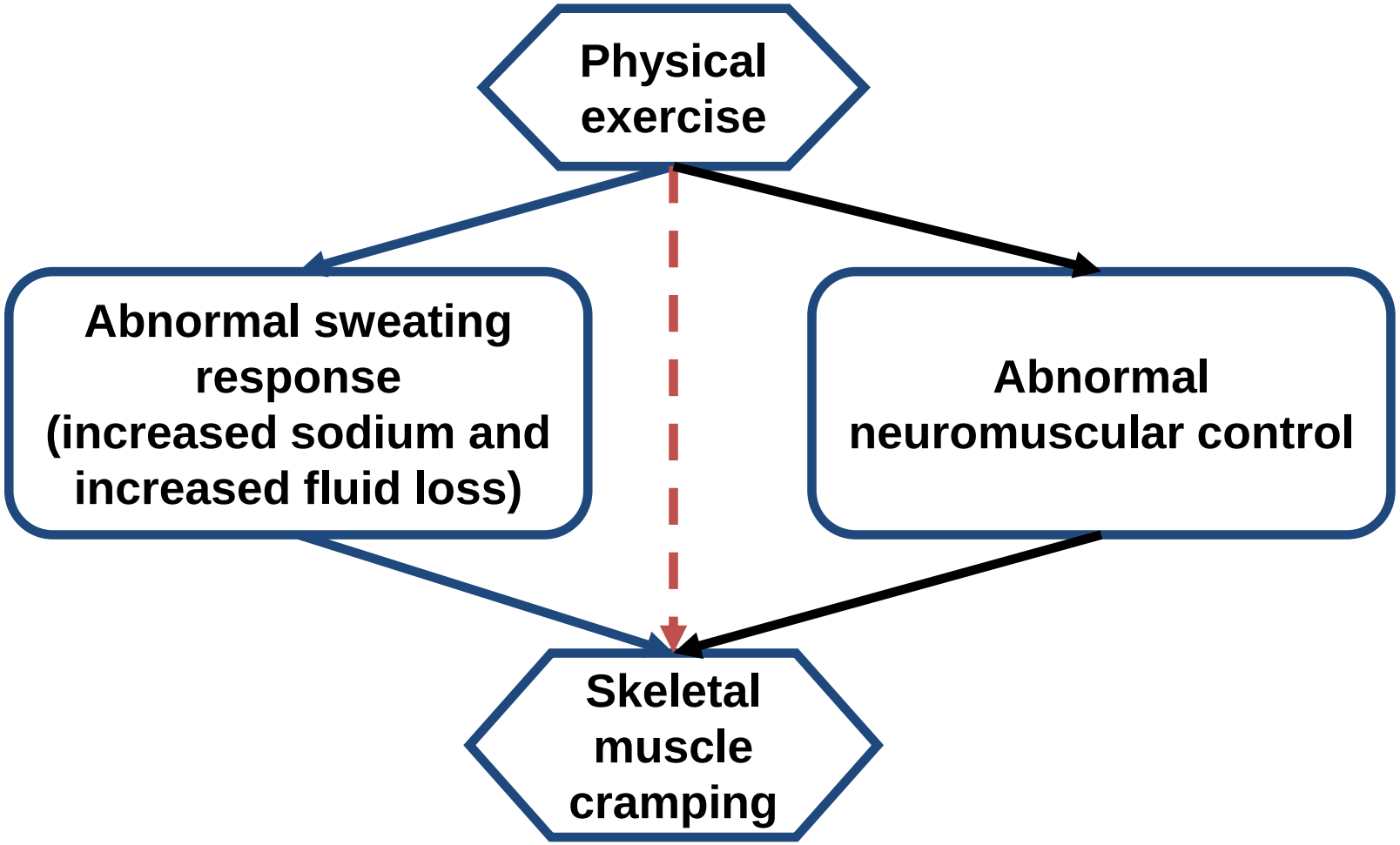
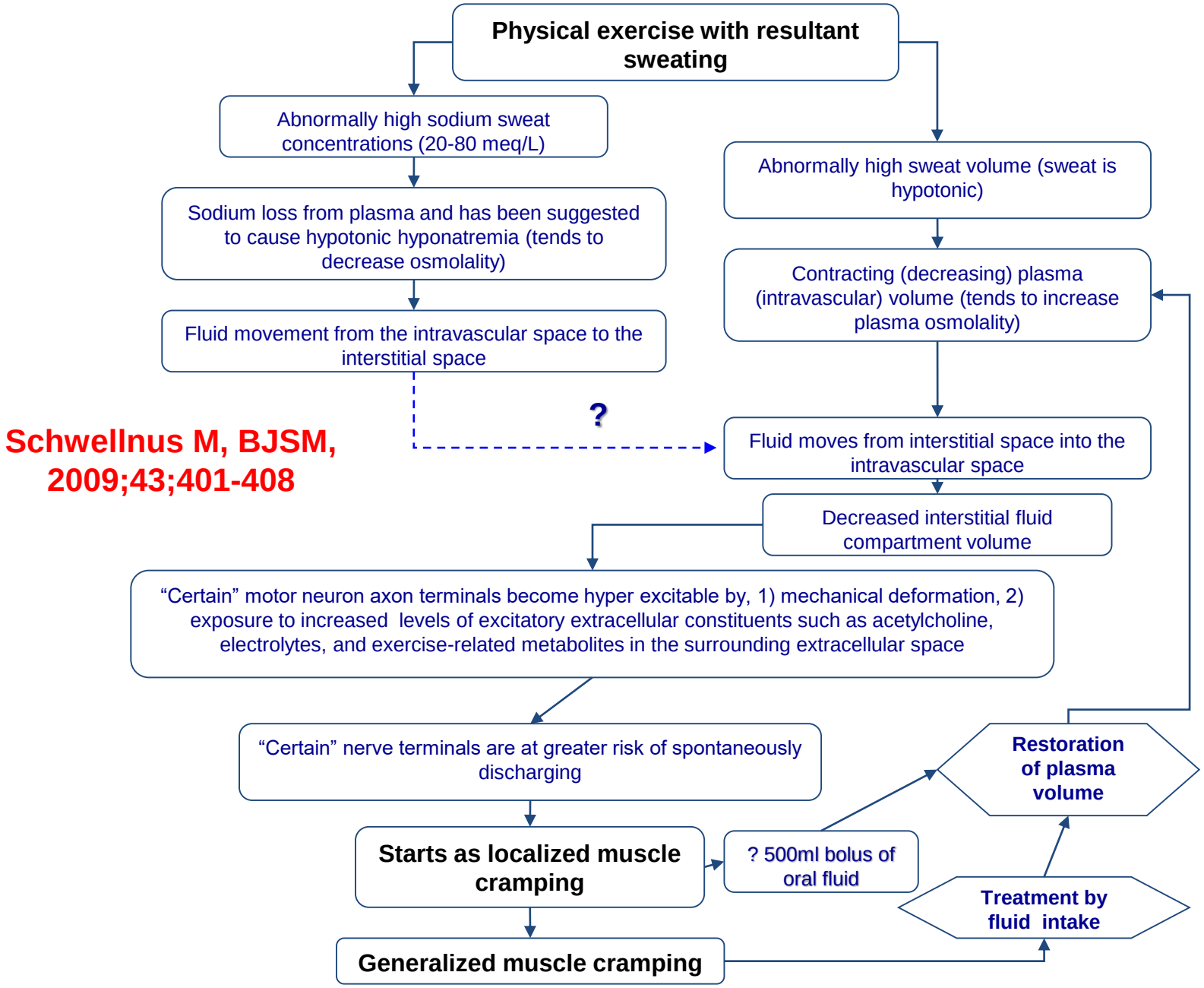
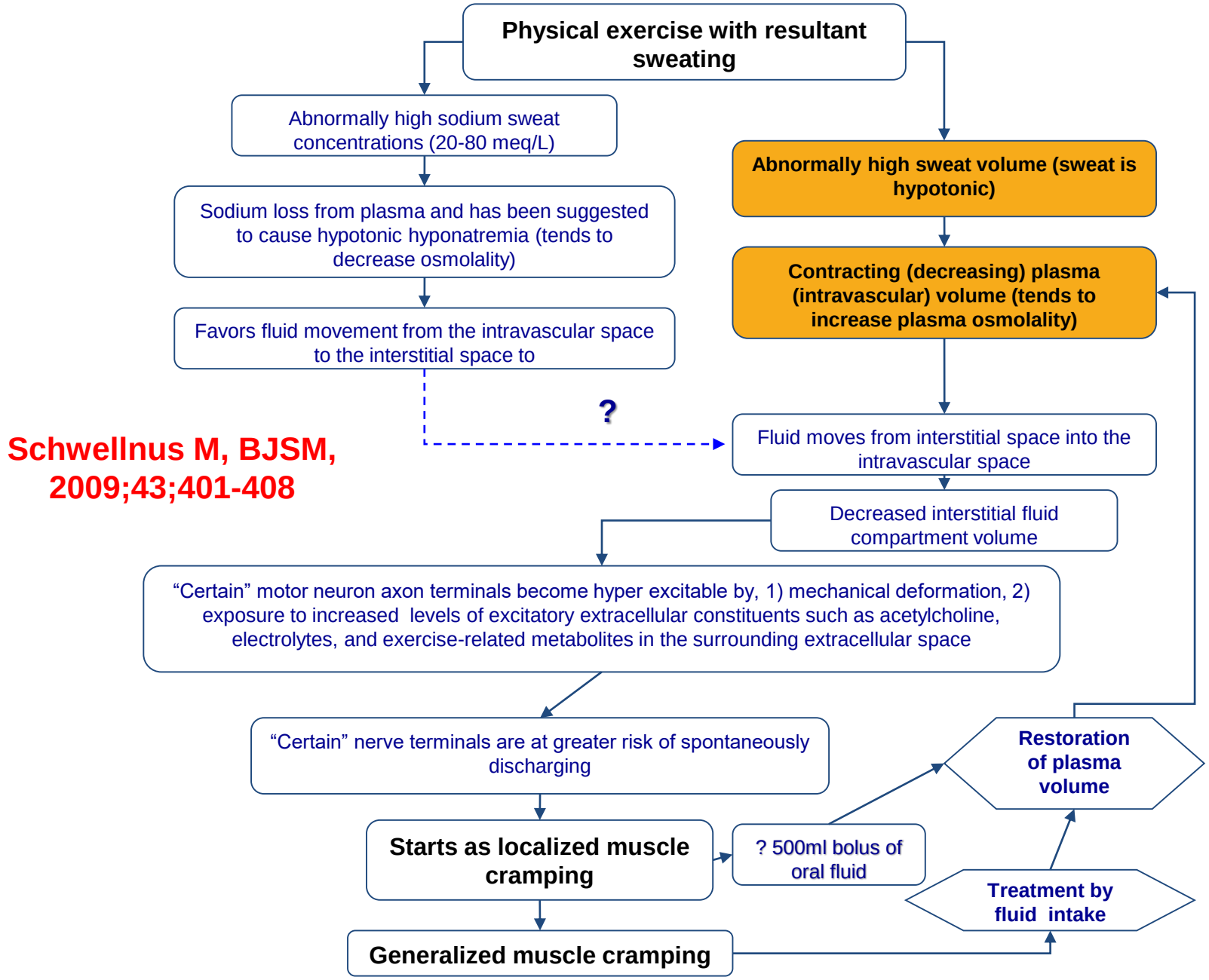


Schwellnus M, BJSM, 2009;43;401-408
Minetto M, et al; 2012, Exerc Sport Sci Rev, 2013; 41(1); 3-10
Edouard P; Sci & Sport, 2014; 29: 299-305
Nelson N et al: Muscle Nerve; 2016: 54: 177-185

Electrolyte deficit / dehydration hypothesis



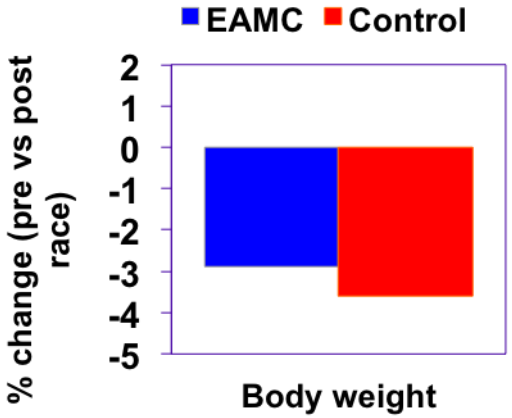
Dehydration hypothesis



Schwellnus M, BJSM, 2009;43;401-408

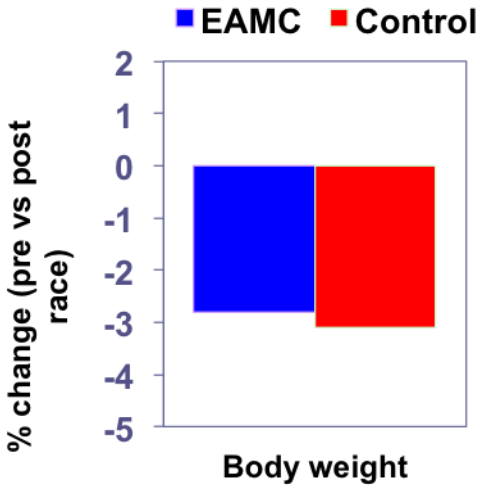
Evidence that athletes suffering from EAMC are more dehydrated compared with controls

Ultra-marathon runners (n=43)



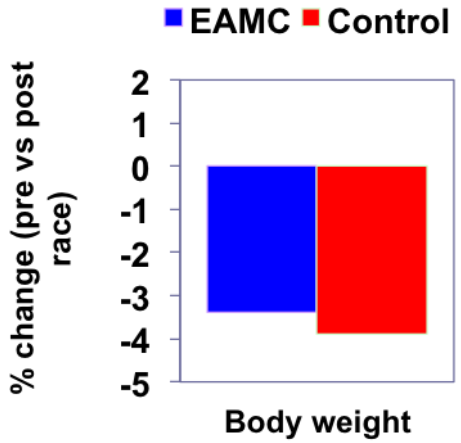
Schwellnus M, Nicol J, et al: Br J Sports Med, 2004, 38: 488-492

Ironman Tri-athletes (n=203)



Schwellnus, M, Drew N, et al Br J Sports Med 2011 45(8); 650-6

Ironman Tri-athletes (n= 18)



Sulzer N, Schwellnus M, et al: MSSE, 2005, 37(7): 1081-1085

Evidence that athletes suffering from EAMC are more dehydrated compared with controls: 2016 study

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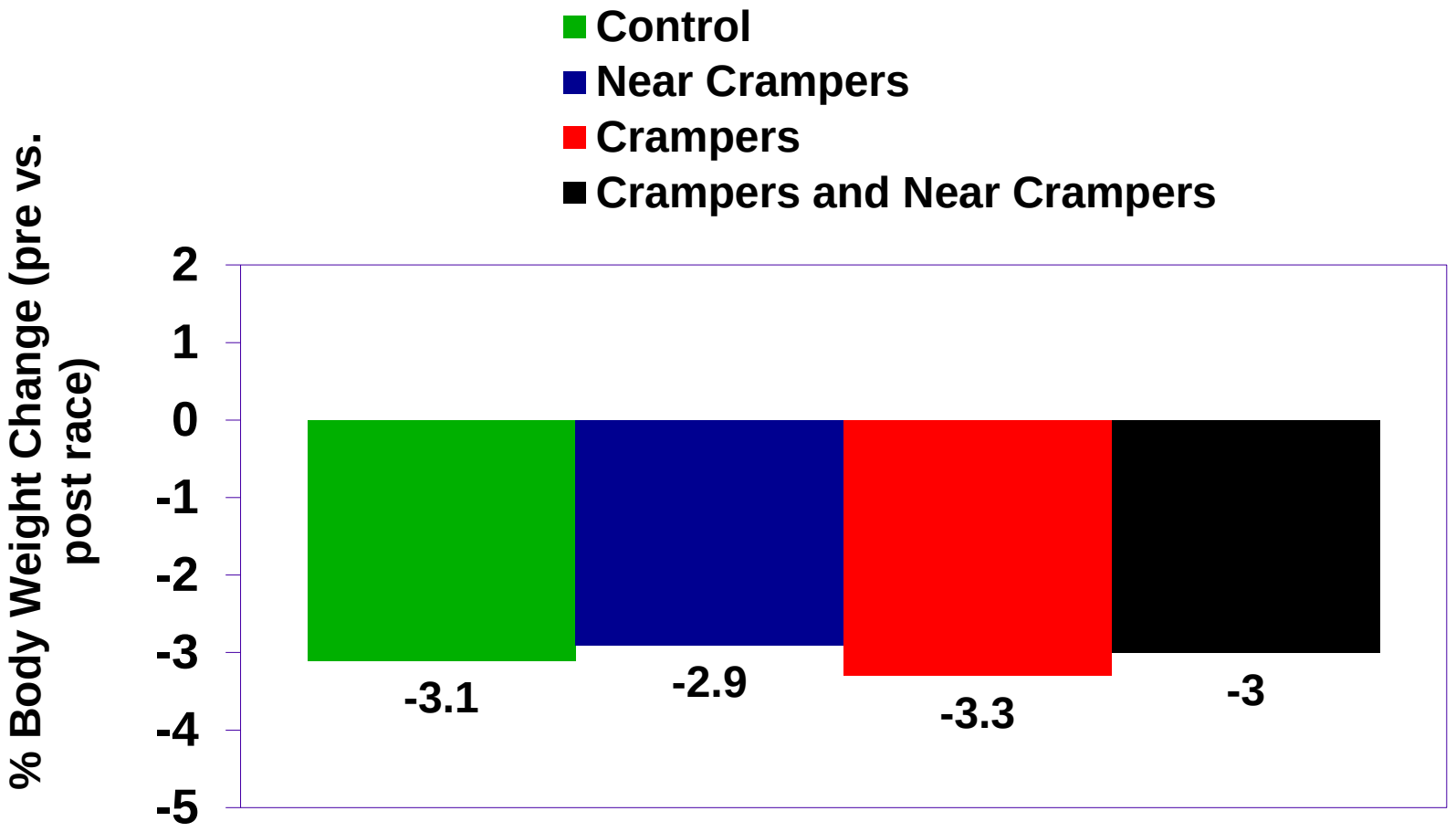
160-km Ultra-marathon runners (n=181)



Hoffman, MD, Stuempfle KJ: Sports Medicine Open 2: 8; 2016

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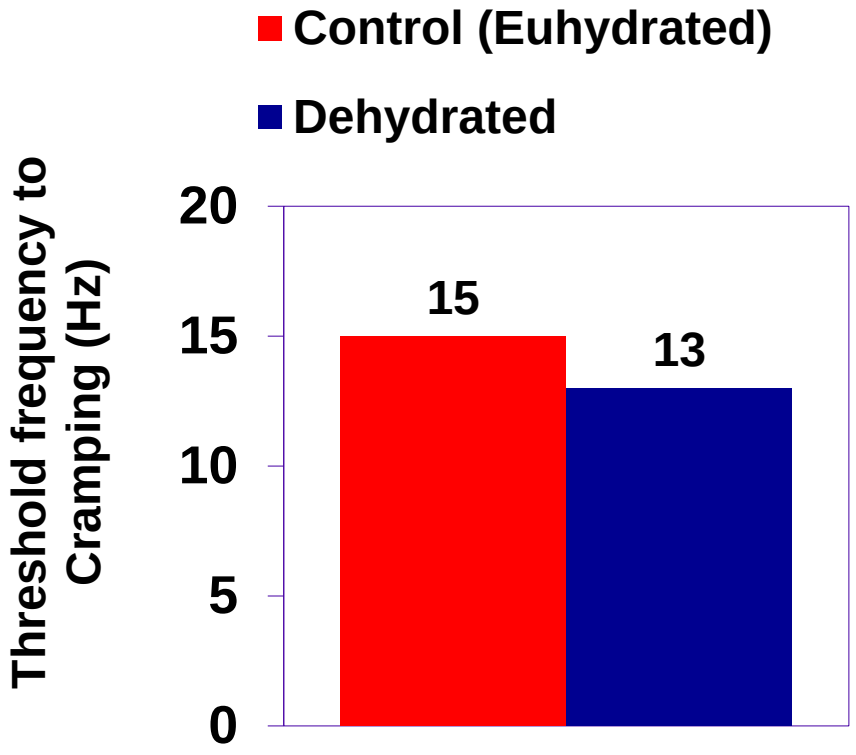
Is more serious dehydration (4.7% BW loss) associated with EAMC susceptibility?

- 10 euhydrated, unacclimated males exercised with their non-dominant limb on a cycle ergometer every 15 min at a moderate intensity until 5% body mass loss or volitional exhaustion
- Dominant limb flexor hallucis brevis cramp threshold frequency, cramp EMG amplitude and cramp intensity were measured
- Cramp variables were re-assessed pre- and post-hypo-hydration (11% PV reduction)



Braulick K, Miller K, et al; BJSM, 2013; 47: 710-714

Electrolyte deficit hypothesis

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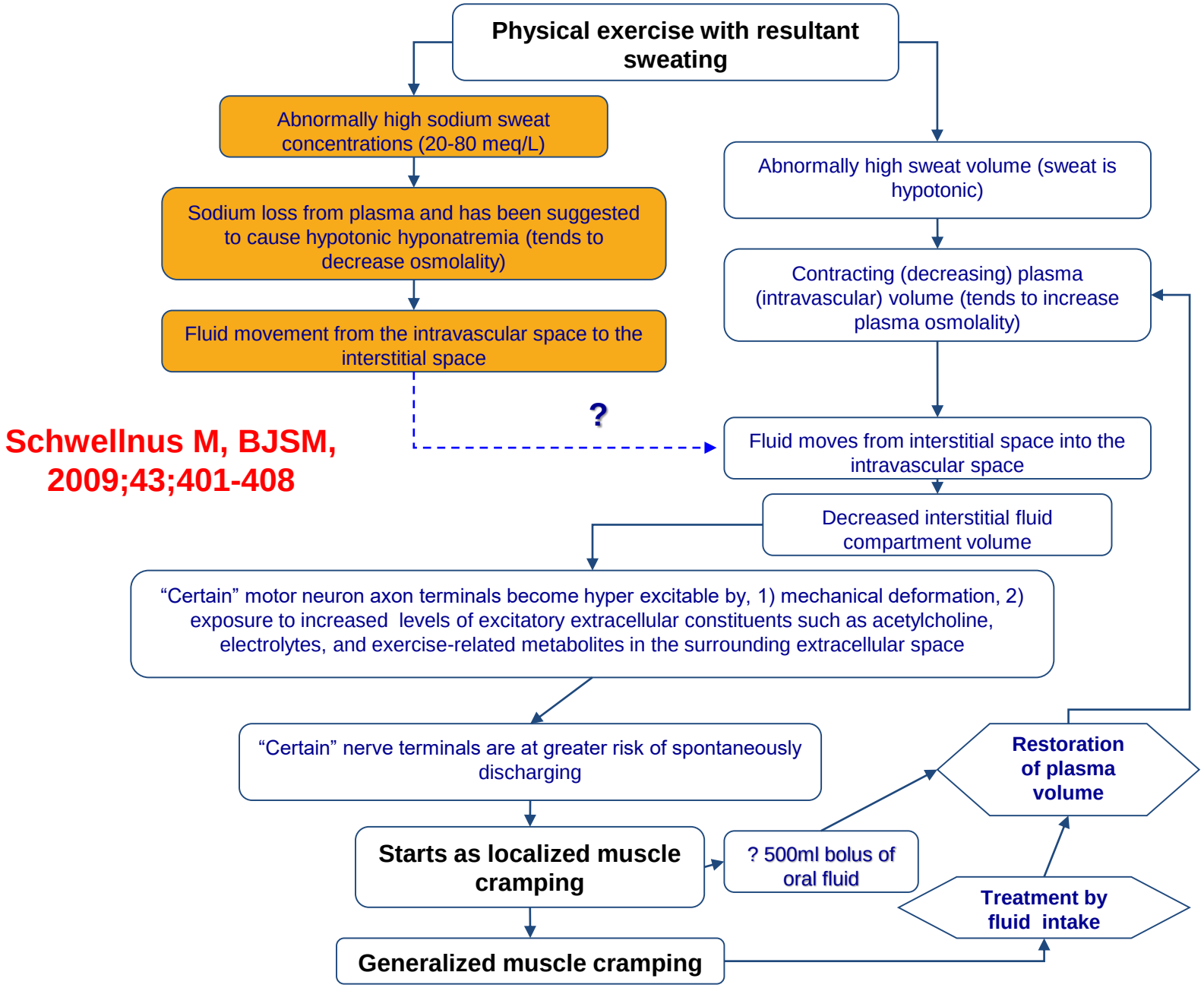

Evidence for serum electrolyte abnormalities associated with EAMC in athletes

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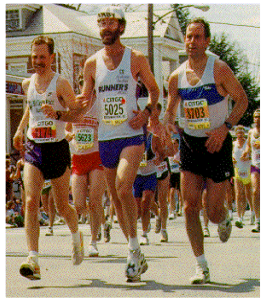
Marathon runners (n=43)

	Crampers (n=21)	Controls (n=22)
Na^+ (mmol/L)	140 (3)	142 (2)
K^+ (mmol/L)	4.9 (0.6)	4.7 (0.5)
Ca^{++} (mmol/L)	2.3 (0.2)	2.2 (0.1)
Mg^{++} (mmol/L)	0.7 (0.1)	0.7 (0.1)
Osmolality (mosmol/L)	280 (16)	284 (10)
Glucose (mmol/L)	6.8 (1.9)	6.5 (2.0)

Schwellnus M, Nicol J, et al: Br J Sports Med, 2004, 38: 488-492



Ironman triathletes (n=18)

	Crampers (n=9)	Controls (n=9)
Na^+ (mmol/L)	140 (2)	143 (3)
K^+ (mmol/L)	4.4 (0.6)	4.2 (0.5)
Mg^{++} (mmol/L)	0.9 (0.2)	0.8 (0.1)
Chloride (mmol/L)	101 (3)	104 (4)
Glucose (mmol/L)	6.8 (1.9)	6.5 (2.0)

Sulzer N, Schwellnus M, et al: MSSE, 2005, 37(7): 1081-1085

Ironman triathletes (n=209)

	Crampers (n=43)	Controls (n=166)
Pre-race Na^+ (mmol/L)	139.8 (1.8)	139.8 (1.5)
Post-race Na^+ (mmol/L)	140.2 (3.4)	139.6 (2.5)
Pre-race K^+ (mmol/L)	4.17 (0.31)	4.12 (0.21)
Post-race K^+ (mmol/L)	4.29 (0.46)	4.20 (0.37)
Pre-race Cl^- (mmol/L)	101.7 (1.7)	101.6 (1.9)
Post-race Cl^- (mmol/L)	100.7 (2.5)	100.5 (2.1)

Schwellnus, M, Drew N, et al Br J Sports Med 2011 45(8); 650-6

Post-race serum sodium concentration is not associated with EAMC in runners

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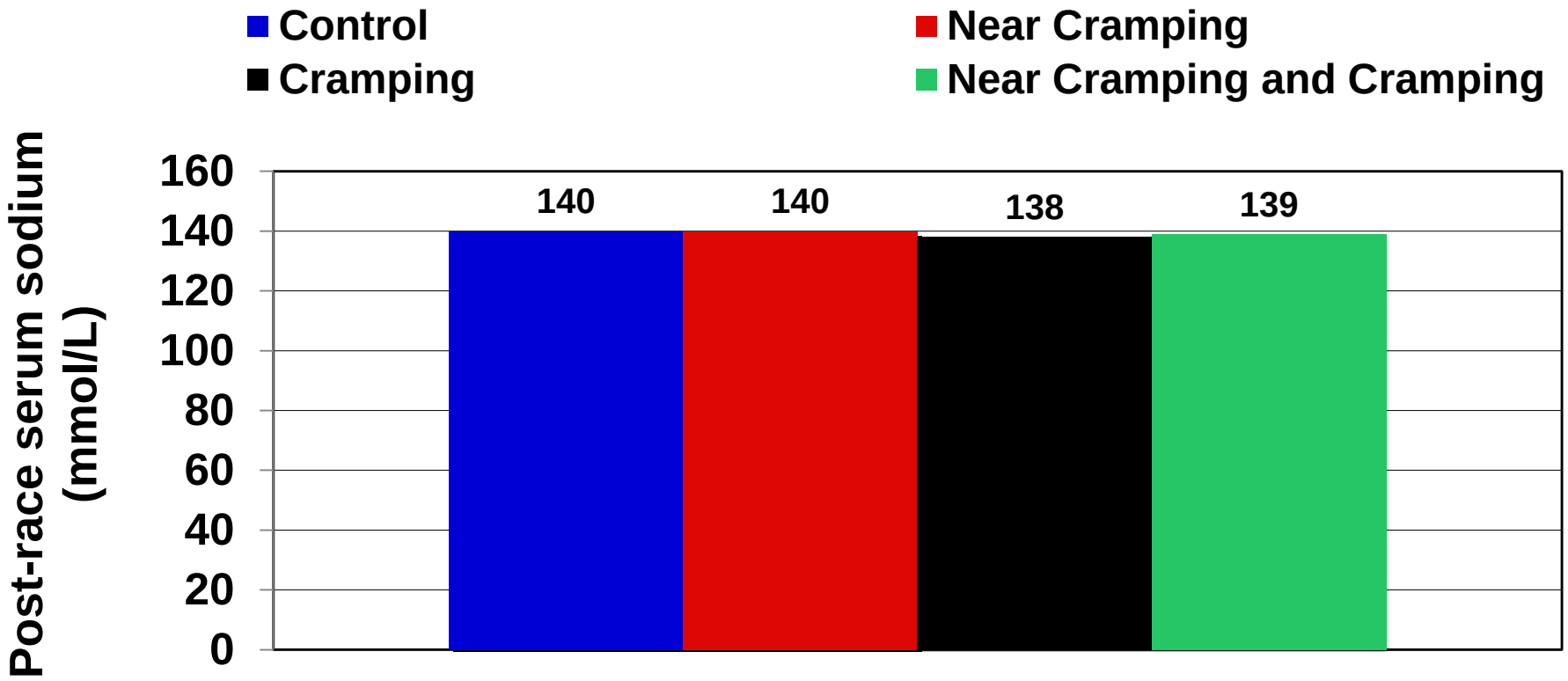
Ultra-marathon runners
181 runners completing a 161km ultra-marathon race



Hoffman, MD, Stuempfle KJ: Sports Medicine Open: 2(8); 2016

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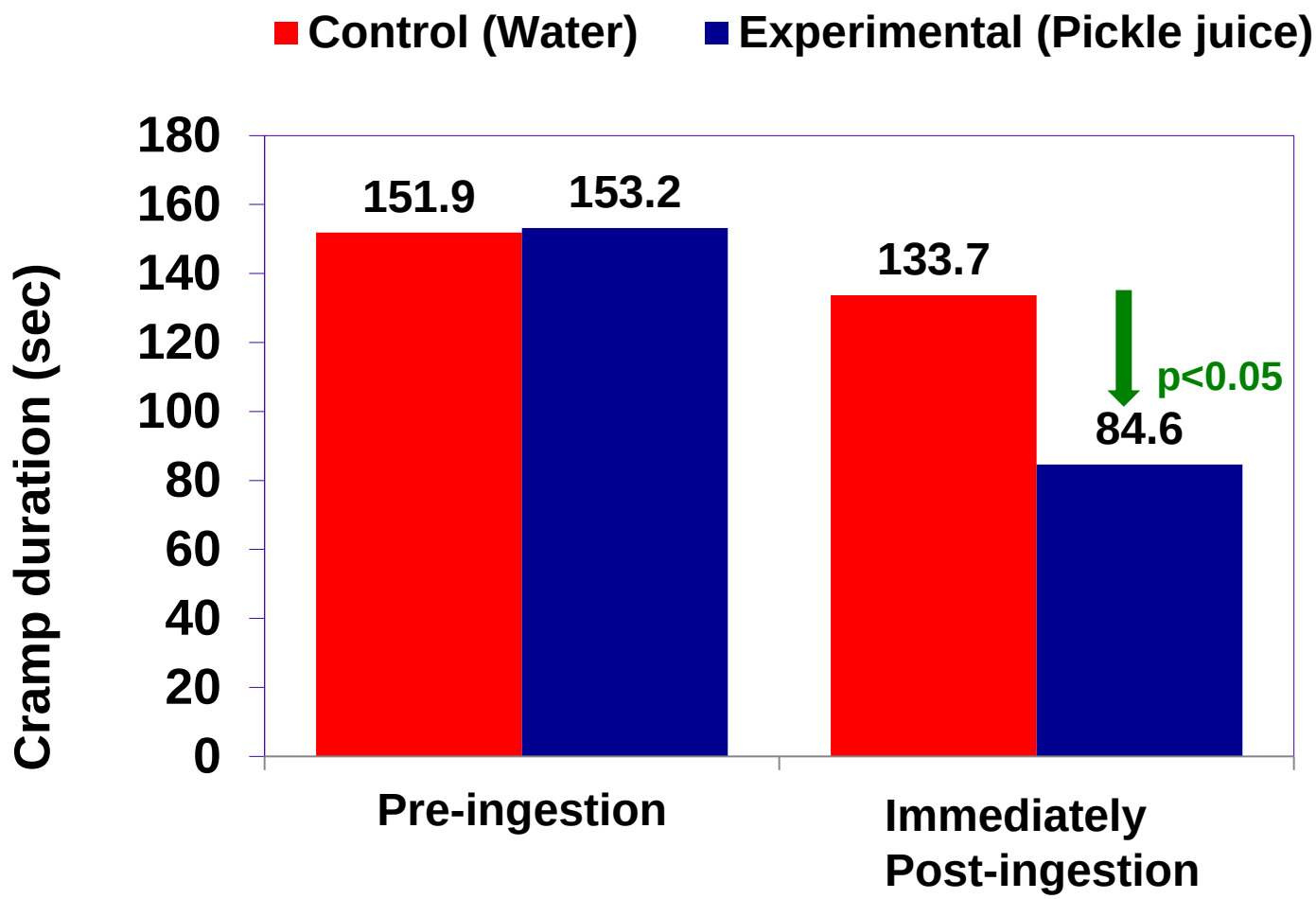
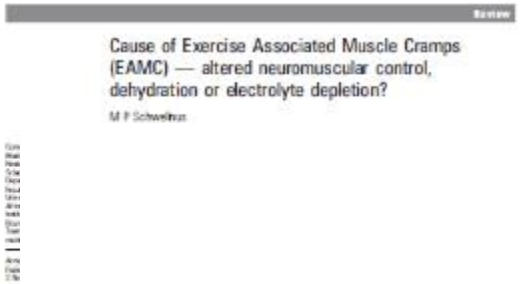
Laboratory study evidence:

Does oral ingestion of a high Na+ and electrolyte solution ("pickle juice") alter cramp duration and EMG activity?



Miller K, et al; MSSE, 2010; 42: 953-961

2017: EAMC and electrolyte abnormalities or dehydration

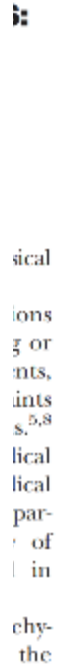


Review

Cause of Exercise Associated Muscle Cramps (EAMC) — altered neuromuscular control, dehydration or electrolyte depletion?

M P Schwellnus

Five reviews (2009, 2013, 2014, 2016 X2) all conclude that evidence supporting the "serum electrolytes and dehydration" hypothesis for EAMC is poor



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Novel finding from Laboratory study:

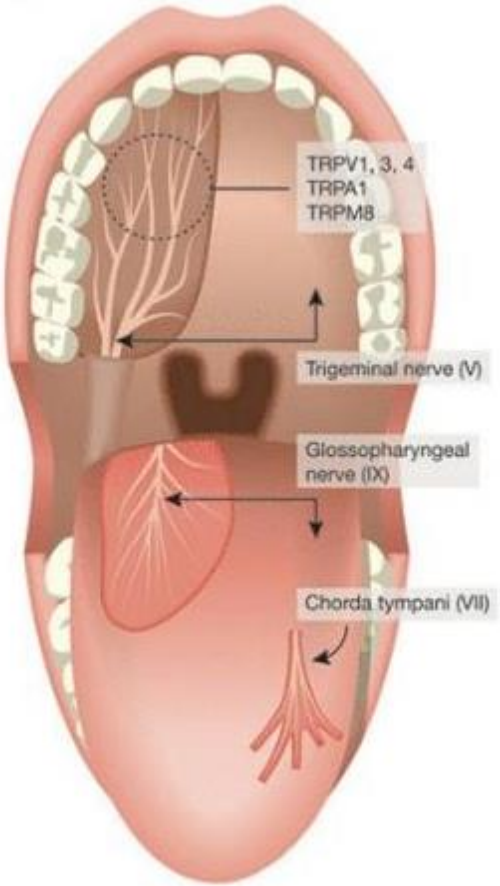
Does oral ingestion of a high Na+ and electrolyte solution ("pickle juice") alter cramp duration and EMG activity?

Rapid inhibition of the electrically induced cramps reflects a neurally mediated reflex that originates in the oropharyngeal region and acts to inhibit the firing of alpha motor neurons of the cramping muscle

Miller K, et al; MSSE, 2010; 42: 953-961

Introducing TRP (Transient Receptor Potential) channels

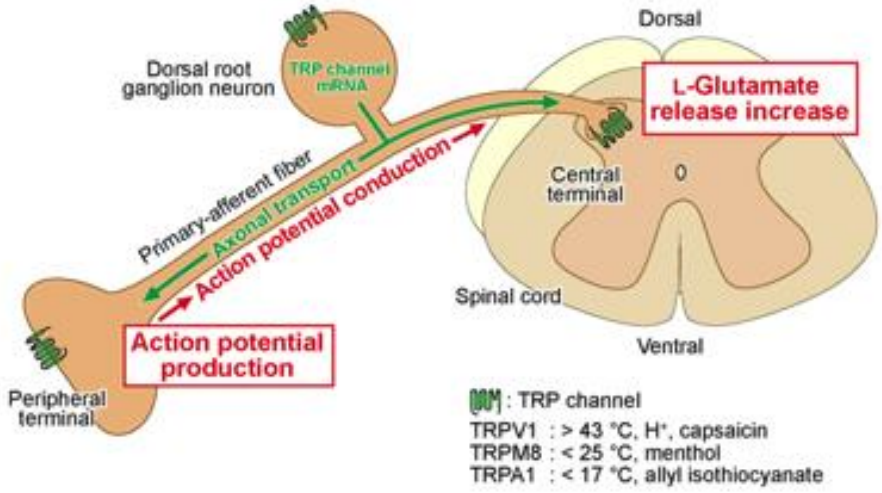
- **Membrane receptors contributing to the transduction of noxious signals on free nerve ending**
- **Sub-populations (TRPV1, TRPA1, and TRPM8) are primary extrinsic afferent nerves in the GIT (mouth, esophagus, stomach, intestine, and colon)**
- **Act as afferent nociceptors for thermal and chemical stimuli (pungent irritants from mustard, onion and garlic, as well as volatile environmental toxins)**



Seminars Immunopath; 2016 ; 38 (3)

TRP channels and possible role EAMC – novel mechanism?

- Transient receptor potential (TRP) agonists (e.g. chemical compounds in “pickle juice”) may have a role in the treatment of acute EAMC
- Stimulation of oral/esophageal TRP ion channels may the the mechanism for the observed reduction in laboratory induced muscle cramps (electrical stimlation) by “pickle juice”
- Clincial trials of TRP agonists in the management of prevention of EAMC are under way
- Beware of treating the symptoms and not the cause!



Alternate hypothesis for the etiology and pathophysiology of EAMC: 1997

"Exercise associated muscle cramping occurs as a result of an imbalance between the excitatory and inhibitory input to the alpha motor neuron"

Schwellnus M et al: J Sports Science, 1997, 15(3): 277-285

Hypothesis that EAMC is related to abnormal neuromuscular control

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1997

Hypothesis that EAMC is caused by sustained abnormal spinal reflex activity, which appears to be secondary to muscle fatigue

Journal of Sports Sciences, 1997, 15, 277-285

Aetiology of skeletal muscle 'cramps' during exercise: A novel hypothesis

M.P. SCHWELLNUS,* E.W. DERMAN and T.D. NOAKES

MRC/UCT Bioenergetics of Exercise Research Unit, University of Cape Town Medical School, Sports Science Institute of South Africa, PO Box 115, Newlands 7725, South Africa

Accepted 3 September 1996

The aetiology of exercise-associated muscle cramps (EAMC), defined as 'painful, spasmodic, involuntary contractions of skeletal muscle during or immediately after physical exercise', has not been well investigated and is therefore not well understood. This review focuses on the physiological basis for skeletal muscle relaxation, a historical perspective and analysis of the commonly postulated causes of EAMC, and known facts about EAMC from recent clinical studies. Historically, the causes of EAMC have been proposed as (1) inherited abnormalities of substrate metabolism ('metabolic theory'), (2) abnormalities of fluid balance ('dehydration theory'), (3) abnormalities of serum electrolyte concentrations ('electrolyte theory') and (4) extreme environmental conditions of heat or cold ('environmental theory'). Detailed analyses of the available scientific literature including data from recent studies do not support these hypotheses for the causes of EAMC. In a recent study, electromyographic (EMG) data obtained from runners during EAMC revealed that baseline activity is increased (between spasms of cramping) and that a reduction in the baseline EMG activity correlates well with clinical recovery. Furthermore, during acute EAMC the EMG activity is high, and passive stretching is effective in reducing EMG activity. This relieves the cramp probably by invoking the inverse stretch reflex. In two animal studies, abnormal reflex activity of the muscle spindle (increased activity) and the Golgi tendon organ (decreased activity) has been observed in fatigued muscle.

We hypothesize that EAMC is caused by sustained abnormal spinal reflex activity which appears to be secondary to muscle fatigue. Local muscle fatigue is therefore responsible for increased muscle spindle afferent and decreased Golgi tendon organ afferent activity. Muscles which cross two joints can more easily be placed in shortened positions during exercise and would therefore decrease the Golgi tendon organ afferent activity. In addition, sustained abnormal reflex activity would explain increased baseline EMG activity between acute bouts of cramping. Finally, passive stretching invokes afferent activity from the Golgi tendon organ, thereby relieving the cramp and decreasing EMG activity.

Keywords: Exercise, fatigue, muscle cramps.

Evidence for the “altered neuromuscular control” hypothesis (1997 - 2017)

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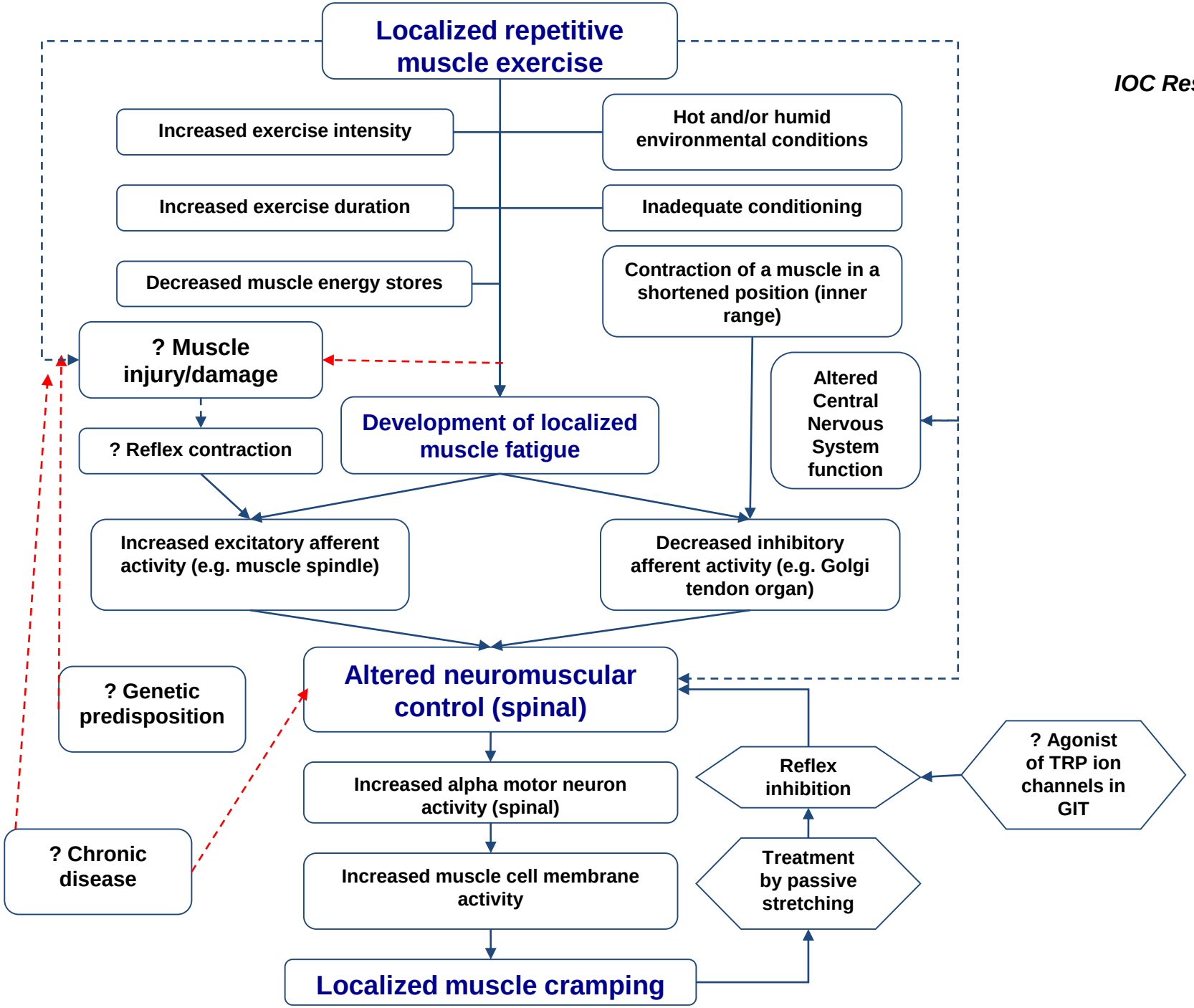
1. Historical data
2. Animal studies
3. Neurological literature (muscle stimulation)
4. EAMC in athletes - laboratory studies:
   - EMG activity during fatiguing exercise in runners
   - Repetitive muscle contraction causes cramping
5. EAMC in athletes - field studies: EMG activity in runners with acute EAMC
6. EAMC in athletes – Risk factors (epidemiological studies)


Localized repetitive muscle exercise
Increased exercise intensity
Hot and/or humid environmental conditions
Increased exercise duration
Inadequate conditioning
Decreased muscle energy stores
Contraction of a muscle in a shortened position (inner range)
? Muscle injury/damage
Altered Central Nervous System function
? Reflex contraction
Development of localized muscle fatigue
Increased excitatory afferent activity (e.g. muscle spindle)
Decreased inhibitory afferent activity (e.g. Golgi tendon organ)
? Genetic predisposition
Altered neuromuscular control (spinal)
Reflex inhibition
? Agonist of TRP ion channels in GIT
Increased alpha motor neuron activity (spinal)
? Chronic disease
Increased muscle cell membrane activity
Treatment by passive stretching
Localized muscle cramping

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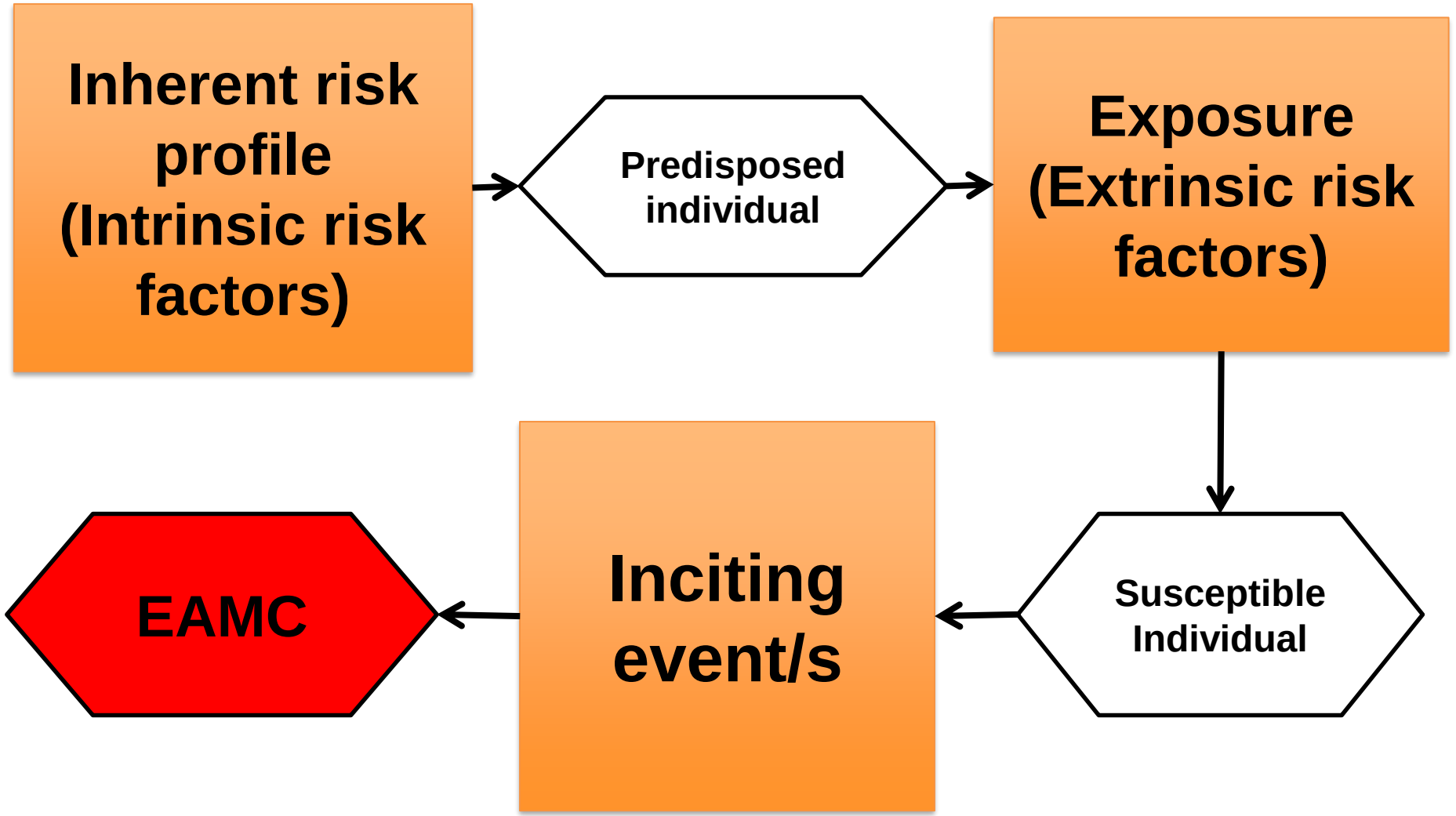
Risk factors for EAMC during exercise – risk model



Risk factors for History of EAMC

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ORIGINAL RESEARCH

Factors Associated With a Self-Reported History of Exercise-Associated Muscle Cramps in Ironman Triathletes: A Case–Control Study

Gavin Shang, MBBCh, MPhil, Malcolm Collins, PhD,*†‡ and Martin P. Schwellnus, MBBCh, MSc(Med), MD*‡*

Factors associated with a history of EAMC in Ironman triathletes were:

a. Exercising at a higher intensity
b. Positive family history
c. History of a soft tissue injury

Shang G, Collins M, Schwellnus M, Clin J Sport Med, 21 (3) May 2011

Risk factors for EAMC

Prospective cohort study in ultra-distance runners

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Original article

Increased running speed and pre-race muscle damage as risk factors for exercise-associated muscle cramps in a 56 km ultra-marathon: a prospective cohort study

Martin P Schwellnus,[1,2] Siddieq Allie,[1] Wayne Derman,[1,2] Malcolm Collins[1–3]

Risk factors associated with EAMC in ultra-distance runners:

a. Exercising at a higher intensity (increased speed)

b. Pre-race muscle damage

Schwellnus M, Allie S, Collins M, Derman W, BJSM, June 2011

Independent Risk Factors for EAMC in Ironman triathletes

Prospective cohort study

IOC Research Centre

Original article

Increased running speed and previous cramps rather than dehydration or serum sodium changes predict exercise-associated muscle cramping: a prospective cohort study in 210 Ironman triathletes

Martin P Schwellnus,[1,2] Nichola Drew,[1] Malcolm Collins[1–3]

Two independent risk factors for the development of self-reported EAMC in Ironman triathletes were:

a. past history of muscle cramping (in particular the number of EAMC reported in the last 10 races)
b. overall faster race time during the Ironman triathlon

Schwellnus, M, Drew N, et al Br J Sports Med 2011 45(8); 650-6

Risk Factors for EAMC in Rugby League Players

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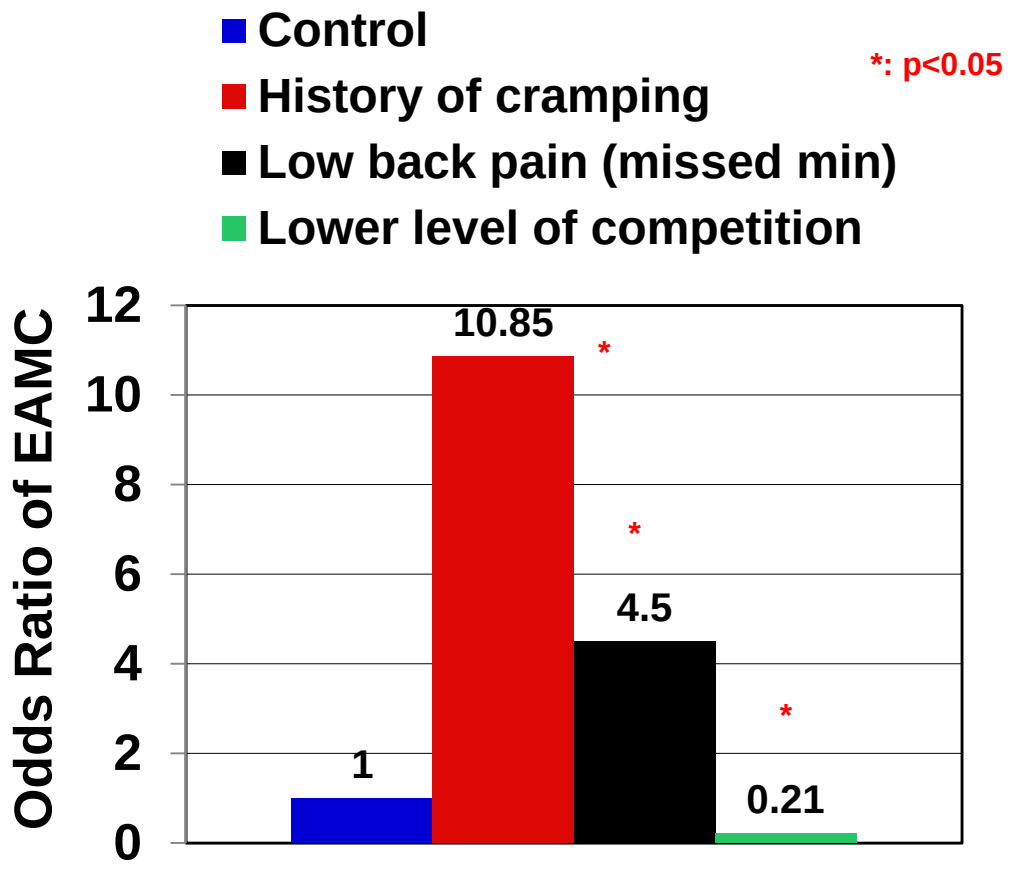
Prospective cohort study over one season

Predictors of EAMC (logistic regression modeling)

- **Competition level**
- **Age**
- **Ethnicity**
- **Playing position**
- **History of cramping**
- **Pre-cramping**
- **Low back pain**
- **Foot orthotic usage,**
- **Foot posture**
- **Foot strike**
- **Muscle flexibility**
- **Calf girth**
- **Hydration status**
- **Number of games played**



Summers K, et al: 2014, J Strength Cond Res, 28(3, 774-783)

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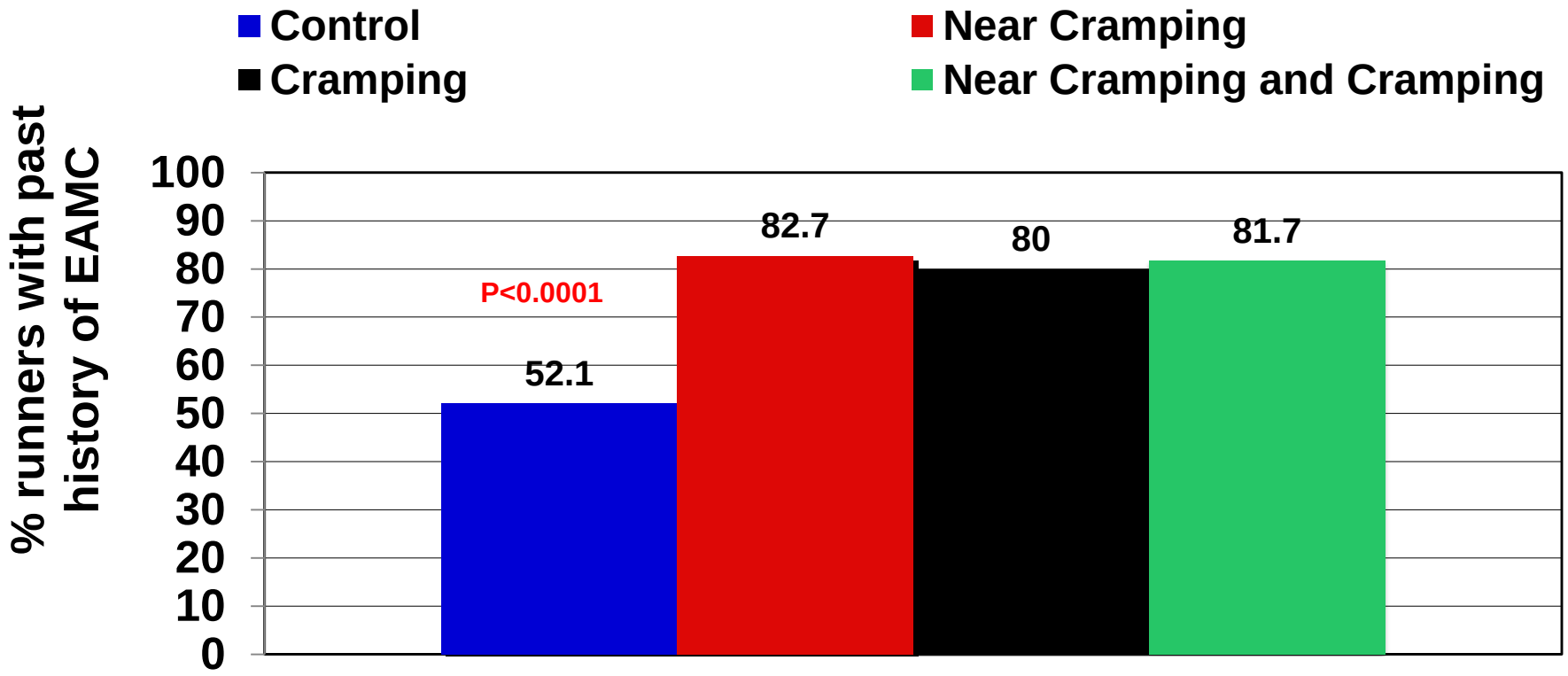
Prior history of EAMC is associated with the development of EAMC

Ultra-marathon runners
181 runners completing a 161km ultra-marathon race



Hoffman, MD, Stuempfle KJ: Sports Medicine Open: 2(8); 2016

Genetic Risk Factors for History of Exercise Associated Muscle Cramping (EAMC) in triathletes

IOC Research Centre

1. The COL5A1 gene is a potential marker for the development of EAMC
2. COL5A1 BstUI RFLP is associated with history of EAMC
3. The CC genotype may be "protective" against a history of developing EAMC
4. These effects may be mediated through the effects that type V collagen exerts on collagen fiber diameter and strength in the endo- and perimysium

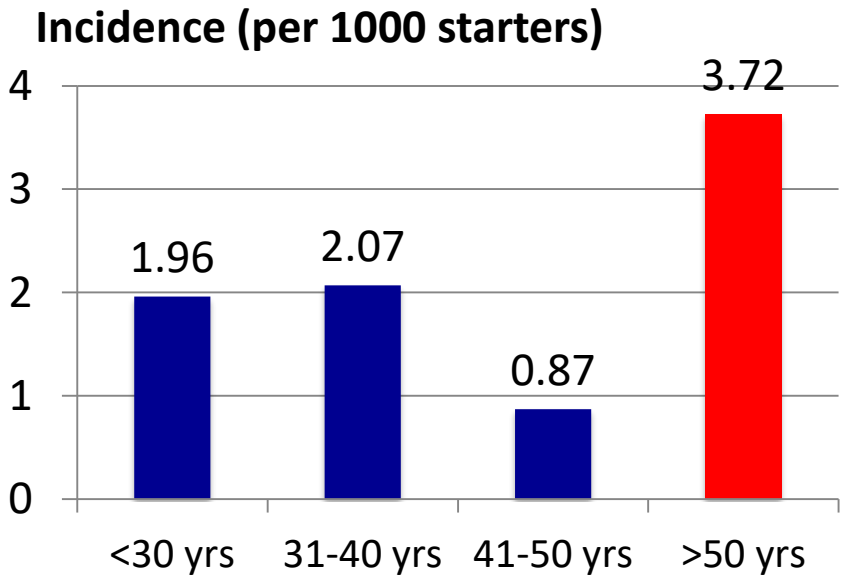
K O'Connell, M Posthumus, M Schwellnus, M Collins; CJSM 2012 (in review)

Risk factors associated with a serious EAMC in recreational 56km distance runners

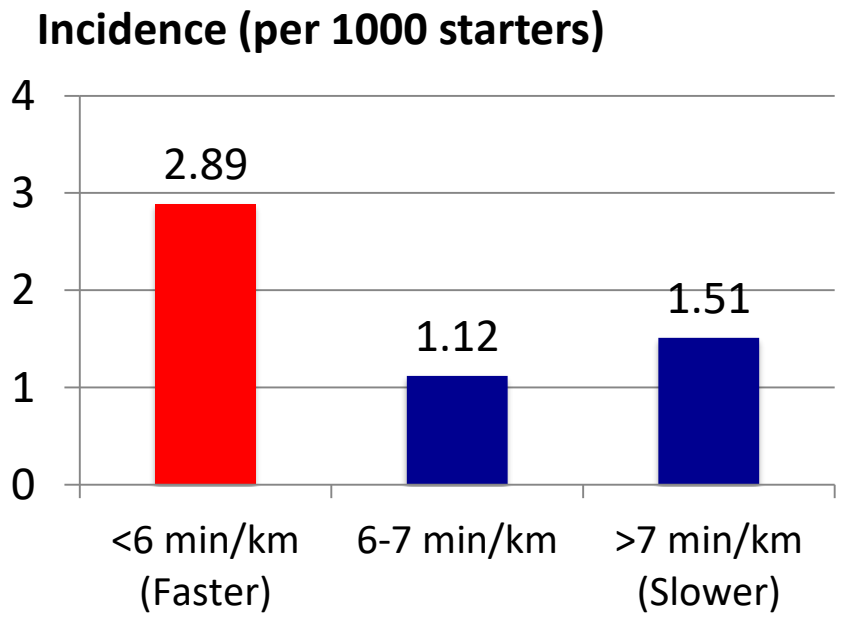
Prospective cohort study in 26 354 runners presenting with serious EAMC

Two independent risk factors

Age group



Running pace

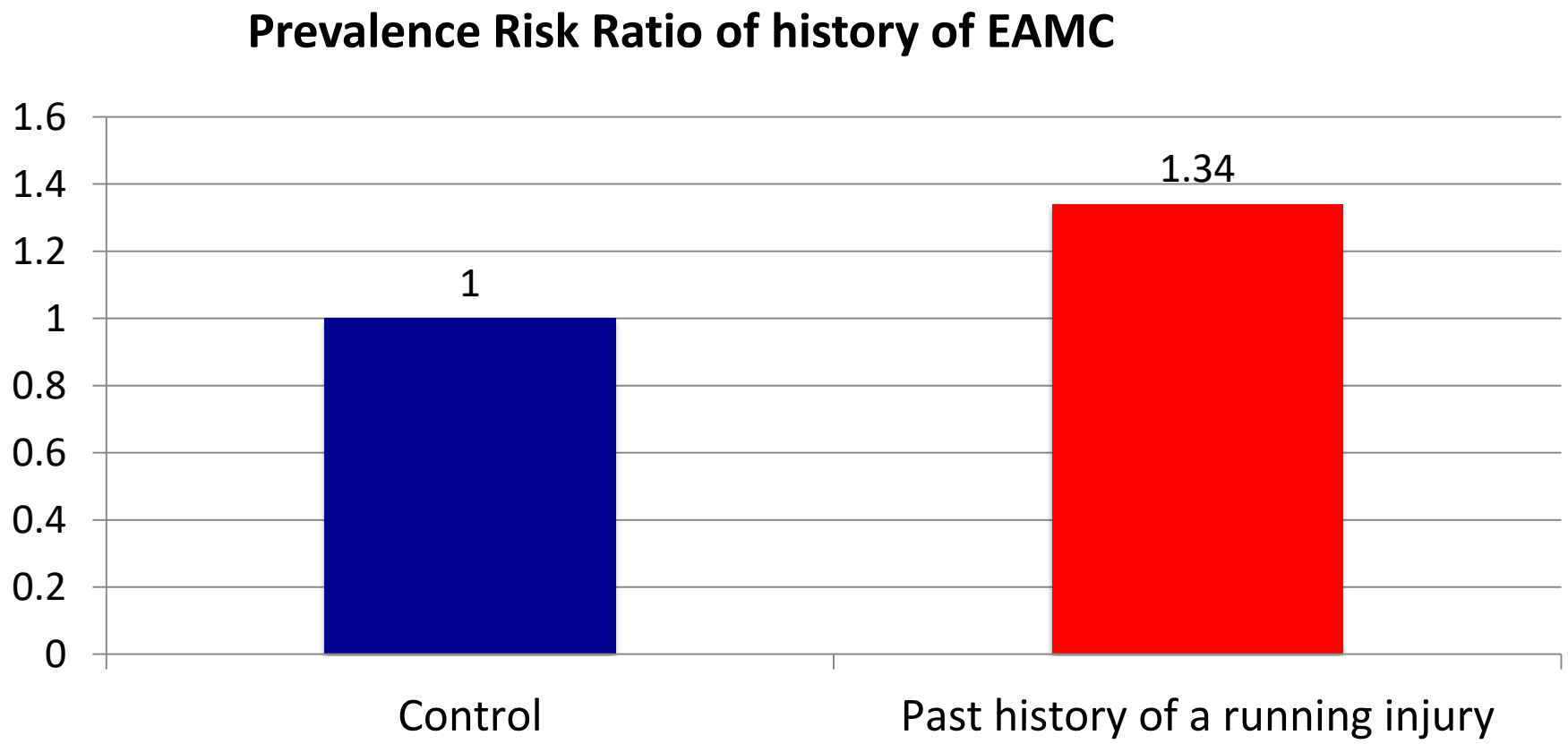


Schwabe K, Schwellnus M, Derman W, Swanevelder S, Jordaan E: Br J Sports Med 2014;48:891–897

IOC Research Centre

Past history of a running injury as a risk factor for EAMC in recreational distance runners

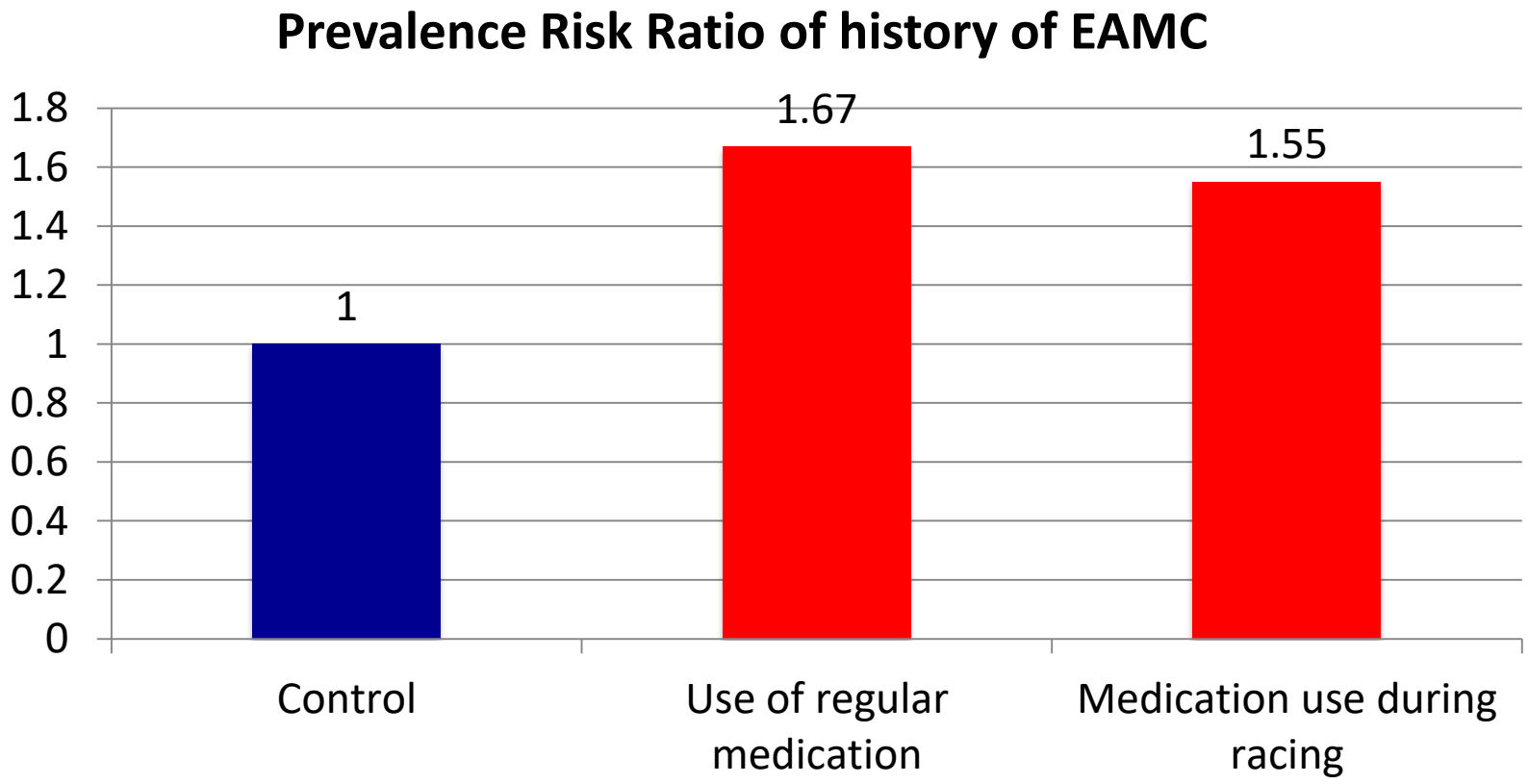
Cross sectional study in 15 778 runners with history of EAMC



Schwellnus M, Swanevelder S, Derman W, Jordaan E; 2017 (in review)

Medication use as a risk factor for EAMC in recreational distance runners

Cross sectional study in 15 778 runners with history of EAMC



Schwellnus M, Swanevelder S, Derman W, Jordaan E; 2017 (in review)

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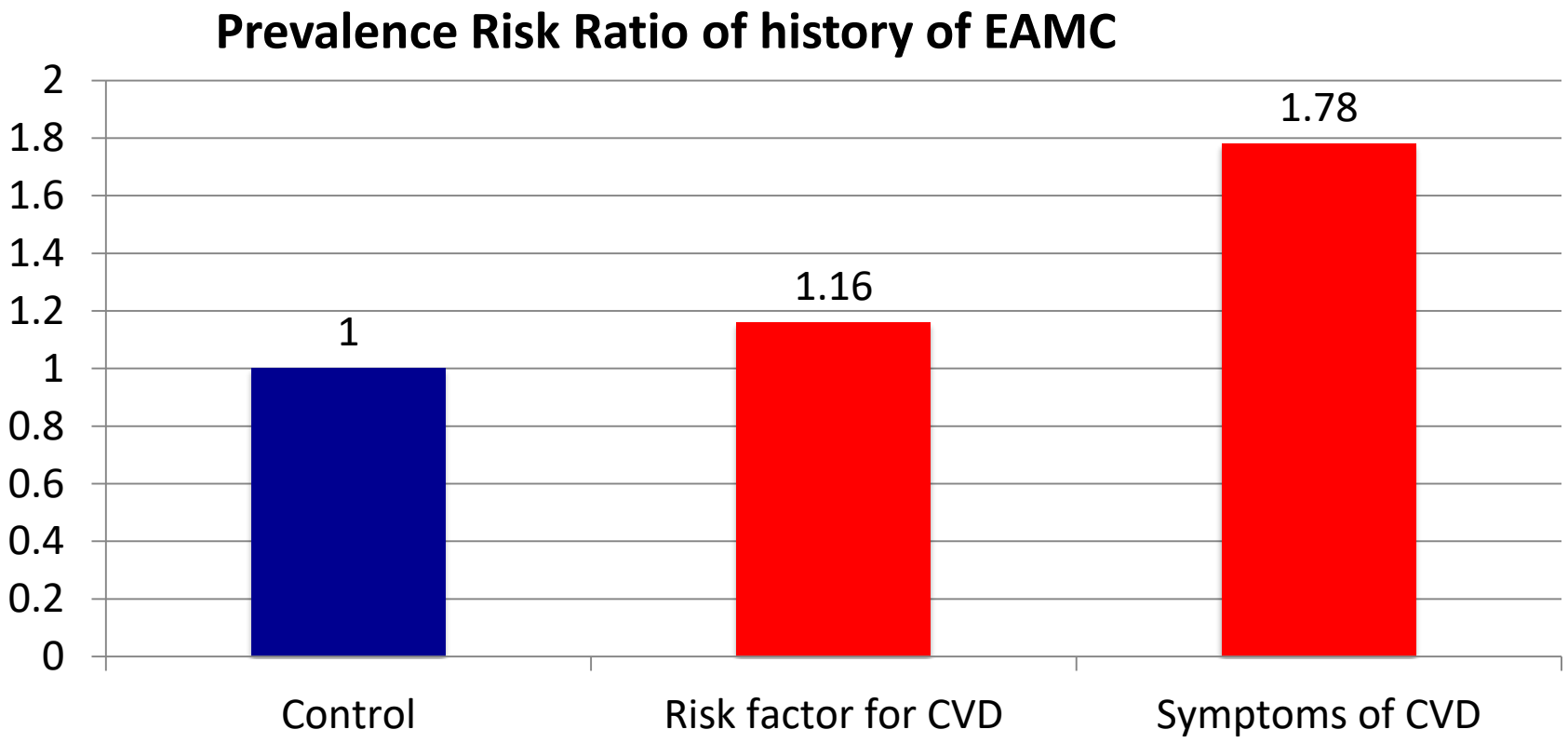
Cardiovascular disease as a risk factor for EAMC in recreational distance runners

Cross sectional study in 15 778 runners with history of EAMC

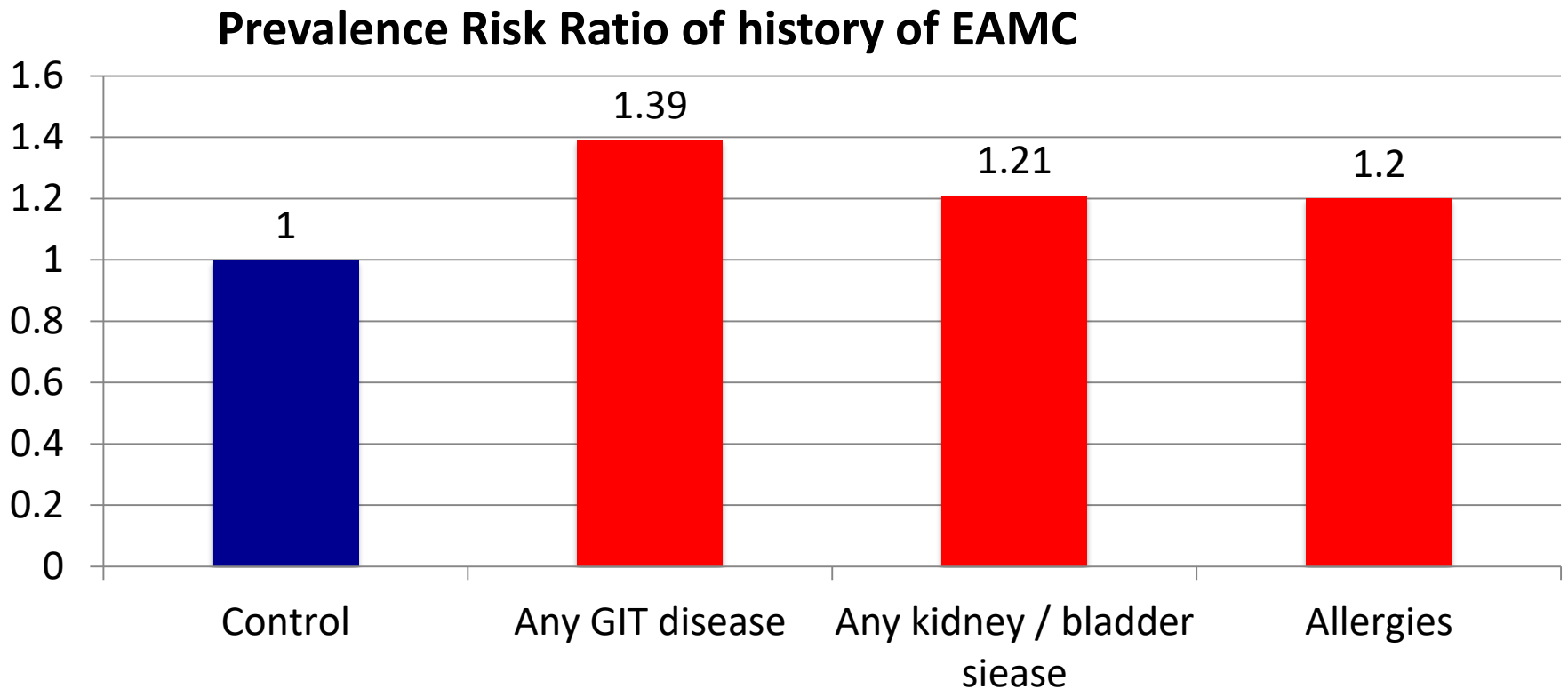


Schwellnus M, Swanevelder S, Derman W, Jordaan E; 2017 (in review)

IOC Research Centre

Other chronic disease as a risk factor for EAMC in recreational distance runners

Cross sectional study in 15 778 runners with history of EAMC



Schwellnus M, Swanevelder S, Derman W, Jordaan E; 2017 (in review)

Summary - Risk factors for EAMC during exercise

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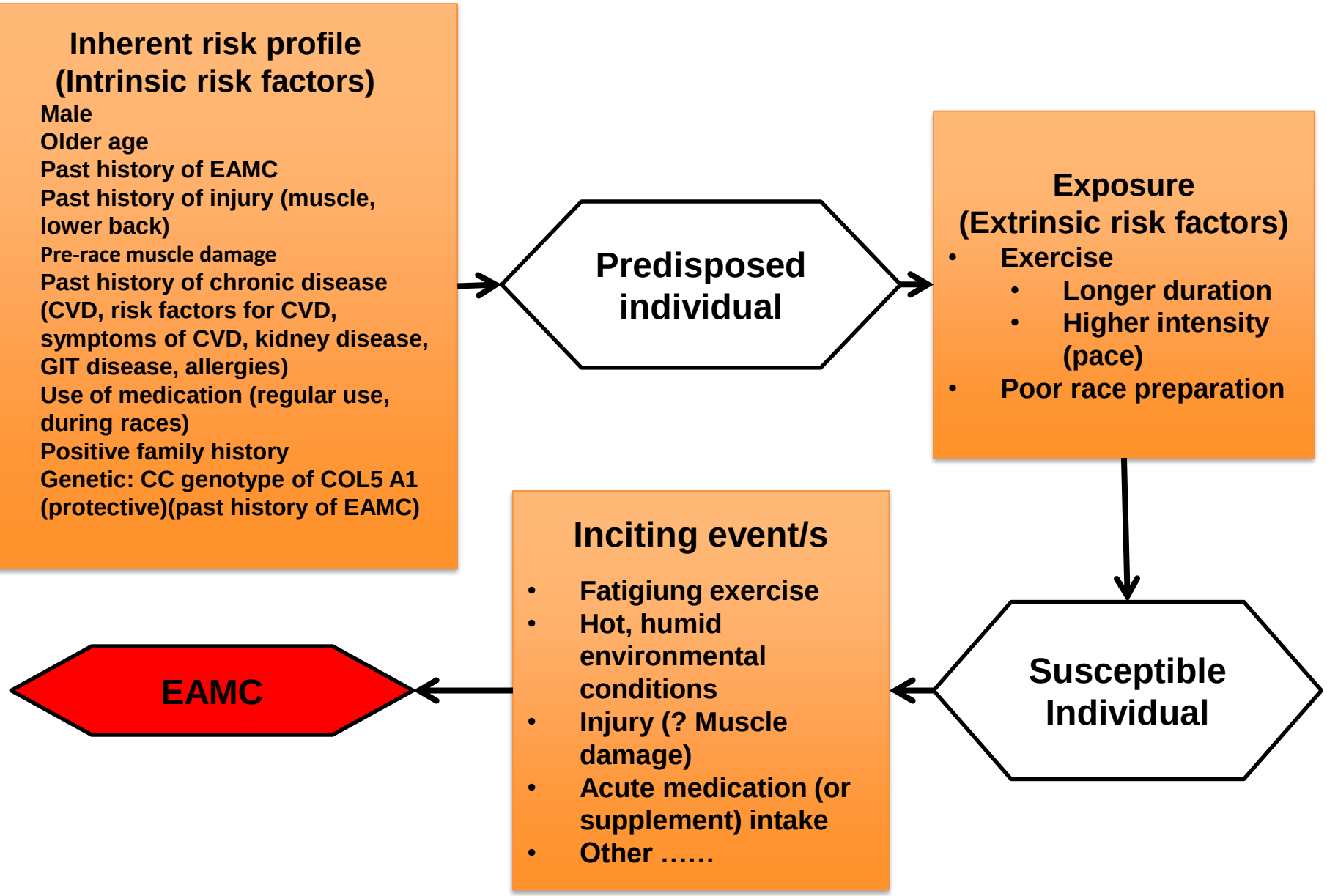

Review of evidence that EAMC is related to abnormal neuromuscular control

IOC Research Centre

2009

Whilst it is clear that further evidence to support the "altered neuromuscular control" hypothesis is also required, research data are accumulating that support this as the principal pathophysiological mechanism for the aetiology of EAMC

Review

Cause of Exercise Associated Muscle Cramps (EAMC) — altered neuromuscular control, dehydration or electrolyte depletion?

M P Schwellnus

Correspondence to:
Martin P Schwellnus, UCT/MRC Research Unit for Exercise Science and Sports Medicine, Department of Human Biology, Faculty of Health Sciences, University of Cape Town, South Africa, 3rd Floor, Sports Science Institute of South Africa, Boundary Road, Newlands, Cape Town, 7700, South Africa; martin.schwellnus@uct.ac.za

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ABSTRACT

Exercise Associated Muscle Cramps (EAMC) is one of the most common conditions that require medical attention during or immediately after sports events. Despite the high prevalence of this condition the aetiology of EAMC in athletes is still not well understood. The purpose of this review is to examine current scientific evidence in support of (1) the "electrolyte depletion" and "dehydration" hypotheses and (2) the "altered neuromuscular control" hypothesis in the aetiology of EAMC. In this review, scientific evidence will, as far as possible, be presented using evidence-based medicine criteria. This is particularly relevant in this field, as the quality of experimental methodology varies considerably among studies that are commonly cited in support of hypotheses to explain the aetiology of EAMC. Scientific evidence in support of the "electrolyte depletion" and "dehydration" hypotheses for the aetiology of EAMC comes mainly from anecdotal clinical observations, case series totalling 18 cases, and one small (n = 10) case-control study. Results from four prospective cohort studies do not support these hypotheses. In addition, the "electrolyte depletion" and "dehydration" hypotheses do not offer plausible pathophysiological mechanisms with supporting scientific evidence that could adequately explain the clinical presentation and management of EAMC. Scientific evidence for the "altered neuromuscular control" hypothesis is based on evidence from research studies in human models of muscle cramping, epidemiological studies in cramping athletes, and animal experimental data. Whilst it is clear that further evidence to support the "altered neuromuscular control" hypothesis is also required, research data are accumulating that support this as the principal pathophysiological mechanism for the aetiology of EAMC.

Exercise Associated Muscle Cramps (EAMC) is one of the most common conditions that require medical attention during or immediately after sports events. EAMC is particularly common in endurance events such as ultra-marathon running and triathlon.[1–4] Despite the high prevalence of this condition the aetiology of EAMC in athletes is still not well understood.

Muscle cramping in athletes may occur as a result of many underlying medical conditions,[5] and therefore not all athletes with muscle cramping suffer from EAMC. However, in the sports medicine literature, cramping during or immediately after exercise is more commonly referred to as Exercise Associated Muscle Cramping (EAMC),[6,7] which has been defined as a "painful, spasmodic and involuntary contraction of skeletal muscle that occurs during or immediately after exercise".[8] This term will be used in this review.

The first reports of muscle cramping related to physical activity were from labourers working on steamships and in mines in hot, humid conditions more than 100 years ago.[9–12] In these early reports it was noted not only that muscle cramping occurred in the heat but also that cramps were accompanied by profuse sweating.[12] These early anecdotal observations led to the development of the traditional "electrolyte depletion" and "dehydration" hypotheses for the aetiology of EAMC. These case reports often related the development of cramping to physical activity performed in hot and humid environmental conditions, and this has led to the terminology "heat cramps" or "exertional heat cramps". This terminology is still used today,[2 4 8 13] often synonymously with EAMC. This is despite the fact that EAMC is known to occur in individuals exercising in moderate to cool temperatures,[4 14] and exposure to extreme cold has also been associated with EAMC in swimmers.[3] It has also been reported that the development of EAMC is not directly related to an increased core temperature.[14] Furthermore, passive heating alone (at rest) does not result in EAMC and cooling does not relieve muscle cramps.[15] It would therefore appear that heat alone is not a direct cause of muscle cramping during exercise, and therefore the term "heat cramps" is a misnomer, and its use should be discouraged.

A novel hypothesis for the aetiology of EAMC was first proposed about 10 years ago.[16] This hypothesis explored evidence that altered neuromuscular control as a result of the development of muscle fatigue may be the primary factor that is associated with the development of EAMC.[16] This "altered neuromuscular control" hypothesis has only recently gained some acceptance and "muscle fatigue" has, in a recent review, been acknowledged as a predisposing factor in the development of EAMC.[6]

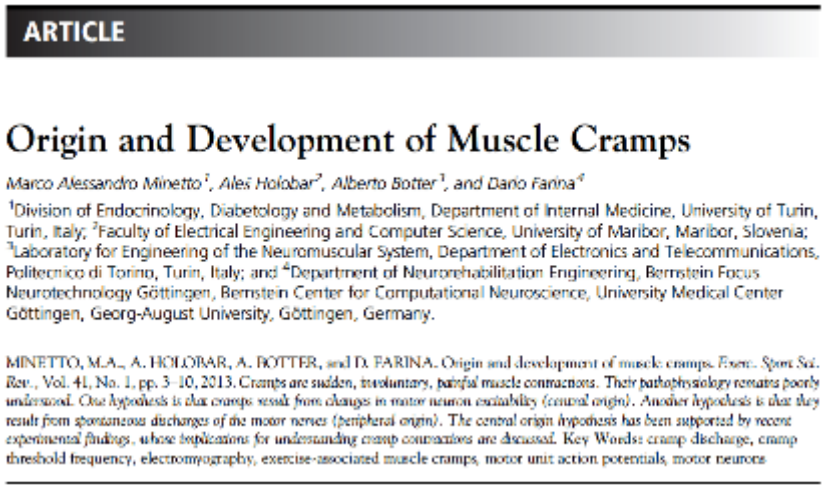
The purpose of this review is to examine current scientific evidence in support of (1) the "electrolyte depletion" and "dehydration" hypotheses" and (2) the "altered neuromuscular control" hypothesis in the aetiology of EAMC. In this review, scientific evidence will, as far as possible, be presented using evidence-based medicine (EBM) criteria.[17] This is particularly relevant in this field, as the quality of experimental methodology varies considerably among studies that are commonly cited in support of hypotheses to explain the aetiology of EAMC.

Review of evidence that EAMC is related to abnormal neuromuscular control

IOC Research Centre

2013

- Recent experimental findings have proved unambiguously the relevance of spinal mechanisms in the generation and development of muscle cramps
- These findings are important for identifying the most effective and safe medications for managing (preventing or reducing the occurrence of) cramps



ARTICLE

Origin and Development of Muscle Cramps

Marco Alessandro Minetto[1], Aleš Holobar[2], Alberto Botter[3], and Dario Farina[4]

[1]Division of Endocrinology, Diabetology and Metabolism, Department of Internal Medicine, University of Turin, Turin, Italy; [2]Faculty of Electrical Engineering and Computer Science, University of Maribor, Maribor, Slovenia; [3]Laboratory for Engineering of the Neuromuscular System, Department of Electronics and Telecommunications, Politecnico di Torino, Turin, Italy; and [4]Department of Neurorehabilitation Engineering, Bernstein Focus Neurotechnology Göttingen, Bernstein Center for Computational Neuroscience, University Medical Center Göttingen, Georg-August University, Göttingen, Germany.

MINETTO, M.A., A. HOLOBAR, A. BOTTER, and D. FARINA. Origin and development of muscle cramps. *Exerc. Sport Sci. Rev.*, Vol. 41, No. 1, pp. 3–10, 2013. *Cramps are sudden, involuntary, painful muscle contractions. Their pathophysiology remains poorly understood. One hypothesis is that cramps result from changes in motor neuron excitability (central origin). Another hypothesis is that they result from spontaneous discharges of the motor nerves (peripheral origin). The central origin hypothesis has been supported by recent experimental findings, whose implications for understanding cramp contractions are discussed.* Key Words: cramp discharge, cramp threshold frequency, electromyography, exercise-associated muscle cramps, motor unit action potentials, motor neurons

Review of evidence that EAMC is related to abnormal neuromuscular control

IOC Research Centre

2014

The "Altered neuromuscular control theory" seems to be the most scientifically acceptable theory, and suggests that EAMC are caused by an imbalance between increased afferent activity (e.g. muscle spindle, Ia) and decreased inhibitory afferent activity (e.g. Golgi tendon organs, Ib) which leads to increased alpha-motor neuron activity and muscle cramping, especially with muscle contraction in a shortened position

Edouard P: Science and Sports; 2014: 29: 299-305

Review of evidence that EAMC is related to abnormal neuromuscular control

IOC Research Centre

2016

EAMC is multifactorial in nature and stems from an imbalance between excitatory drive from muscle spindles and inhibitory drive from Golgi tendon organs to the alpha motor neurons rather than dehydration or electrolyte deficits. This imbalance is believed to stem from neuromuscular overload and fatigue.

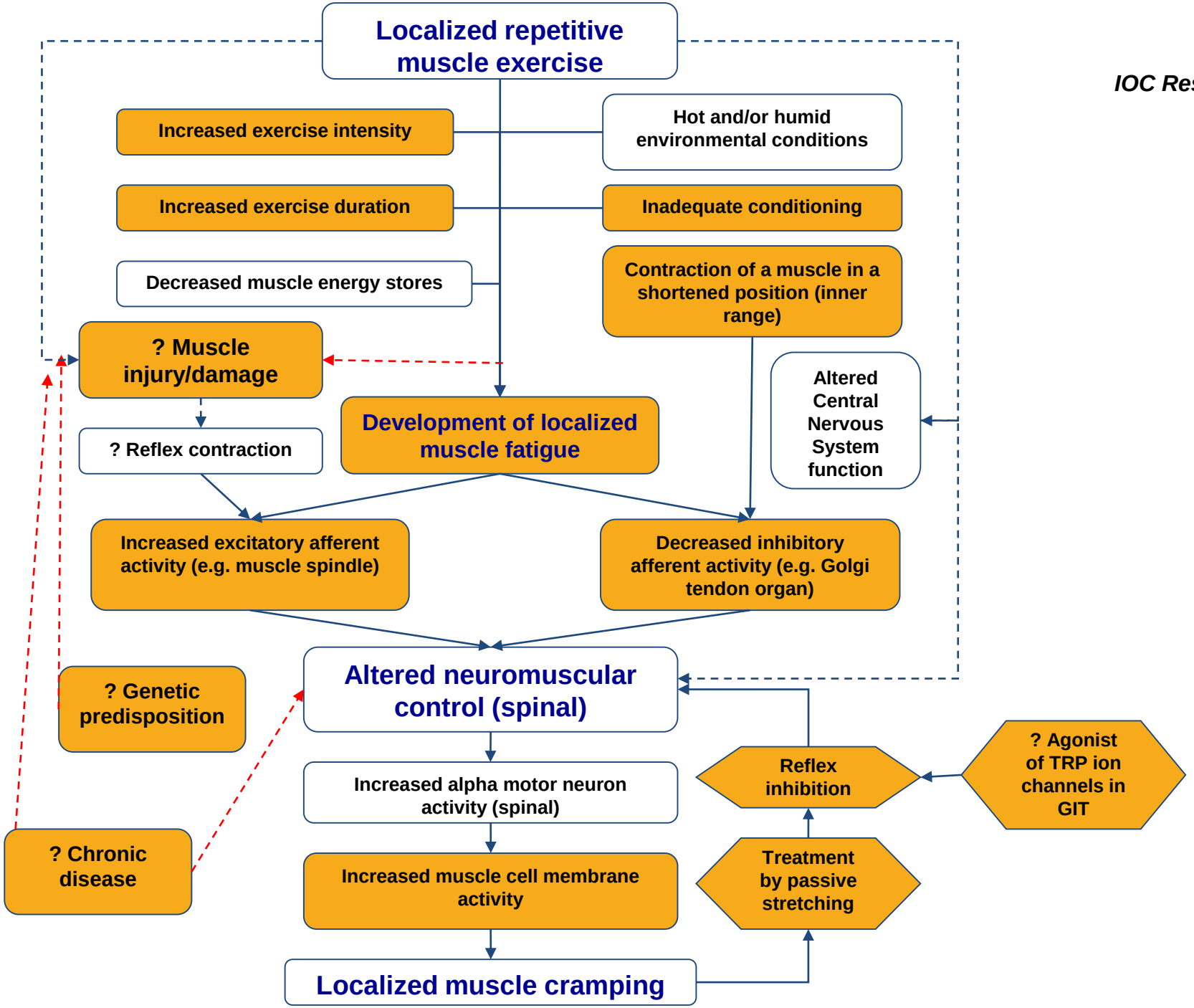
INVITED REVIEW

A NARRATIVE REVIEW OF EXERCISE-ASSOCIATED MUSCLE CRAMPS: FACTORS THAT CONTRIBUTE TO NEUROMUSCULAR FATIGUE AND MANAGEMENT IMPLICATIONS

NICOLE L. NELSON, MSH, LMT, and JAMES R. CHURILLA, PhD, MPH

Clinical and Applied Movement Sciences, Brooks College of Health, University of North Florida, 1 UNF Drive, Jacksonville, Florida 32224-2673, USA

Nelson N et al: Muscle Nerve; 2016: 54: 177-185


Localized repetitive muscle exercise
Increased exercise intensity
Hot and/or humid environmental conditions
Increased exercise duration
Inadequate conditioning
Decreased muscle energy stores
Contraction of a muscle in a shortened position (inner range)
? Muscle injury/damage
? Reflex contraction
Development of localized muscle fatigue
Altered Central Nervous System function
Increased excitatory afferent activity (e.g. muscle spindle)
Decreased inhibitory afferent activity (e.g. Golgi tendon organ)
? Genetic predisposition
Altered neuromuscular control (spinal)
Reflex inhibition
? Agonist of TRP ion channels in GIT
Increased alpha motor neuron activity (spinal)
? Chronic disease
Increased muscle cell membrane activity
Treatment by passive stretching
Localized muscle cramping

Clinical investigation of the athlete with EAMC

- **EAMC is <u>not a diagnosis</u> (it is a clinical syndrome)**
- **Not every athlete with EAMC has 1º or "benign" EAMC**

Clinical investigation of the athlete with EAMC

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Who should be investigated for secondary causes?

- Recurrent cramping
- Cramping associated with collapse, confusion, coma
- Cramping associated with “dark” urine (? myoglobinuria or hematuria)
- History of cramping/spasms at rest
- History of cramping in “non-exercising” muscles
- Cramping associated with other muscle symptoms (fatigue, weakness, swelling, pain)
- Cramping associated with other neurologic or systemic symptoms
- History of generalized (systemic) cramping
- Strong family history of cramping

Clinical investigation of the exercising individual with EAMC

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- **Medical history**

Cramping (onset, duration, muscles, relation to exercise, precipitants)
Neurological history (motor, sensory, co-ordination)
Injury history
Systematic medical history
Drugs and medication
Family history

- **Clinical examination**

General medical examination
Neurological examination
Musculoskeletal examination (muscle pain, stiffness, swelling, weakness)
Systematic comprehensive examination

- **Special investigations**

CBC
Activity markers
Renal function
Thyroid function
Muscle strength / fatigue
Muscle damage (resting and post-exercise CK)
Skeletal muscle biopsy
Others as indicated

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Management of 1º acute EAMC

Non-pharmacologic treatment

1. Reduce intensity (running speed) – "cramp prone" state
2. Stop activity
3. Passive stretching
4. Drinking ad libitum

Other proposed non-pharmacologic treatment methods

1. Hyperventilation / re-breathing
2. Ice / ice massage
3. Walking

Edouard P: Science and Sports; 2014: 29: 299-305

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Management of 1º acute EAMC

Proposed pharmacologic treatment

1. Stimulation of the TRP ion channels (also known as the wasabi receptor) in the oral and esophageal mucosa
   - Clinical trials under way
   - ? Use in 1º and 2º EAMC
   - ? Not treating the cause

Other proposed pharmacological interventions (poor evidence)

1. Sodium
2. Magnesium
3. Quinine

Edouard P: Science and Sports; 2014: 29: 299-305

Clinical approach
Prevention of 1º (“benign’) EAMC

- Identify the possible secondary cause and treat it
- Prevent premature fatigue
  - Training
  - Racing at appropriate exercise intensity
  - Nutrition (? carbohydrate)
  - Other methods
- Prevent muscle damage
  - Tapering
  - Appropriate conditioning
- Prevent injury (muscle)
- Stretching regularly
- Fluid intake (? avoid too much)
- Avoid use of drugs
- ? Thermoregulation

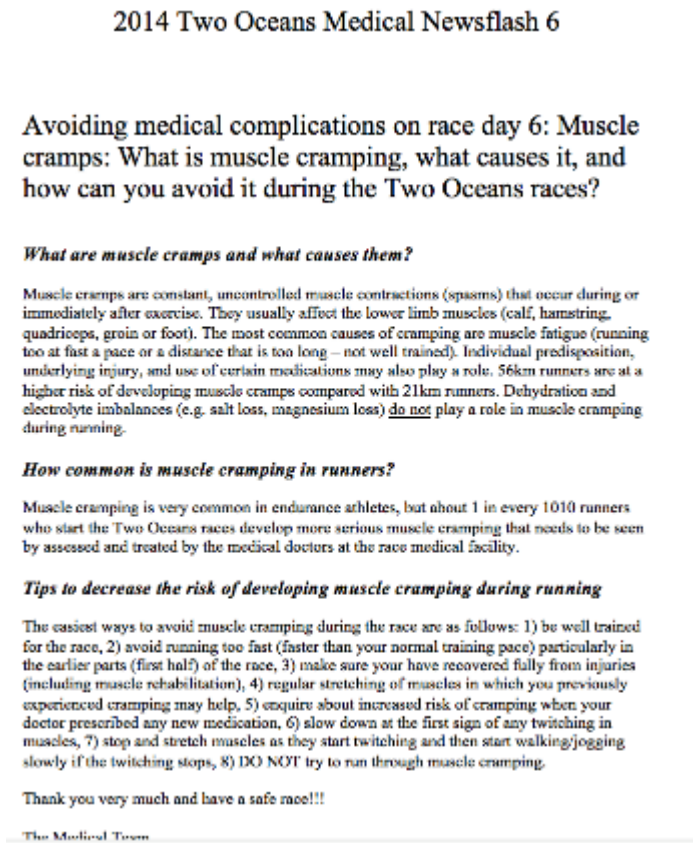
SAFER - EAMC intervention Study

2012 - 2015

IOC Research Centre

EAMC prevention intervention:

1. Be well trained for the race
2. Avoid running too fast (faster than your normal training pace) particularly in the earlier parts (first half) of the race
3. Make sure your have recovered fully from injuries (including muscle rehabilitation)
4. Regular stretching of muscles in which you previously experienced cramping may help
5. Enquire about increased risk of cramping when your doctor prescribed any new medication
6. Slow down at the first sign of any twitching in muscles
7. Stop and stretch muscles as they start twitching and then start walking/jogging slowly if the twitching stops
8. Do not try to run through muscle cramping



2014 Two Oceans Medical Newsflash 6

Avoiding medical complications on race day 6: Muscle cramps: What is muscle cramping, what causes it, and how can you avoid it during the Two Oceans races?

What are muscle cramps and what causes them?

Muscle cramps are constant, uncontrolled muscle contractions (spasms) that occur during or immediately after exercise. They usually affect the lower limb muscles (calf, hamstring, quadriceps, groin or foot). The most common causes of cramping are muscle fatigue (running too at fast a pace or a distance that is too long – not well trained). Individual predisposition, underlying injury, and use of certain medications may also play a role. 56km runners are at a higher risk of developing muscle cramps compared with 21km runners. Dehydration and electrolyte imbalances (e.g. salt loss, magnesium loss) do not play a role in muscle cramping during running.

How common is muscle cramping in runners?

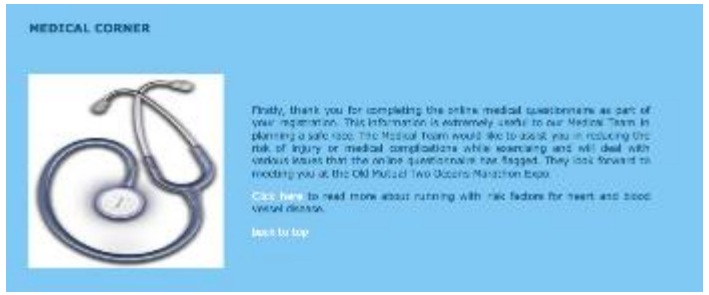
Muscle cramping is very common in endurance athletes, but about 1 in every 1010 runners who start the Two Oceans races develop more serious muscle cramping that needs to be seen by assessed and treated by the medical doctors at the race medical facility.

Tips to decrease the risk of developing muscle cramping during running

The easiest ways to avoid muscle cramping during the race are as follows: 1) be well trained for the race, 2) avoid running too fast (faster than your normal training pace) particularly in the earlier parts (first half) of the race, 3) make sure your have recovered fully from injuries (including muscle rehabilitation), 4) regular stretching of muscles in which you previously experienced cramping may help, 5) enquire about increased risk of cramping when your doctor prescribed any new medication, 6) slow down at the first sign of any twitching in muscles, 7) stop and stretch muscles as they start twitching and then start walking/jogging slowly if the twitching stops, 8) DO NOT try to run through muscle cramping.

Thank you very much and have a safe race!!!

The Medical Team



Pre- vs. post EAMC educational intervention

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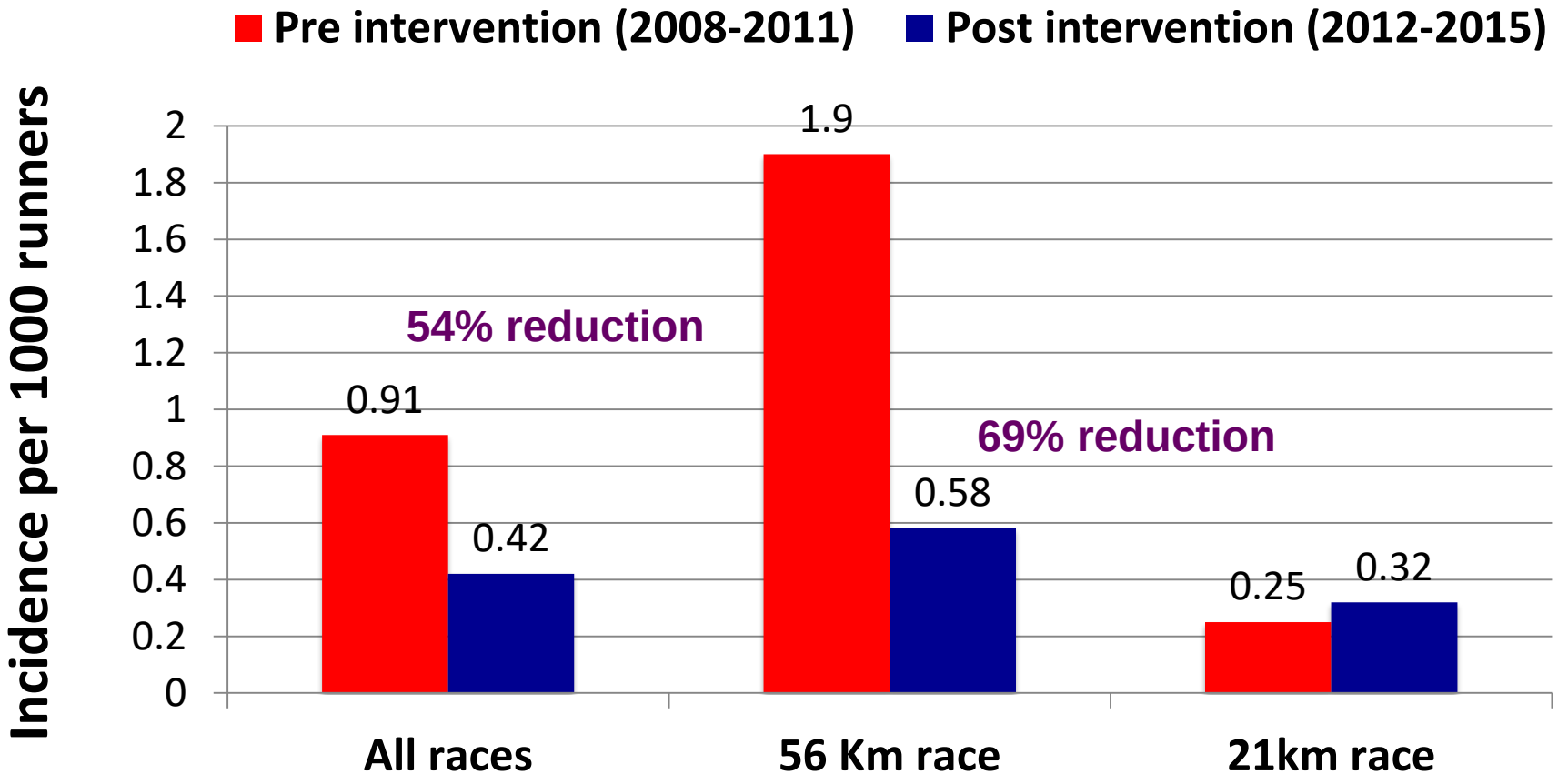
Incidence of serious EAMC



Schwellnus M,, et al, 2016 (in preparation)

Summary

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1. EAMC is common – still under researched
2. Etiology and pathophysiology – multifactorial
3. Accumulating and strong evidence that final common pathway in pathophysiology of EAMC is a neuromuscular control abnormality
4. EAMC is a syndrome – not a diagnosis (many 2^{o} causes)
5. Investigation of recurrent cramping requires careful and comprehensive medical assessment for secondary causes
6. Acute treatment – diagnosis, rest and stretching (? role of TRP ion channel agonists)
7. Prevention – ? Different for primary and secondary, role of education is important

Thank you for your attention

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