Gastrointestinal tract (GIT) symptoms in Ironman Triathletes: A study relating GIT symptoms to changes in splanchnic blood flow

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November 2008

Declaration

I, Helen Mary Wright, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

Signed by candidate (Signature)

Date: 17 November 2008

Acknowledgements

- Professor Martin Schwellnus for his patient guidance and expert supervision

- Professor Malcolm Collins for his expertise and skill

- Yvonne Blomkamp for her cheerful assistance with anything

- Annemarie Nelson for performing all the Doppler ultrasounds and making the collecting of data a pleasant experience

- Andrew for his ongoing encouragement and support

- Dad, Mom, Jane, Andrew, Jill, Dylan and my little work partner, Hanna, for their enthusiasm

- All my triathlete friends for taking part in the study so willingly

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Abbreviations

ATP	Adenosine triphosphate
BMI	Body Mass Index
cm	Centimetre
$cm.s^{-1}$	Centimetre per second
CO_2	Carbon dioxide
CRP	C-Reactive Protein
GIT	Gastrointestinal tract
GIT AS	Asymptomatic for gastrointestinal tract symptoms
GIT S	Symptomatic for gastrointestinal tract symptoms
hr	Hour
hrs/wk	Hours per week
IGC	Indocyanine Green dye Clearance
IgG	Immunoglobulin G
IL-6	Interleukin 6
IMA	Inferior mesenteric artery
kg/m^2	Kilogram per meter squared
km	Kilometre
km/wk	Kilometres per week
LPS	Lipopolysaccharide
$m.s^{-1}$	Meters per second
min	Minute
ml/kg	Millilitres per kilogram
ml/kg/hr	Millilitre per kilogram per hour

mmHg	Millimetres of mercury
NSAIDS	Non-steroidal anti-inflammatory drugs
PB	Personal best
RI	Resistance Index
SMA	Superior mesenteric artery
TAMV	Time average mean velocity
TNF	Tumour Necrosis Factor
VIP	Vasoactive Intestinal Peptide
VO_{2max}	Percentage of maximum output
%	Percentage
<	Less than
>	Greater than
°C	Degrees Celsius

Abstract

Background: Gastrointestinal tract (GIT) symptoms commonly affect endurance athletes such as those competing in the Ironman Triathlon. Although a number of risk factors and the pathophysiological mechanisms for the development of GIT symptoms during exercise have been proposed, scientific evidence in support of these factors and mechanisms is limited. Altered blood flow to the GIT during exercise has been suggested as a possible mechanism for the pathophysiology of GIT symptoms. However, changes in blood flow in the superior mesenteric artery (SMA) and the coeliac artery in athletes presenting with GIT symptoms during exercise has not been previously investigated.

Objectives: The aims of this dissertation were threefold. Firstly, current literature regarding risk factors and pathophysiology of GIT symptoms associated with exercise was reviewed. Secondly, significant risk factors associated with the development of GIT symptoms in Ironman triathletes were identified, and finally, pre- to post-race changes in SMA and coeliac artery blood flow were related to the development of GIT symptoms in triathletes competing in the 2007 South African Ironman Triathlon.

Methods: In the first part of the dissertation, an extensive literature review was conducted using an evidence-based approach. Using selective keywords (gastrointestinal tract symptoms, exercise, risk factors, athletes, triathletes, blood flow) a search was undertaken using the PUBMED database to identify all research publications that relate to the development of GIT symptoms during exercise. The specific focus of the review was on the risk factors and pathophysiological mechanisms for GIT symptoms in endurance athletes. The second and third parts of this dissertation were conducted in the form of a prospective cohort study, where triathletes competing in the the 2007 Ironman Triathlon in South Africa were recruited

in the three days preceding the race. Subjects were asked to complete a questionnaire pertaining to personal details, racing and training history, personal general medical history and medication. A cohort (n=59) then underwent a pre-race heart rate and blood pressure measurement as well as a pre-race haemodynamic assessment (artery diameter, systolic velocity, diastolic velocity and Resistance Index (RI)) of the SMA and coeliac artery using duplex Doppler ultrasound. All the measurements were repeated after the race at the finish line (mean time from race finish to haemodynamic assessment was 1.45±0.5 hrs) and GIT symptoms (nature, classification) were documented as well as the use of medications during the race.

Results: Fifty-nine percent (N= 35) of the triathletes in the cohort reported GIT symptoms during the Ironman Triathlon while 41% (N=24) remained asymptomatic. There was a significant decrease in the diameter of the SMA after the race (P=0.003) and a significant decrease in the RI in the SMA and coeliac artery (P<0.001) in both GIT symptomatic and asymptomatic triathletes. However, there were no significant differences in the haemodynamic measurements between the GIT symptomatic and asymptomatic triathletes. The only significant risk factor for the development of GIT symptoms associated with an Ironman Triathlon in this cohort was younger age (p=0.041). Other risk factors including female gender, high intensity exercise, poorly trained athlete and medication use were not significantly associated with the development of GIT symptoms in this cohort.

Conclusion: The literature with regard risk factors and pathophysiology of GIT symptoms associated with exercise is limited, even though GIT symptoms are commonly experienced by athletes. There is a significant decrease in the diameter of the SMA and a decrease in the RI of the SMA and coeliac artery post-race compared to pre-race. However, these haemodynamic measurements do not differ between GIT

symptomatic and asymptomatic triathletes. Therefore, the pathophysiological hypothesis that altered blood flow is a cause of GIT symptoms is not supported by the results of this study, and other mechanisms for GIT symptoms associated with exercise should be sought.

Keywords*:* Gastrointestinal tract symptoms, blood flow, triathlon, superior mesenteric artery, coeliac artery, ultrasound, Ironman

Chapter 1

Introduction and scope of the thesis

The Ironman Triathlon is an ultra-endurance event which consists of a 3.8km swim, a 180km cycle followed by a 42.2km run. Medical problems associated with ultra-endurance sports are becoming more evident as participation in these events grows [1]. In particular, gastrointestinal tract (GIT) symptoms have been shown to be a common problem reported by triathletes [2, 3]. GIT symptoms are usually mild and self-limiting – however, symptoms can become severe and incapacitating for the athlete [4, 5]. Despite this, research to identify the risk factors for and pathophysiological mechanisms of GIT symptoms associated with exercise, is limited.

GIT symptoms have been classified into upper and lower GIT symptoms [6, 7]. Upper GIT symptoms include nausea, vomiting and heartburn. Lower GIT symptoms include diarrhoea, abdominal cramps, urge to pass stool, bloating and blood in the stool. Risk factors predisposing athletes to GIT symptoms, as well as hypotheses for the underlying pathophysiology, have been suggested for the development of GIT symptoms associated with exercise [4, 6, 8, 9]. Research in both these areas is, however, limited. Therefore our understanding of the aetiology and pathophysiology of GIT symptoms in endurance athletes is, to date, still unclear.

Altered blood flow to the GIT during exercise has been proposed as an underlying mechanism in the development of GIT symptoms [9, 10]. Studies have shown a physiological change in blood flow with exercise in healthy individuals [12, 88] but splanchnic haemodynamics have not been studied in GIT symptomatic athletes.

The focus of this dissertation was to identify risk factors for the development of GIT symptoms in triathletes competing in the 2007 "Spec-Savers" Ironman Triathlon in Port Elizabeth, South Africa. More specifically, a prospective cohort study design was used to determine significant risk factors for GIT symptoms and to investigate and compare the change in splanchnic haemodynamics pre- and post-race in GIT symptomatic and asymptomatic triathletes. This event was chosen as it was a field study and triathletes were exposed to an extended duration of exercise.

An evidence-based review of the literature focusing on postulated risk factors and pathophysiological hypotheses for the development of GIT symptoms associated with exercise is presented in Chapter 2. In Chapter 3, the detailed methodology, results and discussion of the main research study will be presented. Finally, an overall conclusion with practical recommendations and suggestions for future research will be discussed in Chapter 4.

CHAPTER 2

Gastrointestinal symptoms associated with exercise: A review

2.1 INTRODUCTION

It is well established that regular physical activity is an important lifestyle modification in the prevention and management of chronic disease [11, 13]. As a result, the popularity of participation in regular recreational and competitive physical activity has increased [14]. This is also reflected as an increased growth in the participation in endurance events such as the Ironman Triathlon [5, 15].

The modern Ironman Triathlon was born in the mid-1970s out of a debate between cyclists and runners as to who is the better athlete. In response to this debate, a certain John and Judy Collins proposed a race combining these two disciplines and adding a swim leg [16]. The first Ironman Triathlon was held in Kona, Hawaii in 1978, with only 15 participants. Today, entries at Ironman events are capped at 2000, reflecting the growing popularity of the sport [16].

The Ironman Triathlon consists of a 3.8km swim, followed by a 180km road cycle, and finishes with a 42.2km road run. Competitors must finish the race within 17 hours; that is, before midnight on race day. This event ranks as one of the most physically and mentally demanding endurance events. It is

therefore not surprising that medical problems in Ironman triathletes are commonly reported [1]. Compared to single sport ultra-distance events, triathletes can experience a variety of injuries and medical conditions that can occur in each of the three disciplines [2]. It has also been shown that with increasing distances of the triathlon events, i.e. from a sprint distance (750m swim, 20km bike, 5km run) to Olympic distance (1.5km swim, 40km bike, 10km run) and finally, the Ironman distance, the prevalence of medical conditions increases from <2% to 10% to 17% respectively [3].

Furthermore, medical problems can occur during the months of preparation and training, during the race, and also in the recovery period following an Ironman Triathlon [1]. There is a wide spectrum of medical problems that are encountered in endurance triathletes and these medical conditions can affect any of the following systems: cardiovascular, respiratory, gastrointestinal, musculoskeletal, immune, neurological, endocrine, genitourinary, dermatological and haematological [17]. Specific medical problems that have been reported in Ironman triathletes are listed in Table 2.1.

Table 2.1: Medical problems that are experienced by triathletes [1]

- Dehydration
- Muscle cramping
- Hypothermia
- Heat stroke
- Hyponatraemia
- Postural hypotension
- Exposure to ultraviolet light
- Gastrointestinal tract symptoms (GIT)
- Musculoskeletal injuries and minor trauma
- Infection from contaminated water
- Post-race immunosuppression
- Sympathetic nervous system exhaustion
- Haemolysis

The prevalence of medical conditions that occur in triathletes has been reported and the results of these studies show that GIT symptoms are very common [2, 3]. In one study of 110 triathletes, it has been reported that the most common reason for interrupting exercise was due to GIT symptoms [2]. It is important to note, however, that most research in this area has been done on endurance runners [15, 18, 19]. Despite the fact that GIT symptoms are apparently very common in triathletes, relatively little attention has been given to this problem in the medical literature. In particular, there are very few

studies that have reported risk factors, mechanisms, prevention strategies and management of GIT symptoms in triathletes. It is for this reason that this is the focus of investigation in this dissertation, and therefore, the main subject in this review chapter.

2.2 GASTROINTESTINAL TRACT (GIT) SYMPTOMS IN ATHLETES

2.2.1 Introduction

As mentioned, GIT symptoms are common in athletes, especially in endurance athletes [5, 18]. These symptoms can be very frustrating for the athlete as they can occur during training and race conditions [19, 20]. The unexpected nature of the symptoms can be embarrassing to the athlete, can result in medical complications (e.g. fluid and electrolyte loss) and may also impair the performance of the athlete [19]. However, in most instances GIT symptoms are mild and only result in an inconvenience to the athlete [4, 7, 21]. Therefore some athletes consider GIT symptoms almost as a normal part of exercise [2, 22]. GIT symptoms can also be more severe and disabling, forcing athletes to stop racing or abandon training sessions [5]. In one questionnaire that was completed by 279 marathon runners, 20% of athletes felt that GIT symptoms interfered with their performance [19].

In this review, the following aspects relating to GIT symptoms in endurance athletes will be covered: epidemiology, classification and type of GIT symptoms (upper and lower GIT symptoms), risk factors and pathophysiology.

2.2.2 Epidemiology of GIT symptoms in endurance athletes

Incidence is defined as the number of new occurrences of a condition or disease in a population over a period of time [23]. Point prevalence is the measure of the frequency (%) of a condition or disease in a population at a given point in time [23]. Prevalence can also be measured over a period of time, for example, an endurance event such as a marathon – period prevalence or over a lifetime – lifetime prevalence [23].

Several studies have investigated the prevalence of GIT symptoms in runners [15, 18, 19, 24]. It has been shown that GIT symptoms are very common in runners and lifetime prevalence rates as high as 83% have been reported [18]. However, most studies show lifetime prevalence in the range of 20-50% of athletes reporting some form of GIT symptom associated with running [8]. There are limited studies investigating the incidence of GIT symptoms in triathletes during a race. In one cross-sectional study of 110 triathletes the incidence of GIT symptoms during a triathlon was reported as 50% [2].

The incidence of GIT symptoms per 1000 hours of participation [7] and the lifetime prevalence of GIT symptoms has also been investigated in other endurance sports including triathlon, cycling, canoeing, paddling, aerobics

and swimming [2, 5]. In a questionnaire-based study of six different endurance sports, 17% of athletes admitted to the use of prophylactic medication prior to a training session in order to curtail the effect of possible GIT symptoms [7].

Methods of data collection for most of the studies have been in the form of questionnaires and therefore an element of selection bias needs to be taken into account [15]. In summary, the prevalence rate for GIT symptoms in endurance sports is high, thus making GIT symptoms a common and clinically relevant medical problem for the endurance athlete.

2.2.3 Classification and types of GIT symptoms (upper and lower GIT symptoms)

GIT symptoms in athletes can include nausea, vomiting, heartburn, abdominal cramps, bloating, urge to pass stool, diarrhoea and blood in the stool [5, 7, 8]. In most reports, these symptoms have been classified into upper and lower GIT symptoms [6, 7] (Table 2.2.).

Table 2.2: Upper and Lower GIT symptoms

UPPER GIT SYMPTOM	LOWER GIT SYMPTOM
Nausea	Diarrhoea
Vomiting	Bloating
Heartburn	Urge to pass stool
	Abdominal cramps
	Blood in stool

The prevalence of different types of GIT symptoms in athletes (upper and lower) are summarised in Table 2.3.

Table 2.3: The prevalence of upper and lower GIT symptoms in athletes

GIT SYMPTOM		PREVALENCE	REFERENCES
Upper GIT	Nausea	4 – 21%	[5, 18]
	Vomit	2 – 31%	[18, 25]
	Heartburn	8 – 11%	[5, 25]
Lower GIT	Diarrhoea	10 – 30%	[15, 26]
	Urge to pass stool	5 – 63%	[25, 26]
	Abdominal cramps	5 – 67%	[25, 26]
	Blood in stool	2 – 12%	[15, 26]

In most studies, it has been shown that lower GIT symptoms are more common than upper GIT symptoms, and this is particularly evident in runners [7, 15, 18, 24]. Furthermore, the prevalence of upper GIT symptoms tended to

be higher in triathletes than in runners – however, lower GIT symptoms are still more commonly reported than upper GIT symptoms in the triathlete group [4, 25].

In a retrospective cross-sectional study of a group of runners (N=199), a group of cyclists (N=197), and a group of triathletes (N=210) it was shown that triathletes experience more upper GIT symptoms than runners. Each group completed a questionnaire regarding the previous 12 months of training and racing. Prevalence rates of upper GIT symptoms were 36% in runners and 54% in triathletes during the run leg of a triathlon. With respect to these groups, the prevalence of lower GIT symptoms was similar at 71% and 79% respectively [27].

2.2.4 Risk factors for GIT symptoms in endurance athletes

Risk factors have been used in research to identify individuals at higher risk for certain conditions, for example, ligament injury [28]. Risk factors are subdivided into intrinsic and extrinsic risk factors [28]. Intrinsic risk factors are factors originating in the individual, for example, age, gender, and underlying disease [28]. These factors generally cannot be altered by the individual. Extrinsic risk factors are factors originating outside the individual and can be manipulated by the individual [28]. Examples of extrinsic risk factors are diet and environmental conditions [28].

A number of risk factors for GIT symptoms associated with exercise have been identified and are listed in Table 2.4. [5-8, 15, 18]. The risk factors have been divided into intrinsic and extrinsic risk factors.

Table 2.4: Intrinsic and extrinsic risk factors for GIT symptoms associated with exercise

INTRINSIC RISK FACTOR	EXTRINSIC RISK FACTOR
Younger age	High intensity exercise
Female gender	Dehydration
Previous abdominal surgery	Vertical impact sport (running)
Irritable bowel syndrome	Poorly conditioned athlete
Lactose intolerance	Medication
	Dietary factors

The risk factors for the development of GIT symptoms associated with exercise will now be reviewed. Evidence-based medicine (EBM) criteria will be used to evaluate the strength of the evidence for each risk factor [29]. As far as can be ascertained from the existing published literature, this approach has not been followed in any past reviews on risk factors associated with GIT symptoms in endurance athletes.

2.2.4.1 Intrinsic risk factors for GIT symptoms associated with exercise

The main intrinsic risk factors for the development of GIT symptoms associated with exercise are female gender [7, 15, 18], younger age [7, 15,

18, 30], previous abdominal surgery [7], irritable bowel syndrome and lactose intolerance [26].

2.2.4.1.1 Female gender as an intrinsic risk factor for GIT symptoms associated with exercise

It has been reported in a number of studies that female athletes are more likely to be affected by GIT symptoms during exercise than male athletes [7, 15, 18, 19, 31]. In particular, it has been reported that lower GIT symptoms are more common in female than in male athletes [15]. However, scientific evidence for female gender as a risk factor for the development of GIT symptoms is limited.

In one cross-sectional study, 279 leisure time marathon runners were given a questionnaire in order to determine prevalence of GIT symptoms in long-distance running [19]. The 279 subjects comprised 10% of the participants in the marathon race and were selected because they were reported to represent a group of well-trained leisure time runners. Selection criteria were not stated. This study found that 54% of female runners and only 30% of male runners reported GIT symptoms associated with the marathon race [19].

In another cross-sectional study aimed at determining the prevalence of GIT symptoms in a population of marathon runners, 471 out of 1750 runners entering a marathon race (response rate of 27%) completed a questionnaire prior to the race [18]. The questionnaire, with a covering letter detailing the

athletes, in all six endurance sports, had a higher incidence (occurrences per 1000 hours participation) of all GIT symptoms (except vomiting) [7].

The relationship between fluid intake, fluid loss, running distance, running time and the incidence of GIT symptoms during a 25km and 42.2km race was examined in one prospective cohort study [31]. In this study, 114 untrained subjects were followed over 18 months while they trained for the marathon. At one year subjects ran a 25km race and at 18 months they ran a marathon. Only 44 out of the 114 subjects completed the study (drop-out rate of 61.4%). Subjects consisted of 12 females and 32 males, which was a similar ratio to the original group of 114 subjects. The results of this study showed that female runners experienced significantly more GIT symptoms in the 25km race than male runners. However, there was no significant difference in the incidence of GIT symptoms between male and female runners during the marathon [31].

In summary, there is some, but generally limited, scientific evidence that female gender is a risk factor for developing GIT symptoms during exercise. Selection bias is a limitation in three of the four cross-sectional studies that have explored female gender as a risk factor, and small sample size is a further limitation in all these studies. In conclusion, the strength of evidence supporting female gender as a risk factor for GIT symptoms in endurance athletes is limited.

2.2.4.1.2 Younger age as an intrinsic risk factor for GIT symptoms associated with exercise

A second intrinsic risk factor for GIT symptoms in endurance athletes is younger age. In a number of studies, it has been suggested that younger athletes are more likely to suffer from GIT symptoms than older athletes [7, 15, 18, 30]. Furthermore, the postulated explanations for this observation are that younger athletes 1) may perform exercise at a higher relative intensity than older athletes [18], 2) have a poorly "conditioned" GIT compared to older athletes [18], or 3) may be more prone to dehydration due to lack of experience [6]. The scientific evidence for younger age as a risk factor for GIT symptoms, and the possible factors responsible for this observation, will now be reviewed.

In general, there is limited research, mostly from cross-sectional studies, to suggest that younger age is a risk factor for the development of GIT symptoms in endurance athletes.

In one cross-sectional study, 279 leisure time marathon runners were studied to determine the prevalence of GIT symptoms and the effect of running on weight, diet and daily digestive "problems" [19]. The selection of the runners was not stated but the runners were described as being representative of a population of relatively well-trained leisure time runners. Data were collected in questionnaire format; therefore this relied on runners to accurately recall information and may have led to possible recall bias. In this study, younger

age was not a significant risk factor for GIT symptoms associated with running [19].

In two other cross-sectional studies, questionnaires were given to all entrants to a marathon race (the methodology has already been described above in Section 2.2.4.1.1) [15, 18]. The purpose of each of these studies was explained to the runners, respondents were self-selected and the questionnaires relied upon the runner's accurate recall. The response rate was low in one study (27%) [18] and higher in the other study (41.6%) [15]. The results of both these studies showed that younger age was a significant risk factor for lower GIT symptoms associated with running [15, 18]. In another cross-sectional study of triathletes, a questionnaire was given to all 119 entrants of an endurance triathlon race in order to determine the prevalence of GIT symptoms during exercise [5]. As in the previous studies, respondents were self-selected, and there may have been recall bias, but the response rate in this study was higher (59%). The characteristics of the triathletes and the pattern and prevalence of GIT symptoms associated with exercise was determined, and the results did not show an association between younger age and GIT symptoms during exercise [5].

In a final cross-sectional study, the incidence and risk factors of GIT symptoms were assessed by means of a questionnaire survey in 1158 randomly selected athletes from six different endurance sports (response rate=46%) [7]. The results of this study showed a significantly higher

purpose of the study, was delivered with the race information pack to all entrants. Respondents were therefore self-selected, and of the 471 runners only 38 (8%) were female. This study showed that GIT symptoms were experienced by significantly more female compared with male runners ($P<0.05$). However, only 2 out of the 38 females were asymptomatic for GIT symptoms. This study is limited by sample bias and a low response rate. The small sample size of female runners, with only 2 female runners not experiencing symptoms, is most likely as a result of self-selection [18].

Seven-hundred and seven runners in a marathon race of 1700 runners completed a questionnaire as part of another cross-sectional study [15]. This study investigated demographic data, baseline GIT symptoms and GIT symptoms associated with running. The response rate was 41.6% and respondents were self-selected, possibly resulting in some selection bias. Male runners made up 85.2% and female runners 14.8% of respondents. Again, the results of this study showed that lower GIT symptoms were significantly more common in female runners than in male runners [15].

A fourth cross-sectional study investigated the incidence and possible risk factors for GIT symptoms in six endurance sports (aerobics, canoeing, running, triathlons, cycling and swimming) [7]. In this study, questionnaires were handed to a random sample of athletes in each of the six sports. Response rates ranged from 30% to 60%. The subjects consisted of 884 male athletes and 268 female athletes. The results of this study showed that female

incidence of both upper GIT (p=0.0463) and lower GIT (p=0.0004) symptoms in younger compared with older athletes [32].

The relationship between younger age and the development of GIT symptoms in endurance athletes has also been studied in two prospective cohort studies. In one study, stool samples were collected and tested for the presence of occult blood in four stool samples (1 pre- and 3 post-marathon race) in 31 runners [30]. A questionnaire on demographic data, use of non-steroidal anti-inflammatory drugs (NSAIDS) and any history of gastrointestinal disease was completed by the subjects, and finishing times were recorded. The results of this study showed that younger age was a significant risk factor for the development of a positive test for occult blood in the stool sample after the marathon [30].

Finally, GIT bleeding associated with exercise was also studied in a second prospective cohort design in two groups of subjects using qualitative (faecal occult blood) and quantitative techniques (actual faecal haemoglobin measurement) to identify blood in the stool [33]. The first group consisted of 6 subjects who walked 37km on 4 consecutive days and these subjects provided daily faecal samples. The second group consisted of 46 subjects who ran a marathon and provided a pre-race stool sample and two stool samples post-race. The results of this study did not show a significant association between younger age and GIT bleeding associated with exercise [33].

In conclusion, there is some evidence to suggest that younger age is a significant risk factor in the development of GIT symptoms. In general, most studies are limited by their cross-sectional study design, possible selection bias (self-selection) and possible recall bias (questionnaires). Furthermore, results from two well conducted prospective cohort studies are not consistent. Therefore there is some, however limited, evidence that younger age is a significant risk factor for the development of GIT symptoms associated with exercise in endurance athletes.

2.2.4.1.3 Previous abdominal surgery as an intrinsic risk factor for GIT symptoms associated with exercise

Previous abdominal surgery has been proposed as an intrinsic risk factor for the development of GIT symptoms during exercise [7]. In a single cross-sectional study, the incidence and possible risk factors for GIT symptoms in 6 endurance sports was investigated. In this study, 1158 randomly selected athletes responded to a questionnaire survey and the results showed that the development of upper GIT symptoms was associated with a history of previous abdominal surgery. There is no association between the development of lower GIT symptoms and a history of previous abdominal surgery [7]. This is the only study to have reported previous abdominal surgery as a possible intrinsic risk factor for upper GIT symptoms during exercise and therefore further research in this area is needed.

2.2.4.1.4 Irritable bowel syndrome and lactose intolerance as intrinsic risk factors for GIT symptoms associated with exercise

Irritable bowel syndrome and lactose intolerance have been suggested to be associated with the development of GIT symptoms associated with exercise [9]. A questionnaire was completed by 425 runners participating in a 10km running race as part of a cross-sectional study investigating the prevalence and possible risk factors for the development of diarrhoea associated with running [26]. The incidence of lactose intolerance and irritable bowel syndrome in this population was found to be comparable to that of other populations (13-16%). Both conditions were shown to be associated with predominantly pre-race GIT symptoms. It was also shown that irritable bowel syndrome was associated with an increase in the urge to defaecate while running. Lactose intolerance was not shown to increase the risk of GIT symptoms during exercise [26].

There is limited research to support the association between these two conditions and the development of GIT symptoms during exercise and therefore further research is needed in this area.

2.2.4.2 Extrinsic risk factors for GIT symptoms associated with exercise

A number of extrinsic risk factors for the development of GIT symptoms have been suggested. These include exercising at a high intensity [15, 18, 19, 34], dehydration [31, 35], vertical impact sports (running) [2, 7], poorly conditioned

athletes [18, 19, 33] and the use of medication [30, 33]. The scientific evidence for each of these extrinsic risk factors will now be reviewed.

2.2.4.2.1 High intensity exercise as an extrinsic risk factor for GIT symptoms associated with exercise

The association between high intensity exercise and the development of GIT symptoms during exercise among endurance athletes stems from athletes reporting that they experience "tummy troubles" after a "hard" training session or during races [18]. It has also been reported that athletes who are suffering with new onset GIT symptoms relate this to a recent increase in training mileage or increased exercise intensity [36]. Others have also observed that GIT symptoms tend to occur more frequently when exercise is performed at a higher intensity [2, 18, 19, 30], and that athletes with GIT symptoms appear to benefit from a reduction in training intensity, followed by a more gradual increase to the desired level of training. These anecdotal reports indicate that increased exercise intensity is a possible extrinsic risk factor for the development of GIT symptoms during exercise [36]. The scientific evidence supporting a possible association between high intensity exercise and the development of GIT symptoms associated with exercise will now be reviewed.

An analysis of the published literature shows that this association was studied using either cross-sectional study designs (4 studies) or prospective cohort study designs (4 studies). These studies varied considerably in their

methodology, mainly in defining and measuring exercise intensity, and this makes comparison of results between studies difficult.

In the first cross-sectional study, the prevalence of GIT symptoms and the effect of GIT symptoms on weight, diet and everyday digestive complaints were studied in 279 leisure time marathon runners [19]. In this study, intensity of exercise was measured using the finishing times of runners. The results of this study showed that there was a significant association between faster running times (as an indicator of exercise intensity) and the development of GIT symptoms. However, the investigators did not compare the finishing times to previous running times or performances of the athletes. The authors did comment that most runners were thought to have training programmes that were "harder" than what was necessary for their finishing times. This observation indicates that perhaps runners were not racing at a significantly higher relative exercise intensity compared with their training intensity [19].

In three other cross-sectional studies the relationship between GIT symptoms and intensity of exercise was studied using a questionnaire, where intensity of exercise was either subjectively documented as "easy" or "hard", with no clear definition [2, 15, 18]. Furthermore, these data relied on the accurate recall of information on the part of the subject. In the first of these cross-sectional studies, 471 self-selected runners out of 1750 marathon runners (response rate of 27%) completed a pre-race questionnaire to determine the prevalence of GIT symptoms in marathon runners [18]. In the questionnaire, the runners were asked about the frequency of various GIT symptoms during and after an

"easy" and a "hard" run. The authors admitted that this description may have been interpreted as either increased intensity or increased duration of the run. The results of this study did show that there was a significant association between development of GIT symptoms and running a "hard" run [18].

In a second cross-sectional study the occurrence of GIT symptoms during and after "easy" and "hard" training runs and races was investigated in 707 marathon runners [15]. As with many of the other studies, the sample of runners was self-selected (response rate 41.6%) and the questionnaires relied on subjective recall. The results of this study showed that upper GIT symptoms (nausea, vomiting) were associated with a "hard" run, but other GIT symptoms were not found to be more frequent during a "hard" run compared to an "easy" run [15].

In a third cross-sectional study the association between GIT symptoms and intensity of exercise was investigated in 110 triathletes using a pre-race questionnaire (84% response rate) [2]. The aim of this study was to identify GIT symptoms experienced by triathletes during a triathlon and to examine factors that influence the frequency and severity of the GIT symptoms. A limitation of this study was that exercise intensity was documented in a subjective manner, without an exact description of how exercise intensity was measured. The results of this study showed a positive relationship between the intensity of exercise and the development of GIT symptoms [2].

The relationship between exercise intensity and the development of GIT symptoms during exercise was also reported in four prospective cohort studies [30, 31, 34, 37]. In the first of these prospective cohort studies, GIT blood loss in 18 male triathletes during an ultra-distance triathlon race was documented and the incidence was related to training, performance and haematological measures (mainly iron storage-related) [34]. In this study, subjects provided stool samples during training, and pre- and post-race for qualitative testing for occult blood. In addition, a questionnaire was completed and blood samples were taken for haematological analysis during training, and pre- and post-race. In this study, the finishing time was used as a measure of exercise intensity. The results of this study did not show a significant association between exercise intensity and GIT bleeding [34].

In a second prospective cohort study, the relationship between GIT bleeding and exercise intensity (finishing time) was studied in 31 marathon runners [30]. Subjects provided 4 stool samples - one pre-race sample and 3 samples in the 72 hours following the race. The results of this study showed a positive association between faster running times (as a measure of exercise intensity) and GIT bleeding. However, previous running times and training speed were not documented and relative exercise intensity could therefore not be estimated [30].

In the third prospective cohort study, the effect of graded exercise on gastro-oesophageal reflux and oesophageal motility was investigated in 8 trained cyclists [37]. Subjects were required to cycle in a laboratory at 60% VO_{2max} for

1 hour, at 75% VO_{2max} for 45 minutes and at 90% VO_{2max} for 10 minutes. An intra-oesophageal pH monitor and strain gauge transducer were used to monitor oesophageal pH and oesophageal contractions respectively. The results of this study showed that with increasing intensity of exercise, oesophageal contractions decreased in amplitude, size and frequency, while the number of reflux episodes, as well as the duration of acid exposure, increased. These changes became significant at an exercise intensity >90% VO_{2max}. It must be pointed out that despite the changes in measured variables none of the subjects experienced any GIT symptoms during the study [37].

In the final prospective cohort study, 44 randomly selected untrained subjects were followed over an 18-month period as they trained for a 25km race (at one year) and a marathon (at 18 months) [31]. Thirty-eight of the subjects underwent laboratory testing to determine their maximal heart rate and maximal running speed prior to the marathon. Heart rate was monitored in these subjects during the marathon. Therefore average heart rate and running speed were measured against maximal heart rate and running speed, and this percentage was used as a measurement of exercise intensity during the marathon. Fluid intake and GIT symptoms were monitored during the 2 races. The results of this study failed to show a significant association between running at a high intensity and the development of GIT symptoms [31].

In conclusion, there is some but limited evidence that high intensity exercise is a risk factor for the development of GIT symptoms during exercise. The main reasons for this are that 1) the measure of intensity differs between

studies, 2) many studies rely on a subjective assessment of exercise intensity, 3) a number of studies are limited by recall bias and 4) in studies where finishing times were recorded, these times do not equate to exercise intensity and cannot be used as an accurate assessment of exercise intensity. In studies where an objective measure of exercise intensity, such as heart rate during exercise relative to maximum heart rate or percentage of VO_{2max} was used, no association between exercise intensity and the development of GIT symptoms during exercise was demonstrated. Therefore further studies using more objective and reproducible measures of exercise intensity are needed in order to identify whether high intensity exercise is a significant risk factor for GIT symptoms associated with exercise.

2.2.4.2.2 Dehydration as an extrinsic risk factor for GIT symptoms associated with exercise

It has been postulated that GIT symptoms that develop during exercise occur more frequently in the dehydrated athlete [31, 35]. It has also been suggested that the observation that GIT symptoms during running are more common compared with cycling, may be related to the fact that drinking while running is more difficult than while cycling [10, 38]. However, there is little scientific evidence that dehydration may be related to the development of GIT symptoms during exercise, and only two studies [31, 35] have investigated this relationship. The results of these two studies will now be reviewed.

In one prospective cohort study, the incidence of GIT symptoms during running was studied in relation to fluid intake, fluid loss, running distance and marathon finishing time [31]. In this study, 44 untrained subjects were followed for 18 months while training for a marathon and data were then collected when they ran a marathon at 18 months. Fluid intake was measured during the marathon and subjects were weighed before and after the race in order to calculate fluid loss. GIT symptoms occurring during the marathon were recorded, as were heart rates and finishing times. The results of this study showed that as body weight loss exceeded 4-5% (as a measure of dehydration), the incidence of GIT symptoms increased from 50% to 80%. The volume of fluid intake was not found to be associated with GIT symptoms [31].

The association between hydration status and the development of GIT symptoms during exercise was also investigated in a randomised cross-over study [35]. In this study, 15 subjects each participated in 4 experiments on different days over a 3 month period. The four experimental conditions were dehydration at rest and during exercise, and euhydration at rest and during exercise. In the dehydration and exercise experiment, a 4% body water loss was obtained by running at 60% maximum speed in 30°C heat. Thereafter, subjects were given an isotonic carbohydrate-electrolyte drink to consume. Subjects then returned to the treadmill and continued to run at 60% of maximum speed during which time gastric emptying was measured by means of sampling gastric volumes every 10 minutes for 40 minutes via a nasogastric tube. The presence of GIT symptoms was also recorded. In the dehydration and rest experiment 4% body weight loss was achieved by intermittent

exposure to 100°C sauna heat. Once dehydration was achieved, the isotonic carbohydrate-electrolyte drink was given and gastric emptying measured in the same manner as in the dehydration and exercise experiment [35].

In the euhydration experiments subjects rested for 1hour and 50 minutes during which time they drank 250ml water at 20 minutes and 40 minutes [35]. At the 1 hour 50 minutes mark subjects drank the isotonic carbohydrate-electrolyte drink, and then the euhydrated and exercise group ran on the treadmill at 60% maximal speed, while the euhydrated and rest group remained seated. Gastric emptying and the presence of GIT symptoms were measured in the same manner. The results of this study showed a significant slowing in gastric emptying in the dehydration and exercise experiment. GIT symptoms were also only experienced by subjects during the dehydration and exercise experiment [35].

In summary, it appears that there is strong evidence from one prospective cohort study and one randomised clinical trial that GIT symptoms are more common during exercise in the presence of significant dehydration (body weight loss > 4%). Therefore significant dehydration (> 4% body weight loss during exercise) is an extrinsic risk factor for the development of GIT symptoms associated with exercise.

2.2.4.2.3 Vertical impact sport (running compared with cycling or swimming) as an extrinsic risk factor for GIT symptoms associated with exercise

It has been suggested that vertical impact sports, such as running, are associated with more GIT symptoms than non-impact sports [2, 7, 39]. The scientific evidence for this is mainly from cross-sectional studies and will now be reviewed.

In the first retrospective cross-sectional study, the association between GIT symptoms and dietary intake was investigated in 55 male triathletes [40]. The triathletes were interviewed after an endurance triathlon, and the main finding was that most GIT symptoms occurred during the run leg of the race. The main limitations of this study were possible selection bias, recall bias, and no objective measure of vertical oscillation. Furthermore, running is the third component of a triathlon, and confounding factors, such as the development of fatigue or dehydration, could also explain the increased number of GIT symptoms during running, rather than running (vertical impact) alone.

In a second cross-sectional study, the incidence and possible risk factors for GIT symptoms in 6 endurance sports (1158 athletes) was determined using a questionnaire [7]. The main findings of this study was that canoeing, road running and triathlon had a higher incidence of GIT symptoms compared with other sports such as aerobics, cycling and swimming [7].

In the third cross-sectional study among 110 triathletes who participated in a triathlon race, GIT symptoms were reported more frequently, and with increased severity, in the run leg of the triathlon [2].

Finally, the prevalence and severity of GIT symptoms in relation to carbohydrate supplement use and the type of exercise was studied in a double-blind cross-over control study among 32 well-trained triathletes who each underwent 3 identical experiments one week apart [39]. During each experiment, triathletes were given one of 2 carbohydrate supplements or a placebo to drink at specified times before and during a 3-hour exercise session, which consisted of cycling, alternated with running and then repeated. In this study, GIT symptoms were significantly more common, and of longer duration, during running than during cycling [39].

In summary, there is some, but limited evidence to suggest that running (compared with cycling or other non-impact sports) is associated with increased risk of developing GIT symptoms during exercise. In most of the cross-sectional studies, selection bias, recall bias, as well as inability to control for other confounding variables, limits the strength of the evidence. In one intervention trial, running was associated with a greater incidence of GIT symptoms during exercise compared with cycling.

2.2.4.2.4 Poor conditioning as an extrinsic risk factor for GIT symptoms associated with exercise

It has been suggested that poor conditioning (being "unfit") is a risk factor for GIT symptoms during exercise [18, 19, 33]. It has been postulated that this may be due to inadequate adaptation of the GIT to the physiological stresses of exercise training [5]. The evidence that poor conditioning is a risk factor for the development of GIT symptoms associated with exercise will now be reviewed.

In one cross-sectional study, 279 leisure time runners participating in a marathon completed a questionnaire to determine the relationship between GIT symptoms and long-distance running [19]. The results of this study showed that training history was not associated with the development of GIT symptoms. However, in this study it was not clear how the runners were selected and over what time period the "hours of training per week" were recorded, i.e. during the height of training or during tapering [19].

In another cross-sectional study, 471 runners (27% response rate) reported their training history (number of years of running experience and average weekly distance) and the prevalence of GIT symptoms during running [18]. The main findings of this study showed that GIT symptoms were associated with fewer years of running experience, while weekly training distance did not significantly affect the prevalence of GIT symptoms [18].

In a single prospective cohort study, the relationship between GIT bleeding and exercise training was studied in 6 walkers and 46 marathon runners [33]. All the subjects provided stool samples for analysis at various stages of the study, and the marathon runners also completed a questionnaire reporting their weekly training distances. The marathon running group was further subdivided into two groups depending on whether they had taken any medication or not. The results of the study showed that in the marathon running sub-group who had not taken medication, there was no association between training history and the incidence of GIT bleeding [33].

In conclusion, there is weak evidence that poor conditioning [expressed as number of years of training, amount of training per week (time or distance)] is associated with the development of GIT symptoms during exercise. Furthermore, studies mostly rely on subjective recall of training history, which may not be accurate, and no objective measure of training is reported.

2.2.4.2.5 Medication as an extrinsic risk factor for GIT symptoms associated with exercise

The use of non-steroidal anti-inflammatory drugs (NSAIDS) for soft tissue and musculoskeletal injury in endurance athletes is common [30]. It has been suggested that the use of NSAIDS may be a risk factor for GIT symptoms associated with exercise [33], while others have proposed that the use of NSAIDS may protect against GIT symptoms [9]. Evidence-based research with respect to NSAIDS use and GIT symptoms will now be reviewed.

In a prospective cohort study, data on 31 runners taking part in a marathon were collected [30]. This study investigated the prevalence of GIT bleeding after a marathon and possible associated factors. One stool sample was collected before the race and 3 samples were collected in the 72 hours following the race. Stool samples were tested for occult blood by means of a qualitative technique. A questionnaire was also completed and the runners were asked about NSAIDS use. Results found that the use of aspirin and other NSAIDS were not associated with the GIT symptom of GIT bleeding [30].

A second prospective cohort study investigated two groups for faecal occult blood in stool samples before and after either walking 37km on 4 consecutive days (N=6) or running a marathon (N=46) [33]. The marathon runners also completed a questionnaire and with this information were retrospectively subdivided into two sub-groups depending on whether they used medication or not. The prevalence of GIT bleeding was found to be significantly higher in the runners who took medication and more specifically in those who took NSAIDS [33].

Thirty five ultra-endurance runners were studied before, during and after a 100 mile (160km) race [41]. In this prospective cohort study athletes completed a questionnaire before and after the race. They were also required to provide 3 pre-race and 3 post-race stool samples for occult blood testing. Results of this study showed that 80% of the runners with negative faecal occult blood tests used NSAIDS before or during the race, while 24% of the

athletes who tested positive for occult blood in their stool used NSAIDS. Therefore, in this study there was a negative correlation between GIT bleeding and the use of NSAIDS. In contrast to the generally accepted effects of NSAIDS on the GIT, this study showed that there might be a protective role of NSAIDS against GIT symptoms during exercise.

Lastly, in a prospective cohort study of 41 marathon runners' pre- and post-race stool samples, a post-race questionnaire and post-race endoscopy were used to evaluate GIT bleeding associated with endurance running [42]. Nine of the runners had occult positive post-race stool samples. However, there was no relationship between the use of NSAIDS and GIT bleeding in this study.

Therefore there are inconsistent findings where studies reported on the use of medication, such as NSAIDS, as a possible risk factor for the development of, or the protection against, GIT symptoms associated with exercise. Results differ between studies even when the methods of study are similar. Further research is needed to determine the possible effects of medication (including the use of NSAIDS) on the development of GIT symptoms during exercise.

2.2.4.2.6 Dietary factors as extrinsic risk factors for GIT symptoms associated with exercise

It has been suggested that a number of dietary factors, such as type of food [8, 40], timing of the last meal before exercise [2], caffeine intake [22, 43] and other dietary factors [44, 45], may be associated with the development of GIT symptoms during exercise. The scientific evidence for these dietary factors will now be reviewed.

2.2.4.2.6.1 Type of food

It has been suggested that the type of food ingested may play a role in the development of GIT symptoms associated with exercise [22]. Athletes tend to be more aware of their diet and often consume high-fibre diets as part of a healthy lifestyle [8].

Fifty-five ultra-endurance male triathletes were asked questions in a retrospective cross-sectional study to examine the relationship between GIT symptoms and dietary intake [40]. It was shown that a pre-race high-fibre, protein or fat meal was significantly associated with the GIT symptoms of abdominal cramps or nausea. However, this study relied on subjective recall of the meal, the meal constituents and GIT symptoms.

In another cross-sectional study, 110 out of 141 triathletes competing in a triathlon completed a questionnaire. In this study, it was reported that lower

GIT symptoms (diarrhoea and flatulence) were associated with high dietary fibre intake [2]. Once again these results were based on subjective data and recall.

In another cross-sectional study of 279 marathon runners, a questionnaire was used to obtain data about the relationship between GIT symptoms and running [19]. In this study, it was shown that with the commencement of training, eating habits frequently changed. These changes included increased intake of fibre, vegetables and cereals, and a decrease in the intake of fat, sugar and meat. However, these alterations in eating habits did not significantly alter the risk of developing GIT symptoms associated with exercise. The limitations of this study were that long-term dietary habits rather than pre-race meals were primarily investigated. Furthermore, data from this study also relied on accurate recall and subjective reporting.

It has also been suggested that high glycaemic index (GI) foods may increase the risk of GIT symptoms during exercise, but there are no research data to support this [22].

In summary, it appears that the type of food ingested before exercise may play a role in the development of GIT symptoms during exercise. Research to support this hypothesis is limited and further objective research in this area is necessary.

2.2.4.2.6.2 Timing of pre-competition meal

It has been suggested that the timing of the pre-competition meal may be associated with the development of GIT symptoms [2]. In one retrospective cross-sectional study of 55 ultra-endurance male triathletes, it was found that all triathletes who had eaten within 30 minutes before the race, vomited during the swim leg of the race [40]. In a cross-over cohort study of 12 subjects, nausea was measured using a visual analogue scale during cycling in the fasted and the fed state, as well as during varying exercise intensities [46]. The results of this study showed significantly higher nausea scores after eating immediately before exercise and eating 60 minutes before exercise when compared to exercising in the fasted state [46].

Forty-four subjects were followed over an 18-month period while training for a marathon in a prospective cohort study [31]. The timing of the last meal before the race was recorded, as was the occurrence of GIT symptoms during the race. The results of this study did not show a significant association between the timing of the pre-race meal and the development of GIT symptoms during exercise [31].

In summary, results from studies where the relationship between the timing of the last meal before exercise and the development of GIT symptoms during exercise were studied, are not consistent. Further research to define this relationship is necessary.

2.2.4.2.6.3 Caffeine

Caffeine is both a diuretic and a stimulant for the GIT [47]. Caffeine ingestion before or during exercise may, therefore, be a potential risk factor for the development of GIT symptoms during exercise [22, 43]. In a single cross-sectional study, a questionnaire was completed by 110 triathletes to document the relationship between dietary factors (including caffeine) and the development GIT symptoms during exercise [2]. The results of this study showed that lower GIT symptoms (flatulence and diarrhoea) were associated with the ingestion of caffeine. However, neither the timing nor the amount of caffeine that was ingested was reported in this study. Therefore there is very limited evidence that caffeine ingestion is a risk factor for GIT symptoms, and more research is needed.

2.2.4.2.6.4 Other dietary substances as risk factors for GIT symptoms during exercise

A number of other ingested substances have been suggested as risk factors for the development of GIT symptoms during exercise. It has been suggested that the ingestion of excess amounts of vitamin C may cause exercise-related diarrhoea, but there is no conclusive data to support this hypothesis [44]. Similarly, the ingestion of alcohol is mentioned as a possible risk factor for the development of GIT symptoms during exercise, but there are no research data to confirm this [2, 22].

2.2.4.2.6.5 Summary – dietary factors as risk factors for GIT symptoms during exercise

In summary, a number of dietary factors have been postulated as risk factors for the development of GIT symptoms during exercise. These include the type of food consumed and the timing of the meals in relation to the exercise training session or the competition. In general, there are not enough research studies that have investigated these dietary factors, and there is not enough evidence to support the role of dietary factors in the development of GIT symptoms during exercise. This area requires further investigation.

2.2.4.3 Summary of intrinsic and extrinsic risk factors for the development of GIT symptoms associated with exercise

In general, scientific research studies that have investigated intrinsic and extrinsic risk factors for the development of GIT symptoms during exercise are limited. In this section, scientific evidence in support of these intrinsic and extrinsic risk factors for the development of GIT symptoms during exercise was reviewed using an evidence-based approach (classified as strong, limited or weak). In Table 2.5 the evidence for these risk factors is summarised.

There is strong evidence from a limited number of studies to support significant dehydration (body weight loss > 4% during or after exercise) as a risk factor for GIT symptoms during exercise. However, more research studies are still needed to support this finding. There is some, but limited scientific

evidence, to support the following as risk factors for GIT symptoms during exercise: female gender, younger age, high intensity exercise, vertical impact sport and medication use. Poor conditioning, dietary factors and previous abdominal surgery are risk factors for GIT symptoms that are not well supported and evidence is considered weak in these areas.

Therefore further research studies of greater power, such as case control and prospective cohort studies are needed in order to evaluate risk factors adequately. Subject selection needs to be random and subjects should not be self-selected. Data needs to be collected in an objective manner not relying on subject recall. Measurement parameters also need to be standardised. In conclusion, there is very little evidence-based research to support most of these suggested risk factors and further research is essential.

Table 2.5: Summary of the level of evidence for intrinsic and extrinsic risk factors for GIT symptoms associated with exercise

RISK FACTOR	LEVEL OF EVIDENCE
Female gender	Limited
Younger age	Limited
Irritable bowel syndrome and lactose intolerance	Weak
Previous abdominal surgery	Weak
High intensity exercise	Limited
Dehydration	Strong
Vertical impact sport (running)	Limited
Poorly conditioned athlete	Weak
Medication	Limited
Dietary factors	Weak

2.2.5 Pathophysiology of GIT symptoms associated with exercise

The pathophysiology underlying the development of GIT symptoms during exercise is poorly understood [48]. It is likely that there are multiple mechanisms that may be responsible for GIT symptoms associated with exercise [49, 50]. Furthermore, it is difficult to study the physiology of the GIT during exercise as most methods of study of the GIT apply to the resting (non-exercising) condition [9, 51]. It is difficult to adapt these study methods to the exercising individual and to then interpret the results accurately [4]. Therefore there are only a limited number of studies where the pathophysiology of GIT

symptoms associated with exercise have been investigated, and the outcomes of these studies often show conflicting results [8].

A number of hypotheses have been suggested for the development of GIT symptoms associated with exercise. These include the mechanical hypothesis, gastrointestinal motility hypothesis, absorption and secretion hypothesis, neuroendocrine hypothesis, endotoxaemia hypothesis, allergic reaction hypothesis, infectious disease hypothesis and the altered blood flow hypothesis. The scientific evidence for each of these hypotheses as possible pathophysiological mechanisms for the development of GIT symptoms associated with exercise will now be reviewed.

2.2.5.1 Mechanical hypothesis for the development of GIT symptoms associated with exercise

As previously mentioned, it has been observed that vertical impact sports, such as running are associated with more GIT symptoms than gliding sports, such as swimming and cycling [7, 38]. It has, therefore, been suggested that the mechanical movement of the athlete's body during exercise results in vertical oscillation of the GIT, which then precipitates GIT symptoms in vertical impact sports [7]. However, the precise mechanism for the development of GIT symptoms as a result of vertical oscillatory movement is not clear [48]. It has been suggested that mechanical trauma and possible contusion of the abdominal organs (mainly small and large bowel) results in GIT symptoms [8, 52]. It has also been suggested that exercise causes mass

movement of stool into the rectum and this results in the urge to pass stool [15], and that the oscillatory movements result in emptying of the sigmoid colon into the rectum [21]. The evidence in support of the mechanical hypothesis is, however, limited. To date, there are only a few case reports and a single prospective cohort study where the vertical oscillatory model for the development of GIT symptoms associated with exercise has been studied.

In one of the first reports describing a possible mechanical cause for GIT symptoms, a case of a 56-year-old male runner who experienced diarrhoea following a marathon was reported [53]. In this runner, the authors suggested that the mechanical contact of the caecum against the anterior abdominal wall resulted in local trauma, analogous to exercise-induced haematuria from the bladder [54]. This mechanical contact was suggested as the cause of the GIT symptoms in this athlete and this has been termed the "caecal slap" syndrome [53].

Hypertrophy of the retroperitoneal psoas muscle in an athlete has also been suggested as another possible mechanism that may cause mechanical trauma to the GIT during exercise [55]. In one case study of a 36-year-old runner who experienced mainly lower GIT symptoms during running, it was hypothesised that the colon was mechanically displaced and compressed by the increased muscle mass of the hypertrophied psoas muscle (as seen on contrast X-ray images) causing GIT symptoms during exercise in this athlete [55].

Two case reports of caecal volvulus in competitive athletes have also been reported [56]. In these cases, it has been suggested that the combination of a very lean mesentery and the mechanical bouncing of running may have been responsible for the volvulus [56].

All these reports are, however, case studies, and there are no other studies (case control or prospective cohort studies) to support the hypothesis that the caecal slap syndrome, psoas hypertrophy or caecal volvulus are mechanisms that may explain the cause of GIT symptoms associated with exercise.

It has also been suggested that mechanical stimulation may induce the release of the GIT hormone, vasoactive intestinal peptide (VIP) [57]. This hormone is associated with increased colonic motility, decreased absorption and increased secretion, which have been suggested to result in secretory diarrhoea [58]. In animal interventional studies, it has been shown that distension of the stomach, as well as mechanical stimulation of the mucosa of the stomach, small and large intestine can result in significant release of VIP [57, 59]. The possible role of VIP and other GIT hormones in the development of GIT symptoms associated with exercise will be discussed in further detail in Section 2.2.5.4.

In a single prospective cohort study, which was designed to investigate the mechanical hypothesis for GIT symptoms associated with exercise, six athletes were monitored during cycling and running using an accelerometer [60]. In this study, the accelerometer was placed on the abdomen and

vibration in three planes was monitored during running and cycling. The results of this study showed that running resulted in more than double the vibration compared with cycling [60]. However, GIT symptoms were not reported during the study [60].

In another prospective cohort study, it was shown that GIT symptoms were more frequent during running than cycling in an experiment where subjects alternated between running and cycling [39]. Therefore the increased vibration during running may be associated with GIT symptoms, but this has not been confirmed in case control or prospective cohort studies in runners with or without GIT symptoms.

In summary, scientific evidence supporting the mechanical hypothesis for the development of GIT symptoms associated with exercise is limited. Evidence only comes from case report or series and one prospective cohort study. Furthermore, there is no clear link between the mechanical effects of vertical oscillation and the development of GIT symptoms in athletes. However, it appears that many clinicians support the mechanical model because of the apparent strong association between running and the development of GIT symptoms [8, 61]. It is also important to note that the mechanical hypothesis does not explain the pathophysiology of GIT symptoms in athletes participating in non-impact endurance sports.

2.2.5.2 Gastrointestinal motility hypothesis for the development of GIT symptoms associated with exercise

The gastrointestinal motility hypothesis has been put forward as another possible explanation for the development of GIT symptoms associated with exercise [62]. It has been suggested that exercise affects the intrinsic motility of the GIT, which then results in GIT symptoms [4]. The exact mechanism by which motility is affected is uncertain, but may be due to alterations in blood hormone concentrations, changes in blood supply to the GIT or as a result of exercise-induced changes in the autonomic nervous system [62, 63]. It is important to consider that the motility in each component of the GIT including oesophagus, stomach, small and large bowel, may be affected. Therefore, the effects of exercise on motility in each separate component of the GIT will now be briefly reviewed.

2.2.5.2.1 Exercise and oesophageal function

It has been suggested that the upper GIT symptoms of heartburn and nausea are related to abnormalities in oeophageal motility that occur during exercise [4]. The effect of exercise on oesophageal function and evidence that this may be a potential mechanism for development of GIT symptoms associated with exercise will now be discussed.

It has been shown that gastro-oesophageal reflux increases with exercise [64]. In a prospective cohort study, 8 trained and 9 untrained subjects

underwent graded cycling exercise [37]. In this study protocol, the intensity of cycling was increased from 60% to 75% and then to 90% VO_{2max} with a rest period between each bout of cycling. Gastro-oesophageal reflux and oesophageal motility were measured throughout by means of an intra-oesophageal pH monitor and a 3 strain gauge transducer. The results of this study showed that the number and duration of reflux events increased with increasing intensity of exercise, and that there was a decrease in the frequency, amplitude and duration of oesophageal contractions with increasing exercise intensity. However, in this study, there was no difference in the responses between the two groups (trained and untrained) and both groups were asymptomatic for GIT symptoms during exercise [37].

Although blood concentrations of GIT hormones were also measured in this study, there was no association between reflux and changes in hormone levels in response to the exercise bouts [37]. Therefore this study demonstrated a change in oesophageal function (increased number and duration of reflux events and decrease in oesophageal contractions associated with increasing intensity of exercise) but this was unrelated to GIT symptoms [37].

The effect of fasting compared with eating before exercise on gastro-oesophageal reflux has also been studied. In a prospective cohort study investigating gastro-oesophageal reflux in different types of exercise, a total of 17 subjects were studied [51]. An intra-oesophageal pH monitor was used to record reflux events. All exercise sessions were performed at greater than

70% VO_{2max} and GIT symptoms were recorded during the exercise session. Ten subjects rowed for 30 minutes, 11 subjects ran in a fasted state for 60 minutes and 9 subjects ran in a post-prandial state for 60 minutes. If a subject took part in more than one session, this was not done on the same day. The results of this study showed an increase in gastro-oesophageal reflux associated with all 3 forms of exercise compared to resting, that post-prandial running was associated with significantly more reflux than fasted running and rowing, GIT symptoms were experienced by 3 subjects but this did not correlate with reflux events, and reflux during fasted running predisposed subjects to more severe reflux during post-prandial running. Therefore, this study showed a change in gastro-oesophageal reflux associated with exercise but there was no association between reflux and the development of GIT symptoms during exercise [51].

A single study showed an association between gastro-oesophageal reflux events and the symptom of belching [65]. In this randomised single-blinded study, 14 subjects were given either placebo or ranitidine 300mg (H2 Blocker) and then performed a 1 hour treadmill run at 70-85% VO_{2max}. The result of this study showed that there were significantly less reflux events in the subjects who had taken Ranitidine but there was no effect on the symptom of belching [65].

It has been suggested that the gastro-oesophageal reflux events during exercise are due to the mechanical nature of exercise, raised intra-abdominal

pressure, slowed gastric emptying or possibly alteration in lower oesophageal sphincter pressure [66].

Evidence that exercise decreases lower oesophageal sphincter pressure comes from a prospective cohort study [67]. In this study, the effect of exercise on oesophageal peristalsis and lower oesophageal sphincter pressure was studied in 6 male subjects. A 3 lumen polyvinyl manometry catheter was used to record pressure changes and peristalsis before, immediately after, and one hour after subjects had run for 2 hours on a treadmill at 50% VO_{2max}. The results of the study showed an increase in lower oesophageal pressure immediately post-exercise, no alteration in peristalsis during exercise compared to pre-exercise measurements, and none of the subjects experienced any GIT symptoms [67].

In another prospective cohort study 7 cyclists performed four 5-minute bouts of cycling at 90% VO_{2max} with a rest of 1-3 minutes between each bout [68]. The second and third bout was followed by the ingestion of 600 ml and 200 ml respectively of sports drink. Pressure measurements of the lower oesophageal sphincter were taken before, during and after exercise bouts. The results showed a decrease in lower oesophageal sphincter pressure associated with high intensity exercise, and the ingestion of fluid did not affect the decrease in pressure [68].

In another study, 10 well-trained subjects were studied in a cross-over study to investigate the effect exercise has on various components of GIT function

[69]. In this study, oesophageal motility and gastro-oesophageal reflux events were measured by means of a transnasal catheter with pressure, and pH sensors that were connected to a data recorder. Subjects took part in two protocols: The exercise protocol involved resting for 60 minutes followed by cycling for 90 minutes at >80% VO_{2max} followed by 210 minutes of rest, and the rest protocol subjects rested for the entire time mentioned. Diet was standardised for the 24 hours preceding the study. The results of the study showed a decrease in lower oesophageal pressure and an increase in peristaltic velocity during exercise. There was no significant difference in reflux events in this study [69].

In conclusion, the effect of exercise on gastro-oesophageal reflux events, oesophageal peristalsis and lower oesophageal sphincter pressure is not consistent from the studies where this has been investigated. It has been suggested that the intensity of exercise may play a role in the altered function of the oesophagus [69] but the precise role of exercise intensity in the development of GIT symptoms is not clear. Further research is needed to document the association between oesophageal function in GIT symptomatic and asymptomatic subjects at varying levels of exercise intensities and types of exercise.

2.2.5.2.2 Exercise and gastric function

The GIT plays an important role in the efficient delivery of fluid, energy and electrolytes to the body during endurance exercise [21]. The delivery of

gastric contents to the intestine for absorption is thought to be under the control of the duodenum [38]. The duodenum has receptors for pH, carbohydrates, amino acids, fatty acids and osmolality [38]. It has been suggested that a delay in gastric emptying may be a possible mechanism for the development of GIT symptoms associated with exercise [31, 38]. Therefore factors which may delay gastric emptying will now be reviewed briefly (Table 2.6).

Table 2.6: Factors affecting gastric emptying

Factors resulting in delayed gastric emptying
High intensity exercise
Hyperosmolality
Dehydration
Caloric content
Raised temperature
Reduced volume

2.2.5.2.2.1 High intensity exercise

It has been suggested that exercise at high intensity delays gastric emptying [6, 70]. In a cross-over study investigating the effect of varying exercise intensities on gastric emptying, 10 male subjects took part in two experimental protocols [70]. The protocols took place on separate days and were either a rest protocol or an exercise protocol. The protocols were divided into six 15-minute bouts. Prior to each 15-minute bout, 400ml of water was consumed.

The exercise protocol consisted of 3 bouts of graded walking from 28% to 41% to 56% VO_{2max} followed by 3 bouts of graded running from 57% to 65% to 75% VO_{2max}. The results showed an increase in gastric emptying at all intensities of walking and running, except at an intensity of 75% VO_{2max}. The increase in gastric emptying was similarly increased at these intensities. However, at 75% VO_{2max} gastric emptying was found to decrease significantly. Therefore at exercise intensities equal or greater than 75% VO_{2max}, gastric emptying will decrease significantly [70].

2.2.5.2.2.2 Hyperosmolality

Delayed gastric emptying can result in a delay in the delivery of substrate for energy metabolism, as well as upper GIT symptoms during exercise. Therefore the effect of the osmolality of ingested fluid during exercise on gastric emptying has been studied. In one study, gastric emptying of an isotonic and a hypertonic drink during running and cycling at 70% VO_{2max} for 80 minutes was compared in a randomised clinical trial [71]. There was a significant reduction in gastric emptying of the hypertonic drink while the isotonic drink emptied at a rate similar to water [71]. In another randomised cross-over study the effect of osmolality and temperature on gastric emptying was investigated in 5 trained athletes who ran for 2 hours at 65% VO_{2max} in 35°C heat. In a randomised fashion subjects were given 10% glucose polymer, 10% glucose or sweetened water [72]. In a fourth intervention, in 25°C temperature, subjects were given sweetened water to drink. Gastric emptying was significantly reduced in the glucose experiment, while

exercising in the heat was also associated with a slower gastric emptying compared with the cooler conditions [72]. Therefore hyperosmolar solutions, as well as exercising in the heat, can reduce gastric emptying. However, a direct causal link between these conditions and an increased incidence of GIT symptoms during exercise has not been established.

2.2.5.2.2.3 Dehydration

It has also been suggested that dehydration is associated with delayed gastric emptying [35]. In a randomised cross-over study, 15 subjects participated in each of 4 experiments; euhydrated-rest, euhydrated-exercise, dehydrated-rest and dehydrated-exercise [35]. During the euhydrated experiments, subjects were given water to drink at 20 and 40 minutes during an initial 2-hour rest period. In order to dehydrate the subjects the dehydrated-exercise group cycled at 60% VO_{2max} in 30°C heat and the dehydrated-rest group was exposed to 100°C sauna heat until subjects had lost 4% body weight as an indication of body water loss. Thereafter all subjects were given an isotonic carbohydrate electrolyte beverage to drink (8ml/kg). Following this, the euhydrated-exercise and dehydrated-exercise groups began the exercise session (running on a treadmill at 60% VO_{2max}) and the euhydrated-rest and dehydrated-rest groups began the rest session. Gastric emptying was measured every 10 minutes for 40 minutes by means of a nasogastric tube utilising the double-sampling technique in all subjects [73]. The results of this study showed a significant decrease in gastric emptying in only the dehydrated-exercise group. It was concluded that the effect of exercise and

dehydration are additive in delaying gastric emptying. GIT symptoms were only reported during the dehydrated-exercise protocol and six subjects were affected (37.5%). Therefore the results of this study support the hypothesis that dehydration results in delayed gastric emptying and that delayed gastric emptying is a possible mechanism in the development of GIT symptoms associated with exercise [35].

2.2.5.2.2.4 Caloric content

It has been suggested that the type of carbohydrate ingested may alter gastric emptying [45]. In one prospective cohort study gastric emptying was determined in 6 subjects after the ingestion of test meals containing glucose, fructose, lactose, galactose, maltose or sucrose [45]. Glucose was found to slow gastric emptying down far more than galactose, while fructose ingestion had the least effect on gastric emptying. Therefore the type of carbohydrate can affect the rate of gastric emptying and may be related to the risk of developing GIT symptoms during exercise.

2.2.5.2.2.5 Raised ambient temperature

As previously mentioned, exercising in the heat may reduce the rate of gastric emptying. The effect of heat and hypohydration on gastric emptying was studied in 10 well-trained subjects. In this study, subjects ran for 15 minutes on a treadmill at 50% VO_{2max} in three ambient temperatures (18°, 35° and 49°C heat) [74]. Gastric emptying was significantly reduced while exercising

in the 49°C condition, and the higher the ambient temperature, the more significant the reduction in the rate of gastric emptying [74].

2.2.5.2.2.6 Reduced gastric volume

It has also been suggested that reduced gastric volume as a result of ingesting less fluid may delay gastric emptying [75]. In a cross-over study, 8 subjects cycled for 2 hours at 70% VO_{2max} on three different occasions, while consuming 11.5ml/kg/hr, 17.1ml/kg/hr or 23ml/kg/hr of a 7.5% carbohydrate solution every 15 minutes. The results showed that gastric emptying was fastest in the group who drank the highest volume of fluid and slowest in the group who drank the least amount of fluid [75].

In conclusion, there are many factors that may affect gastric emptying during exercise. However, in only one study, the effects of delayed gastric emptying, as a result of dehydration, was associated with the development of GIT symptoms during exercise. Scientific evidence linking other factors that affect gastric emptying to the development of GIT symptoms during exercise is limited, and this requires further investigation.

2.2.5.2.3 Exercise and function of the small and large bowel

It has been postulated that exercise may affect the motility of the small and large bowel, and that these effects may be responsible for the development of

GIT symptoms during exercise [6]. However, there is very limited scientific evidence to support this hypothesis, and this will now be reviewed.

The most common method of documenting the effect of exercise on small and large bowel motility is to investigate the effect of exercise on orocaecal transit time or whole gut transit time. Orocaecal transit time is the transit time from mouth to caecum, and this can be measured using the hydrogen breath test. The hydrogen breath test measures the hydrogen concentration after the ingestion of lactulose and this represents small bowel transit time [76]. The effects of exercise on orocaecal transit time using this method has been reported in three studies [77-79].

In the first of these three studies, 7 subjects underwent testing during rest and exercise on separate days [77]. Exercise sessions consisted of cycling for 5 minutes and then resting for 5 minutes. This cycle was repeated for 6 hours. Hydrogen concentration was measured every 10 minutes in both experiments. The results showed no change in small bowel transit time between the rest and exercise interventions [77].

In the second study, continuous hydrogen concentration was measured in 12 subjects during a 2 hour rest and exercise (walking on a treadmill at 5.6km/hr with 2% gradient for 2 hours) session [78]. In this study there was a significant decrease in orocaecal transit time in the exercise session [78].

In the third study, the hydrogen concentrations of 23 subjects were measured every 15 minutes during either an exercise session (walking for 60min at 4.5km/hour) or resting for 60 minutes [79]. Orocaecal transit time in this study was found to increase during the exercise session.

In a final study, the effect of exercise on various aspects of GIT function, including measurement of the orocaecal transit time by means of the hydrogen breath test, was studied in 10 well-trained subjects [69]. Subjects took part in two protocols consisting of a rest protocol and an exercise (rest for 60 minutes followed by cycling for 90 minutes at >80% VO_{2max} followed by 210 minutes rest) protocol. Diet was standardised for the 24 hours preceding the study and hydrogen concentration was measured every 15 minutes during the test protocols. The findings were that there was no significant difference in orocaecal transit time between the rest and the exercise experiments [69].

As mentioned, the effect of exercise on small and large bowel motility can also be measured using whole gut transit time. Whole gut transit time is studied using the excretion of radio-opaque markers [80]. This methodology was employed in a number of studies. In one study, 10 subjects took part in 3 experiments each lasting 1 week [81]. The experiments consisted of either running or cycling at 50% VO_{2max} or resting for 1 hour of every day for a week. Dietary fibre and fluid intake were recorded. Stool samples were collected, weighed and X-rayed. The results of this study showed that there was a significant decrease in whole gut transit time in the running and cycling experiments compared with the resting experiment. However, there was no

difference in whole gut transit time between running and cycling conditions [81].

Finally, a pH-sensitive radio-telemetry capsule can be used to measure small bowel transit time and if this is combined with the radio-opaque marker method to measure whole gut transit time, the colon transit time can be calculated. In one study, the effects of an exercise bout on these motility parameters have been studied [62]. Small bowel transit time and colonic transit time were measured in 11 trained female athletes who participated in either a 1-hour cross country run at approximately 70% VO_{2max} or a 6-hour rest period randomly on separate occasions [62]. In this study, 6 athletes reported GIT symptoms during the exercise experiment, but there was no significant difference in the transit times of small bowel and colon between the rest and exercise period. Therefore in this study, exercise did not affect small and large bowel transit times, and GIT symptoms were subsequently not associated with change in transit times [62].

In conclusion, the effects of exercise on the measurement of small and large bowel transit times vary. Transit times have been shown to increase, decrease or remain unchanged with exercise [8]. The reason for these varied results is not clear but may be due to differences in populations studied, methodology used, exercise type, exercise intensity, training status and method of analysis of transit time [48, 62].

In summary, there is limited evidence that alterations in motility in segments of the small and large bowel occur as a result of exercise. Furthermore, there is weak or no evidence that these alterations might be a contributing factor to the development of GIT symptoms during exercise [8]. Further research in this area is needed.

2.2.5.3 Absorption and secretion hypothesis

Absorption and secretion of osmotically active substances from and into the lumen respectively is part of the normal functioning of the GIT [48]. It has been postulated that GIT symptoms during exercise may be as a result of changes in this absorption and/or secretory function of the GIT [10, 17]. A number of mechanisms whereby exercise could possibly alter the absorption and/or secretory function of the GIT have also been proposed and include reduction of blood flow, reduced transit time, direct damage to brush border enzymes and altered GIT hormone levels [4, 10].

It has been suggested that reduced blood flow to the GIT during exercise [12] can alter ATP-fuelled sodium and potassium pumps, resulting in decreased glucose absorption [38]. If glucose remains in the GIT lumen this can exert an osmotic pull on intravascular fluid, and movement of fluid from the intravascular compartment into the GIT lumen may result in the development of osmotic diarrhoea [38]. It has also been suggested that if carbohydrate is not absorbed in the small intestine due to reduced perfusion, glucose will be off-loaded into the colon [62], where colonic bacteria will ferment the

carbohydrate. The formation of excess gas may then cause GIT symptoms [10]. However, there is only limited scientific data to support these mechanisms and their role in the gastrointestinal secretion and absorption hypothesis for the development of GIT symptoms during exercise [8].

In one prospective cohort study, the effect of exercise on absorption of water, glucose and electrolytes was investigated in 5 subjects who ran for 1 hour at 70% VO_{2max} while receiving a constant infusion of test liquid combined with a non-absorbable marker [82]. A triple lumen catheter was used to measure the contents of the GIT beyond the jejunum before and during exercise. In this study, there was no difference in luminal contents (water, glucose and electrolytes) at rest and during exercise [82].

In another study the relationship between pepsinogens, endurance running and the development of GIT symptoms during exercise was investigated in a prospective cohort study [83]. In this study, blood samples were taken at various stages of a marathon and GIT symptoms were recorded in 13 male subjects. It was found that altered hormone levels were not associated with GIT symptoms. Of interest, it was noted in this study that 4 subjects who consumed hyperosmotic beverages during the marathon did not report any GIT symptoms [83].

In another study, gastric acid secretion was unchanged and absorption of triglycerides (as detected on blood samples) was similar in subjects who

either cycled (45 minutes at 50-70% VO_{2max}) or rested for 45 minutes after eating a steak [84].

In summary, there are limited data available that absorption and secretion is altered during exercise, and that this can cause GIT symptoms during exercise. In studies where this hypothesis was investigated, exercise did not alter the absorption or secretory function of the GIT [62].

2.2.5.4 Neuroendocrine hypothesis

The control of the GIT is primarily under the influence of GIT hormones [38], and the release of these hormones is controlled by the autonomic nervous system [38]. It has, therefore, also been suggested that exercise may alter the secretion of GIT hormones and that this may cause the development of GIT symptoms during exercise [83]. The evidence for the neuroendocrine hypothesis as a cause of GIT symptoms during exercise will now be reviewed.

Table 2.7: Neuroendocrine control of the GIT

GIT HORMONE	AUTONOMIC NERVOUS SYSTEM
Vasoactive Intestinal Polypeptide (VIP)	Adrenalin
Gastrin	Noradrenalin
Motilin	
Pancreatic polypeptide	
Somatostatin	
Glucagon	
Insulin	
Secretin	
Peptide histidine isoleucine	
Neurokinin A	
Pancreastatin	
Glucagon-like peptide 1	
Enteroglucagon	
Neurotensin	
Gastric inhibitory peptide	

GIT hormones and the autonomic nervous system neurotransmitters involved in the neuroendocrine control of the GIT are listed in Table 2.7. At rest, GIT hormones play a role in the control of absorption, secretion and motility of the GIT [48]. A detailed discussion of the physiology, including the factors that may alter the stimulation of each hormone, varies and is beyond the scope of this review. However, there are two relevant stimuli, which may affect the

release of these hormones during exercise. These two stimuli are ischemia and mechanical irritation.

In two separate animal studies, bowel ischemia, as well as mechanical stimulation of the mucosa of the small bowel and rectum, resulted in the release of vasoactive intestinal peptide (VIP) into the portal circulation [57, 85]. Raised levels of VIP can cause a decrease in absorption, increased secretion and increased colonic motility. This can result in the development of secretory diarrhoea [9, 58].

The relationship between exercise, GIT symptoms and neuroendocrine factors has been investigated in a number of studies [58, 63, 83, 86]. In one study, the GIT hormone response was investigated in 7 trained runners who ran 30km at a speed of 15km/hr compared with the response of a control group of 5 subjects who were exposed to 20 minutes of dry sauna heat of 80°C [63]. Blood samples taken before and at various intervals during running and during heat exposure showed that there was no change in hormone levels in the sauna group, but that running resulted in an increased blood concentration of the following hormones and neurotransmitters: VIP, gastrin, motilin, somatostatin, glucagon, pancreatic polypeptide noradrenalin and adrenalin. The levels of the following hormones remained unchanged enteroglucagon, neurotensin, gastric inhibitory peptide and insulin. GIT symptoms were not reported by any of the runners or control subjects [63].

In a prospective cohort study, the relationship between marathon running and GIT hormone response was investigated in 26 runners participating in a marathon race [58]. Blood samples were taken pre- and immediately post-race for the following hormones: VIP, gastrin, neurokinin A, pancreastatin, insulin, glucagon-like peptide 1, secretin and pancreatic polypeptide. The results showed that blood concentrations of all the hormones increased after the marathon except insulin. In this study, 8/26 runners reported GIT symptoms during the race. However, there was no significant association between the development of GIT symptoms during the race, and blood hormone concentrations [58].

In a similar prospective cohort study [86], blood samples were taken before and after a 67km running race in 89 runners. In this study the effects of running on GIT hormones and neurotransmitters were investigated for gastrin, VIP, peptide histidine isoleucine, motilin, cortisol, adrenalin and noradrenalin. The results of this study showed that the blood concentrations of all the hormones and neurotransmitters increased after the run except for noradrenalin. GIT symptoms were reported in 33% of the runners but once again there was no significant correlation between the development of GIT symptoms and blood concentrations of hormones or neurotransmitters. The one exception was that decreased noradrenalin levels were associated with abdominal cramps. However, this was attributed to a possible slower running pace as a result of the abdominal cramps rather than a cause of the abdominal cramps [86].

In a final study, blood samples were taken at intervals before and after an endurance mountain marathon (7 days pre-race at sea level, 24 hours pre-race at altitude, immediately post-race and 24 hours post-race) in 13 runners [83]. Blood concentrations of pepsinogen 1, pepsinogen 11, cortisol and gastrin were measured. A control group of 5 subjects travelling with the runners was included in the study to control for travel, altitude, acclimatisation, food and beverages consumed. Runners and controls were also asked to report GIT symptoms during the study period. The results of this study showed that runners had significant increases in blood gastrin and cortisol levels and significant decreases in blood pepsinogen levels after the race while blood hormone levels in the control group remained stable. Forty-six% of runners reported GIT symptoms during and 62% runners reported GIT symptoms after the race. Again, there was no significant association between GIT symptoms and blood hormone levels in the runners [83].

In conclusion, there is strong evidence that exercise results in increases in the blood concentration of a number of hormones and neurotransmitters. It has been suggested that these changes in hormone concentrations may be a result of the metabolic demand of exercise [58, 83] and reduced clearance secondary to decreased blood flow during exercise to the liver and kidneys [38]. There is also strong evidence that there is no causal link between these increases in blood hormone and neurotransmitter concentrations and the development of GIT symptoms during exercise.

2.2.5.5 Endotoxaemia hypothesis

The basis of the endotoxaemia hypothesis is that gram negative bacteria from the GIT gain access to the circulation during exercise, resulting in endotoxaemia, which is proposed to cause GIT symptoms associated with exercise [87]. It is suggested that either a reduced blood supply to the GIT during exercise or mechanical trauma can alter the integrity of the gut mucosa resulting in access of colonic bacteria to the circulation [87, 88]. The symptoms of endotoxaemia include fever, rigors, dizziness, nausea, vomiting, diarrhoea, abdominal cramps, and symptoms of severe sepsis [89].

In a prospective cohort study of 18 triathletes, the relationship between endotoxaemia and strenuous exercise was investigated [90]. Blood samples, taken from the subjects before and immediately after an ultra-endurance triathlon, showed an increase in serum lipopolysaccharide (LPS) and a decrease in serum anti-LPS immunoglobin G (IgG) concentrations. LPS and anti-LPS IgG are indicators of endotoxaemia [87]. However, GIT symptoms were not recorded in these subjects. The authors suggested that high intensity training may have resulted in exposure to LPS with the resultant production of IgG antibodies. Following re-exposure to the antigen (LPS) during the race, the IgG antibodies attach to the antigen (LPS) and levels of free IgG subsequently decrease. The results of this study suggest that endotoxaemia may follow strenuous exercise, but there was no causal link to the development of GIT symptoms during exercise [90].

In another prospective cohort study, the relationship between GIT symptoms and endotoxaemia was investigated in 29 triathletes who were studied before and after an ultra-endurance triathlon [87]. A questionnaire that included questions about GIT symptoms was completed by the subjects pre- and post-race, and markers of acute phase reaction and release of cytokines were measured. Blood samples were obtained pre- and post-race (immediately, 1 hour, 2 hours and 15-20 hours post-race) for LPS, anti-LPS IgG, Tumour Necrosis Factor (TNF), interleukn-6 (IL-6), C-reactive protein (CRP) and pre-albumin. The main findings were that there was a decrease in anti-LPS IgG and an increase in LPS serum concentrations but only in a range that is considered as a mild endotoxaemia. IL-6 was also significantly raised after the race. Reported GIT symptoms during the race were not associated with LPS levels, but more severe GIT symptoms were found to be associated with IL-6 levels. It was therefore concluded that endurance exercise may result in a mild endotoxaemia but a direct relationship between endotoxaemia and the development of GIT symptoms during exercise could not be established. It was also postulated that the raised IL-6 levels may be part of an acute phase reaction following muscle damage and that this is probably unrelated to endotoxaemia [87].

In summary, there is little evidence from only two studies to support the hypothesis that endotoxaemia is causally related to the development of GIT symptoms during exercise.

2.2.5.6 Allergic reaction hypothesis

It has been suggested that histamine release, which is associated with exercise-induced anaphylaxis, may act on the smooth muscle of the intestine and cause abdominal cramps and diarrhoea during exercise [61, 91]. However, this allergic reaction hypothesis as the underlying mechanism for the development of GIT symptoms associated with exercise is not supported by scientific evidence.

2.2.5.7 Infective hypothesis

It is well established that athletes may be exposed to infectious agents during exercise, and this may cause gastrointestinal infections resulting in symptoms. Infective agents as a cause of GIT symptoms during exercise have been particularly prevalent in triathletes who may swim in open bodies of water as part of their training or racing [17]. A number of infective agents have been identified as possible causes of GIT infection and include parasitic infections, such as Entamoeba histolytica, giardia lamblia or other bacterial infections [43, 92].

In one case study, a 48-year-old runner reported a 4 month history of lower GIT symptoms of abdominal cramps and diarrhoea associated with running [92]. A stool sample from this individual showed Entamoeba histolytica as the infecting agent and the cause of his symptoms [92].

This single case study and other anecdotal reports of infective agents in athletes as causes of GIT symptoms support the infective hypothesis in isolated sports events such as swimming and canoeing in open water events. However, this hypothesis does not explain the GIT symptoms that are associated with exercise in the majority of athletes, including runners.

2.2.5.8 Blood flow hypothesis

2.2.5.8.1 Anatomy

The arterial blood supply to the GIT is via three main vessels. Together these make up the splanchnic blood supply to the GIT [93]. The coeliac artery is the first main branch off the abdominal aorta and it leaves the aorta anteriorly at the level of the twelfth thoracic vertebra. It is a short, wide vessel. Innervation of the artery is from the autonomic nervous system via the coeliac plexus. This artery supplies the embryological foregut. The coeliac artery divides into the splenic artery, the left gastric artery, and the common hepatic artery. These vessels each supply the following structures: splenic artery (spleen, pancreas, and stomach), left gastric artery (stomach and oesophagus) and the common hepatic artery (stomach, duodenum, liver, and gallbladder).

The superior mesenteric artery (SMA) supplies the mid-gut. This vessel leaves the aorta just below the coeliac artery at the level of the first lumbar vertebra. Its distribution extends from the second half of the duodenum to the distal third of the transverse colon and therefore supplies the duodenum, pancreas, jejunum, ileum, caecum, appendix, ascending colon and 2/3 of the transverse

colon. The SMA supplies a large component of the small and large bowel and therefore has an important role in the well being of the GIT.

The inferior mesenteric artery (IMA) arises 4cm proximal to the bifurcation of the abdominal aorta, and this artery supplies the hindgut. Its supply extends from the distal third of the transverse colon to the upper part of the anal canal and therefore provides blood supply to the transverse colon, the descending colon, sigmoid, rectum and upper anus. In contrast to the coeliac artery and the SMA, the IMA is very difficult to visualise using duplex Doppler ultrasound. The SMA and the IMA are both innervated by sympathetic afferent branches and are, therefore, under the control of the autonomic nervous system.

2.2.5.8.2 Normal GIT blood flow at rest and during exercise

At rest the blood flow through the SMA is approximately 500ml/min. This was shown in a study of 70 subjects where duplex Doppler ultrasound was used to measure the blood flow in the SMA [94]. In a similar study duplex Doppler ultrasound was also used to assess blood flow in the SMA before and after a meal in 56 subjects [95]. After a solid meal, SMA blood flow was shown to increase by more than 100% [95].

The smooth muscle of the splanchnic blood vessels is under the control of the sympathetic nervous system [96]. Stimulation of adrenergic alpha 1 receptors result in vasoconstriction and reduced blood flow to the GIT. An acute exercise bout is associated with the release of noradrenalin and adrenalin that

stimulate splanchnic vasoconstriction and reduced blood flow. As a result, blood is redistributed to skeletal muscle and skin during exercise [96].

Splanchnic blood flow has been shown to reduce by as much as 80% of resting values at maximal exercise [12]. Treadmill running at 70% $VO2_{max}$ resulted in a drop in splanchnic blood flow by 60-70% of resting values when 10 subjects were studied and blood flow was measured by Indocyanine Green dye Elimination technique (IGE) [88]. In a more recent case control study of 16 subjects exercising at 60-80% $VO2_{max}$, duplex Doppler ultrasound was used to assess the change in blood flow in the SMA at rest and exercise. Results showed a decrease in blood flow of 43% immediately after exercise and 24% at ten minutes post-exercise [97]. Another study compared change in blood flow with sub-maximal exercise in the SMA and coeliac artery using duplex Doppler ultrasound to splanchnic blood flow (SMA + coeliac artery) using Indocyanine Green dye Elimination technique [98]. In this study data were collected in 8 subjects. Results showed correlation between the two methods of investigation and that there was a 25% reduction in SMA and 50% reduction in coeliac artery blood flow with exercise.

In summary, there is strong evidence that there is a physiological decrease in splanchnic blood flow during an acute exercise bout and it appears that reductions in blood flow are greater in the coeliac artery compared with the SMA. The effect of prolonged duration exercise, such as an ultra-triathlon, on GIT blood flow has not been studied.

2.2.5.8.3 Evidence to support the blood flow hypothesis

The redistribution of blood away from the GIT to skeletal muscle and skin during exercise is a normal physiological response to exercise [12]. However, it has been suggested that this decrease in blood flow may result in ischemic damage to the GIT and this may be associated with the development of GIT symptoms during exercise [9, 10]. It has been postulated that a reduction in blood flow would diminish the provision of oxygen and energy to GIT cells and together with the accumulation of metabolic waste products this may result in cell damage and death [6]. If this occurs, absorption, secretion and motility of the GIT could be affected and GIT symptoms could develop during exercise [6, 48]. A reduction in blood flow to the GIT during exercise may therefore be an underlying mechanism in a number of the hypotheses for the development of GIT symptoms during exercise that have already been reviewed. However, scientific evidence supporting the reduced blood flow hypothesis in the development of GIT symptoms associated with exercise is very limited and will now be reviewed.

2.2.5.8.3.1 Training and exercise intensity

As previously mentioned, the redistribution of blood away from the GIT to the skeletal muscles during exercise is under the control of the sympathetic nervous system [99]. Noradrenalin released during exercise results in vasoconstriction of the splanchnic vessels [99]. Following exercise training, noradrenalin concentrations in the blood are less elevated than in the

untrained state, for the same exercise load [100]. Therefore, following regular training, less blood may be diverted away from the GIT during exercise at the same exercise load [12]. This has been confirmed in one study where blood flow using Indocyanine Green dye Elimination (IGE) from the hepatic system as a measure of splanchnic blood flow was measured in sedentary men before and after training [88]. Before training, blood flow during moderate intensity exercise was decreased by 40% but this was less (reduction of 30% at the same absolute work load) after a period of training. Highly trained subjects were also evaluated in the same way in this study and a reduction in blood flow of only 15% was documented during exercise. It can therefore be concluded that with regular exercise training, splanchnic vasoconstriction is reduced and the effects of an acute exercise bout on blood flow to the GIT are less (at the same absolute workload) [88].

Apart from training status, the reduction in blood flow to the GIT is also affected by exercise intensity. High intensity exercise is associated with greater increases in blood noradrenalin concentrations and this will result in increased sympathetic activity, which causes splanchnic vasoconstriction [101]. The relationship between changes in GIT blood flow and increasing exercise intensity has been investigated [88]. Exercise at maximal exercise intensity was associated with a reduction in splanchnic blood flow by as much as 80% [12].

Evidence that GIT symptoms are more common in untrained athletes [18] and that high intensity exercise is more likely to be associated with GIT symptoms

[15, 18, 19] has already been reviewed in this chapter (Section 2.2.4.2.4 and Section 2.2.4.2.1 respectively). It should be noted, that three common risk factors associated with the development of GIT symptoms during exercise, may in fact, be linked through a reduction in splanchnic blood flow during exercise. These risk factors are 1) level of conditioning, 2) intensity of exercise and 3) dehydration. However, there are no studies that have investigated the relationship between a reduction in splanchnic blood flow and the development of GIT symptoms during exercise. It is for this reason that the focus of this thesis is to explore the possible causal relationship between decreased splanchnic blood flow during exercise and the development of GIT symptoms during exercise.

2.2.5.8.3.2 GIT bleeding and endoscopic findings

The most severe, and potentially life threatening GIT symptom associated with exercise, is GIT bleeding [4]. GIT bleeding is mostly occult but it can be macroscopic haematochesia or malaena [4]. In a study of marathon runners, which will be described below, GIT bleeding was found to be significantly associated with GIT symptoms during exercise [42]. It has been suggested therefore that GIT bleeding is part of the spectrum of GIT symptoms associated with exercise [43]. Endoscopic examination is the technique of choice to investigate subjects after endurance exercise for the presence of GIT bleeding, and a number of case studies have been reported [102-104].

In one case study, features in keeping with ischemic colitis (colonoscopy and biopsy) were documented in a 34 year old runner who presented with diarrhoea and GIT bleeding during exercise [102]. Similarly, a lesion in the caecum which on histology showed mucosal ischemia was reported in a 33 year old runner who presented with diarrhoea and GIT bleeding [103] while haemorrhagic gastritis was demonstrated on gastroscopy in a runner who reported malaena stools following an endurance race [104].

In one prospective cohort study, GIT bleeding associated with running was studied in 41 marathon runners [42]. Following the marathon, 9 subjects were found to have positive faecal occult blood stool specimens and 3 subjects underwent gastroscopy and colonoscopy within 48 hours after the marathon. Two subjects had gastric lesions and one had a lesion at the splenic flexure of the colon. Histology of these lesions showed evidence of ischemic changes in the gut mucosa. During a follow-up endoscopy one month later, the lesions had disappeared completely. The transient nature of these lesions suggests that the cause of these lesions was ischemia during the marathon [42].

In another prospective cohort study, 7 athletes from varying sporting backgrounds were studied before and after running (a single training run of varying distance, duration and intensity) [105]. Endoscopic evaluation and biopsy of the upper GIT was performed on the 7 subjects before and within 15 minutes after the training session. Although only 1 subject reported abdominal cramps during the run, there was evidence of pathological histology results in the post-run biopsy specimens of all the subjects. The main histological

features were in keeping with vascular changes but they were not related to GIT symptoms in this study [105].

In conclusion, endoscopic changes suggestive of gut ischemia have been documented following exercise. However, there is only weak evidence to link these changes directly to the development of GIT symptoms during exercise. Further investigation is required to determine the relationship between decreased blood flow, ischemia and the development of GIT symptoms during exercise.

2.2.5.8.3.3 Dehydration and reduced blood flow during exercise

Dehydration during exercise may lead to reduced intravascular volume [6]. If the blood supply to the gut is already reduced from redistribution to skeletal muscle and skin, a decrease in intravascular volume can diminish splanchnic blood supply further [8]. In a prospective cohort study (previously discussed in Section 2.2.4.2.3 - Dehydration as an extrinsic risk factor for GIT symptoms associated with exercise) fluid intake, fluid loss and the development of GIT symptoms during a marathon were studied in 44 subjects [31]. The incidence of GIT symptoms increased significantly once body water loss exceeded 4-5%. Indirectly, the results of this study support the reduction in blood flow as a possible cause for the development of GIT symptoms during exercise [31].

2.2.5.8.3.4 Decreased iron absorption

A prospective cohort study investigated GIT blood loss associated with an ultra-distance triathlon race and its relation to training, performance and haematological measures (mainly iron storage related) [34]. Seventeen ultra-distance triathletes had stool samples collected for qualitative faecal occult blood testing and blood taken for haematological analysis during training, pre-race and post-race. Eighty percent of the subjects had occult positive stools post-race. Ten subjects had markedly reduced serum ferritin levels, which are a marker of body iron stores. All subjects were considered healthy and to have an adequate diet. It was postulated that ischemic damage, which was thought to be the underlying cause of the GIT bleeding, was also damaging the GIT villi. As a result, absorption of iron from the gut was reduced. This was supported by the fact that despite adequate oral iron supplements, serum ferritin levels did not improve [34].

2.2.5.8.3.5 Gastric mucosal pH

The effect of exercise on the pH of gastric mucosa was studied in a prospective cohort study [106] in which 4 oarsmen rowed for 30 minutes at maximum output. A tonometric probe was passed into the stomach via the oesophagus and measured gastric CO_2 tension. Arterial blood gas and tonometry readings were taken every ten minutes during and after exercise for 20 minutes. GIT symptoms were not recorded in this study. Results were calculated using the Henderson-Hasselbach equation. This study showed a

significant drop in gastric pH with high intensity exercise to levels comparable with chronic intestinal ischemia, thus indicating minimal splanchnic blood flow to gastric mucosa during high intensity exercise [106].

2.2.5.8.4 Measuring splanchnic blood flow during and after exercise

In general, there is little information regarding sphlanchnic haemodynamics because of the technical difficulties in measuring splanchnic blood flow during or after exercise [94, 107]. Most methods of measuring splanchnic blood flow are demanding and invasive and are difficult to apply practically in clinical and/or field research studies [108]. Transcutanous duplex Doppler ultrasound was first used in 1982 and this technique is now used widely in research and clinical practice [94]. This method and other possible methods of measuring splanchnic haemodynamics will now be briefly discussed.

In the past, dye dilutional techniques, a spill-over angiography reflux method and the video dilution technique have been used to measure splanchnic blood flow [94]. However, these methods require arterial catheterisation and are therefore invasive and difficult to use in healthy subjects who perform exercise.

The Indocyanine Green dye Elimination (IGE) technique has been used to estimate splanchnic blood flow by means of injecting dye into the SMA and then measuring clearance in the superior mesenteric vein [94]. However, this technique is invasive and time-consuming [98]. Furthermore, the results using

this technique are influenced by the venous system and have been shown to overestimate blood flow [94].

Transcutanous duplex Doppler ultrasound has been used successfully in the assessment of both superficial and deep vessels (brachial, carotid, aorta and fetal vessels) [94]. The SMA is particularly amenable to duplex Doppler ultrasound because of its size and location [109]. Duplex Doppler ultrasound consists of a real-time two-dimensional scanner and a pulsed Doppler flowmeter [107]. The real-time scanner is used to locate the vessel in B mode and to identify the angle of isonisation which is the angle between the incident Doppler beam and the long axis of the vessel [107]. This angle should be <60° for accurate measurement [109]. In the assessment of the SMA, the vessel is identified and a point approximately 2cm from its origin is used for measurements [94, 107].

A study investigating the short- and long-term coefficient of variability of duplex Doppler ultrasound of the SMA was performed [94]. Twenty-one subjects had 5 measurements taken over a 1-hour period and this was used to determine short-term coefficient of variability. In this study, 18 subjects underwent 3 measurements each on separate occasions 2 weeks apart, and these data were used to calculate long-term coefficient of variability. Results showed less than 10% variability for both short- and long-term assessments. Therefore duplex Doppler ultrasound of the SMA can be considered a reproducible method of investigating splanchnic haemodynamics [94].

In one study, the effect of cycling on splanchnic blood flow in the fasted and fed state was studied in 8 subjects using both duplex Doppler ultrasound and the Indocyanine Green dye Elimination technique [98]. In this study, the results of the two techniques were found to be comparable [98]. The only limitation of duplex Doppler ultrasound was the technical difficulty experienced with increased respiratory rate following exercise [98]. This was easily overcome by asking the subjects to briefly hold their breath during inspiration while measurements were taken [98]. The advantages of duplex Doppler ultrasound are that it is simple, portable, non-invasive, reproducible, and instantaneous [94, 107, 109]. Therefore duplex Doppler ultrasound has been shown to be an acceptable and accurate method for the assessment of splanchnic haemodynamics [97].

Duplex Doppler makes use of various measurements to assess blood flow. Resistance Index (RI) has been used as an estimation of blood flow [110]. The SMA is a resistance vessel and RI is indicative of the downstream resistance in the SMA [110]. RI is calculated from systolic and diastolic velocities that are measured on the same image and are independent of the angle of isonisation [110].

$$RI = \frac{\text{Systolic velocity} - \text{Diastolic velocity}}{\text{Systolic velocity}}$$

As resistance to flow increases, RI approaches one.

This is a quick and easy method and is considered an accurate measurement of mesenteric blood flow [110]. Other studies have used the following formula to calculate SMA blood flow [94, 98].

$$\text{Flow} = \text{pie} \times \text{diameter} \times \text{TAMV} \times 60$$

In this equation, the diameter and time average mean velocity (TAMV) are required for the calculation. This measurement is dependent on the angle of isonisation and therefore requires accurate positioning of the ultrasound probe for acceptable measurement [97, 109]. At least two images are required for this measurement. Therefore more time and skill is required for this measurement.

In conclusion, duplex Doppler ultrasound is a well accepted and reproducible method of measuring splanchnic haemodynamics. RI has been shown to be a simple and acceptable measure of blood flow.

2.2.5 Summary

In summary, a review of the literature with regard the classification, epidemiology, risk factors and pathophysiology for the development of GIT symptoms associated with exercise has shown the following:

- GIT symptoms during exercise are common in both endurance runners and other athletes including triathletes
- GIT symptoms associated with exercise can be classified as upper and lower GIT symptoms

- Lower GIT symptoms are more common in athletes
- Intrinsic and extrinsic risk factors for the development of GIT symptoms during exercise have been suggested but, in general, scientific data supporting these factors is limited
- A number of hypotheses have been proposed for the pathophysiology of GIT symptoms and these include the mechanical hypothesis, gastrointestinal motility hypothesis, absorption and secretion hypothesis, neuroendocrine hypothesis, endotoxaemia hypothesis, allergic reaction hypothesis, infectious disease hypothesis and the altered blood flow hypothesis
- There is limited scientific research to support these hypotheses and further research is required
- One of the more promising hypotheses for the development of GIT symptoms during exercise is related to changes in blood flow to the GIT that may occur during exercise - however, this requires further investigation
- Duplex Doppler ultrasound is considered a simple, non-invasive, reproducible and acceptable measure to study blood flow in the splanchnic blood vessels (SMA and coeliac artery)
- Changes in splanchnic blood flow in athletes who develop GIT symptoms during exercise have to our knowledge not been studied

Chapter 3

Are pre- and post-exercise changes in splanchnic blood flow related to the development of GIT symptoms in Ironman triathletes? – A prospective cohort study

3.1 INTRODUCTION

There is a marked increase in the participation in endurance sports events, such as the Ironman Triathlon [5, 15]. With the growth in popularity in these events, medical problems associated with endurance sports are becoming more apparent, and the appropriate diagnosis and management of athletes is of primary importance to the sports physician [1]. It has been shown that GIT symptoms are commonly reported by athletes [5, 18] and can range from mild to severe [4, 5]. Despite the fact that GIT symptoms are commonly reported, research is limited with regard to the risk factors, pathophysiology and management of the GIT symptoms associated with exercise.

GIT symptoms during exercise have been classified as upper (nausea, vomiting, heartburn) and lower (diarrhoea, bloating, urge to pass stool, abdominal cramps, blood in the stool) GIT symptoms [6, 7]. Lower GIT symptoms have been shown to be more common than upper GIT symptoms, especially in runners [7, 15, 18, 24].

Several intrinsic and extrinsic risk factors for the development of GIT symptoms during exercise have been suggested (reviewed in Chapter 2). In summary, intrinsic risk factors include female gender, younger age, previous abdominal surgery, irritable bowel syndrome and lactose intolerance, while extrinsic risk factors include high intensity exercise, dehydration, vertical impact sport, poorly conditioned athlete, medication and dietary factors [5-8, 15, 18]. However, research is limited, and published studies frequently are limited due to methodological constraints.

Various hypotheses have been suggested for the underlying pathophysiology of GIT symptoms associated with exercise [8]. These hypotheses have been reviewed in Chapter 2 and include the mechanical hypothesis, gastrointestinal motility hypothesis, absorption and secretion hypothesis, neuroendocrine hypothesis, endotoxaemia hypothesis, allergic reaction hypothesis, infectious disease hypothesis and the altered blood flow hypothesis.

A detailed review of the literature (Chapter 2) indicates that reduced blood flow to the GIT during exercise may be a likely pathophysiological mechanism for the development of GIT symptoms during exercise. Although studies have shown that significant physiological changes in blood flow occur in response to an acute exercise bout [12, 88] there are no studies that 1) have investigated the effects of prolonged exercise on splanchnic blood flow, and 2) have specifically linked the development of GIT symptoms during prolonged exercise to alterations in splanchnic blood flow. Therefore further research in this area is required.

The primary aim of this study was to document if changes (pre- to post-exercise) in blood flow in the SMA and coeliac artery are related to the development of GIT symptoms in triathletes competing in an Ironman Triathlon. A secondary aim was to identify intrinsic and extrinsic risk factors associated with the development of GIT symptoms in Ironman triathletes.

3.2 METHODS

3.2.1 Type of study

This research study was a prospective cohort study.

3.2.2 Subjects

Subjects for the study were recruited from the potential 1566 triathletes who entered the "Spec-Savers" South African Ironman Triathlon held in Port Elizabeth in March 2007. This ultra-endurance race consists of a 3,8km swim, a 180km road cycle followed by a 42,2km road run. Entrants, of which 75% were male and 25% were female, were informed of the research project via email 2 months prior to the race. They could also access information about the study via the official Ironman website [16] (Appendix A). The information given to the triathletes included a detailed description of the study and the study procedure (Appendix B), a consent form (Appendix C) and a questionnaire (Appendix D). Contact details for further information or queries about the study were also made available on the web page. The study protocol was approved by both the Research Ethics Committee of the University of Cape Town (reference REC 002/2007) (Appendix E) and the official

organisers of the Port Elizabeth "Spec-Savers" South African Ironman Triathlon that included the general organising committee and the medical subcommittee.

Triathletes were recruited in the three days preceding the race. A designated medical research area was set up adjacent to the registration area. Triathletes were approached and invited to be a part of the study while they waited to register for the race. The study and procedure were then explained to them and any questions answered. Each triathlete was then asked to sign informed consent prior to enrolment into the study. Some triathletes had already completed the questionnaire made available to them on the website. The others were asked to complete the questionnaire at the registration venue, or they could return the completed questionnaire anytime prior to the race. Pre-race heart rate and blood pressure and haemodynamic assessment of SMA and coeliac artery using duplex Doppler ultrasound were then performed and recorded (Appendix F1) (see Section 3.2.6).

At completion of the race, the triathletes were asked to report as soon as possible to the allocated area for the post-race assessment. The ultrasound machine was set up just after the finish line in the medical tent and the location was signposted. The triathletes had their heart rate and blood pressure measured and a duplex Doppler ultrasound of the SMA and coeliac artery was repeated and recorded (Appendix F2) (see Section 3.2.6).

3.2.3 Pilot study

Two weeks prior to the 2007 "Spec-Savers" South Africa Ironman Triathlon a pilot study was performed. Four triathletes in training for the Ironman Triathlon volunteered to participate in this pilot study. Each triathlete underwent a pre- and post-exercise haemodynamic assessment of the SMA by means of duplex Doppler ultrasound scan. At the pre-exercise assessment, heart rate and blood pressure were recorded and a duplex Doppler ultrasound of the SMA was done.

Measurements taken included:

1) Blood vessel diameter (mm)
2) Systolic velocity (cms^{-1})
3) Diastolic velocity (cms^{-1})
4) RI (calculated by the ultrasound machine) (see Section 3.2.6).

Following the pre-exercise assessment, the triathletes ran 1km followed by running down and up 4 flights of stairs twice and then 1km back. They were asked to run at approximately 80% of maximum effort. Immediately after the run, heart rate and blood pressure were measured and a duplex Doppler ultrasound of the SMA was repeated using the same parameters of measurement.

The pilot study allowed the investigator and the ultrasonographer to establish an efficient sequence of events and enabled them to identify possible practical problems they may encounter. For example, the movement caused by heavy respiration

following exertion was overcome by asking the triathletes to hold their breath in mid-inspiration [98].

3.2.4 Questionnaire and pre- and post-race assessment history

A questionnaire was completed by the triathletes prior to the race. The questionnaire was adapted from a previously validated format [111-113]. The information gained from the questionnaire was used for various research projects being conducted at the 2007 Ironman Triathlon. Out of the 1566 entrants 166 (11%) volunteered and then completed and returned the questionnaire. The minority of the triathletes completed the questionnaire from the Ironman website. Most triathletes filled in their information in the three days prior to the race and handed the questionnaire to the research team at the registration venue.

For the purpose of this study the following sections of the questionnaire were of relevance and information from these sections was used:

(A) Personal details (including age, height, weight, gender and occupation)

(B) Racing and training history

(E) Personal general medical history and

(C) History of medication use

In the questionnaire the triathletes were asked for their self-predicted times for the overall race and for each leg of the Ironman Triathlon. With regards training, the triathletes were asked about volume of training in hours and distance, in each discipline, in the preceding 15 weeks and in the final 1 week before the race. The

number of days per week spent training, during the 15 weeks prior to the race, was sought. The triathletes were also asked about the number of working hours per week in the 15 weeks leading up to the race.

In the racing section of the questionnaire, triathletes were asked about previous personal best times in triathlons (standard and Ironman) and running events (10km, 21.1km and 42.2km) in their careers and in the previous 12 months and 15 weeks leading up to the race. The number of triathlons (standard and Ironman) competed in over the past 2 years and the number of triathlons (standard and Ironman) and running events (10km, 21.1km and 42.2km) competed in, in their careers was sought. The year in which they first competed in triathlons (standard and Ironman) and running events (10km, 21.1km and 42.2km) was also asked. The triathletes were asked for their personal best time in a cycle race between 80km and 120km in the 15 weeks prior to the Ironman Triathlon.

The personal general medical history of the questionnaire enquired specifically about GIT symptoms associated with exercise. The use of medication during any triathlon and/or in the week prior to the race was sought. Triathletes were asked whether they had experienced previous collapse associated with exercise. A previous history of abdominal surgery was also enquired about.

During the pre-race haemodynamic assessment, triathletes were further asked about previous GIT symptoms associated with exercise including nausea, vomiting, abdominal cramps, diarrhoea, urge to pass stool and bloating. The presence of GIT

symptoms in the three days prior to the race was also documented and if present, the triathlete was excluded from the cohort.

During the post-race haemodynamic assessment, triathletes were asked about any GIT symptoms they experienced during the race, including which symptom they experienced (including nausea, vomit, abdominal cramps, diarrhoea, urge to pass stool, bloating and blood in the stool) and in which leg of the race the symptom occurred. The use of medication during the race was reported, as well as the type of medication used.

3.2.5 Pre- and post-race heart rate and blood pressure (systolic and diastolic)

Resting supine heart rate (bpm) and blood pressure (mmHg) – systolic and diastolic - were measured and recorded in the cohort of triathletes pre- and post-race while a duplex Doppler ultrasound was being done.

3.2.6 Pre- and post-race haemodynamic assessment of the SMA and coeliac artery

An ultrasonographer, experienced in vascular ultrasound, performed all the duplex Doppler ultrasound scans pre- and post-race. A Toshiba Nemio XG Colour Doppler machine (Tecmed: Physical address - 109 Vasco Boulevard, Goodwood, Cape Town: Postal address - P.O Box 610, Goodwood, Cape Town 7460: Tel.: +27 21 592 2464: Email: capetown@tecmed.co.za) was used for all the scans. A linear vascular probe was used for the measurements. Measurements were taken as necessary at 60

degrees according to the optimal angle of isonisation.

The pre-race assessment took place in the designated medical research area adjacent to the registration area. The time since last ingestion of fluid or food was recorded. For the haemodynamic assessment the triathletes lay supine with the head flat to relax the abdominal muscles. The linear probe was applied to the epigastric area and the SMA was identified. Measurements taken included:

1) Blood vessel diameter (mm)
2) Systolic velocity (cms^{-1})
3) Diastolic velocity (cms^{-1})
4) RI was calculated by the ultrasound machine using the following equation:

$$RI = \frac{\text{Systolic velocity} - \text{Diastolic velocity}}{\text{Systolic velocity}}$$

The coeliac artery was then identified and the same parameters measured.

Asking the subject to hold their breath in mid-inspiration optimised identification and visualisation of the arteries.

Post-race haemodynamic assessment took place in the medical tent in a well signposted area. The exact time of the haemodynamic assessment was recorded in order to calculate time delay after finishing the race. The same measurements as above, except for the diameter of the coeliac artery, were measured and recorded. The diameter of the coeliac artery was not measured due to time constraints.

3.2.7 Environmental conditions on race day

Weather conditions on race day were supplied by the South African Weather Service. The sea water temperature was 20°C. The average air temperature during the race was 24°C with minimum of 17°C and maximum of 30°C. The average wind speed was 5m.s^{-1} and the relative humidity was 65%.

3.2.8 Statistical analysis of data

All the data was entered on to an Excel spreadsheet (Microsoft 2003) and analysed using the Statistica 7.0 (Stat-soft Inc, Tulsa, Oklahoma, USA) or GraphPad InStat 2.05a (GraphPad Software, San Diego, California, USA) statistical programs. All normally distributed numerical data are represented by the mean ± standard deviation, with the number of subjects in parenthesis and a one-way analysis of variance (ANOVA) was used to determine any significant differences between groups. Categorical data are expressed as frequencies, and significant differences between groups were analysed using the Pearson's chi-square or Fisher's exact tests. A repeated-measures ANOVA was used to investigate differences in the pre- and post-race measurements between the GIT symptomatic group and asymptomatic groups. Statistical significance was accepted when $p<0.05$.

3.3 RESULTS

3.3.1 Subject characteristics and GIT symptoms

Sixty four triathletes underwent pre-race and post-race haemodynamic assessment of the SMA and coeliac artery using Doppler ultrasound. Five of the triathletes reported GIT symptoms in the three days leading up to the race and were therefore excluded from the subsequent analysis. Of these 5 triathletes, 4 triathletes reported GIT symptoms during the race and 1 was asymptomatic. Of the 59 triathletes who were finally included in this study, 78% (N=46) completed the pre-race questionnaire. Thirty-five of the 59 triathletes (59%) experienced GIT symptoms during the race (GIT S=35), while 24/59 (41%) did not (GIT AS=24).

The general characteristics of the GIT S and the GIT AS groups are depicted in Table 3.1. There were no significant differences between the two groups with respect to height, body weight, BMI, gender and percentage time spent standing, sitting, walking or performing manual labour during occupation. The symptomatic group was however, significantly younger than the asymptomatic group (P=0.041).

Table 3.1: The general characteristics and occupational history of the GIT symptomatic (GIT S) and asymptomatic (GIT AS) triathletes

	GIT S GROUP (N=35)	GIT AS GROUP (N=24)	P-value
Age (years)	37.3 ± 9.2 (35)	42.3 ± 8.8 (24)	0.041
Height (cm) [a]	181.3 ± 8.4 (26)	179.3 ± 7.8 (19)	0.434
Weight (kg) [a]	77.1 ± 9.3 (25)	75.5 ± 8.9 (18)	0.576
BMI (kg/m^2) [b]	23.3 ± 1.8 (25)	23.5 ± 2.7 (18)	0.743
Gender (% males)	82.9 (35)	95.8 (24)	0.223
Occupation Time Sitting (%)	53.9 ±32.7 (26)	62.2 ± 29.4 (19)	0.383
Occupation Time Standing (%)	23.6 ± 22.5 (26)	14.4 ± 13.3 (19)	0.117
Occupation Time Walking (%)	17.7 ± 18.2 (26)	17.1 ± 16.1 (19)	0.909
Manual Labour (%)	4.6 ± 9.5 (26)	6.6 ± 12.9 (19)	0.559

Gender and occupation are expressed as a frequency (%). Other values are expressed as average ± standard deviation. The number of subjects (N) is in parentheses.
[a] Weight and height are the athletes' self-reported normal values.
[b] Body mass index (BMI) is calculated as weight (kg) divided by height (cm) squared.

The number of triathletes reporting GIT symptoms during each leg of the Ironman Triathlon is shown in Table 3.2. At least one GIT symptom was experienced by 12% (N=7) of triathletes in the swim leg of the race, 25% (N=7) of triathletes in the cycle leg of the race and 44% (N=26) of triathletes in the run leg of the race. Twenty percent (N=12) of the triathletes experienced upper GIT symptoms and 37% (N=22) experienced lower GIT symptoms. Upper GIT symptoms were reported by 9% (N=5) of the triathletes during the swim and run legs, while only 5% (N=3) of the triathletes reported at least one upper GIT symptom during the cycle leg of the race. Lower GIT symptoms were reported by 29% (N=17) and 20% (N=12) of the triathletes during the run and cycle legs respectively and only 3% (N=2) of triathletes reported at least one

lower GIT symptom during the swim leg of the race. The upper GIT symptom, vomiting (7%, N=4), was the most common symptom during the swim leg, while the lower GIT symptom of abdominal cramps was the most common symptom during the cycle (19%, N=11) and run (19%, N=11) legs of the race. Abdominal cramps was also the most common symptom reported by the triathletes during the entire race (17%, N=10). Within the symptomatic group, 66% (N=23) of the triathletes reported one GIT symptom, 31% (N=11) reported two GIT symptoms and 3% (N=1) reported three GIT symptoms during the race.

Since most of the triathletes (44%) reported their GIT symptoms during the run leg of the race, the data were re-analysed using this sub-group. There were no significant differences between the age (P=0.220), height (P=0.364), weight (P=0.287), BMI (P=0.899) and gender (P=0.963) of the GIT run symptomatic and asymptomatic sub-groups (Appendix G Table G.1). Lower GIT symptoms were reported in 37% of triathletes and therefore the data were also re-analysed for this sub-group. Similarly, there were no significant differences found between the lower GIT symptomatic and asymptomatic sub-groups with regard age (P=0.187), height (P=0.523), weight (P=0.838), BMI (P=0.442) and gender (P=0.898) (Appendix G Table G.2).

Table 3.2: The relative (%) and actual (N) number of triathletes reporting GIT symptoms in each leg of the Ironman Triathlon

		SWIM	CYCLE	RUN	TOTAL
UPPER GIT SYMPTOMS		8.5 (5)	5.1 (3)	8.5 (5)	20.3 (12)
	Nausea	3.4 (2)	3.4 (2)	6.8 (4)	11.9 (7)
	Vomit	6.8 (4)	1.7 (1)	1.7 (1)	10.2 (6)
LOWER GIT SYMPTOMS		3.4 (2)	20.3 (12)	28.8 (17)	37.3 (22)
	Abdominal Cramps	3.4 (2)	18.6 (11)	18.6 (11)	16.9 (10)
	Diarrhoea	1.7 (1)	3.4 (2)	10.2 (6)	10.2 (6)
	Urge	0.0 (0)	0.0 (0) [a]	6.8 (4)	6.8 (4)
	Bloat	0.0 (0)	6.8 (4)	11.9 (7)	11.9 (7)
	Blood in Stool	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
TOTAL		11.9 (7)	25.4 (15)	44.1 (26)	59.3 (35)

Values are expressed as a frequency (%) with the number of subjects (N) is in parentheses. [a] The presence or absence of this symptom was only reported by 58 of the 59 triathletes.
Some triathletes experienced more than one symptom and/or one symptom in more than one leg of the race.

3.3.2 Actual and predicted 2007 South African Ironman Triathlon performance

The pre-race self-predicted performance times and the actual 2007 South African Ironman Triathlon performance times for the overall race, as well as the swim, cycle and run legs of the GIT symptomatic and asymptomatic groups are shown in Table 3.3. When co-varied for age there was no significant difference between the GIT S and the GIT AS groups with regard to their predicted race times and actual race times. Similarly, when their actual times were expressed relative to their predicted times, there were no significant differences in the overall swim and cycle times between the two groups. There were also no significant differences between the

overall predicted (P=0.985) or actual (P=0.399) times, as well as the swim (P≥0.611), cycle (P≥0.634) or run (P≥0.249) predicted and actual times of the GIT S and the GIT AS run leg sub-groups (Appendix G Table G.3). In the lower GIT S and AS sub-groups there were also no significant differences in the overall predicted (P=0.561) or actual (P=0.501) times and the swim (P≥0.529), cycle (P≥0.539), run (P≥0.312) predicted and actual times (Appendix G Table G.4).

There was, however, a tendency for the average relative predicted run time of the GIT S group to be longer than the GIT AS group (P=0.064), suggesting that the GIT S group ran slower than they had initially planned (Table 3.3). There was also a tendency for those triathletes who developed GIT symptoms during the run leg of the race to run slower than they had initially planned (P=0.094). The overall (P=0.440), swim (P=0.950) and cycle (P=0.812) relative predicted times were, however, similarly matched between the two groups (Appendix G Table G.3). Triathletes who developed lower GIT symptoms during the race did not show a significant difference in the relative predicted overall (P=0.273), swim (P=0.564), cycle (P=0.438) and run (P=0.120) times compared to the asymptomatic group (Appendix G Table G.4).

Table 3.3: The predicted, as reported in the pre-race questionnaire, and actual performance times of the GIT symptomatic and asymptomatic triathletes

		GIT S GROUP (N=35)	GIT AS GROUP (N=24)	P-value	Co-varied P-value [a]
Predicted Times	**Overall** (min)	746.2 ± 87.4 (26)	756.6 ± 110.7(19)	0.726	0.803
	Swim (min)	86.3 ± 16.6 (26)	83.7 ± 16.7 (19)	0.598	0.348
	Cycle (min)	385.6 ± 46.2 (26)	389.5 ± 49.4 (19)	0.787	0.755
	Run (min)	267.9 ± 44.1(26)	278.7 ± 49.6 (19)	0.446	0.866
Actual Times	**Overall** (min)	801.9 ± 98.4 (35)	784.1 ± 96.0 (24)	0.493	0.275
	Swim (min)	97.4 ± 18.3 (35)	93.8 ± 15.6 (24)	0.434	0.192
	Cycle (min)	394.7 ± 39.5 (35)	392.4 ± 41.2 (24)	0.831	0.584
	Run (min)	291.5 ± 53.7 (35)	279.3 ± 41.8 (24)	0.354	0.275
% Predicted Times	**Overall** (%) [b]	107.8 ± 11.7 (26)	104.2 ± 7.7 (19)	0.253	n.d.
	Swim (%) [b]	114.8 ± 14.4 (26)	114.0 ± 13.7 (19)	0.862	n.d.
	Cycle (%) [b]	101.8 ± 11.0 (26)	100.3 ± 6.4 (19)	0.599	n.d.
	Run (%) [b]	110.5 ± 17.4 (26)	101.9 ± 10.8 (19)	0.064	n.d.

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.
[a] Co-varied for age.
[b] Actual times expresses relative to the predicted split and overall times.
n.d., not determined.

3.3.3 Training and performance history

The triathletes' swimming, cycling, running and total training duration and distances during the final 1 week and 15 weeks before the 2007 South African Ironman Triathlon, are shown in Table 3.4. There were no significant differences between the GIT S and GIT AS groups with regard time spent swimming, cycling and running, as well as the overall training time, during the 15 weeks or 1 week before the race.

There were also no significant differences in their training swimming and cycling distances, as well as the overall distance trained, between the two groups during the 15 weeks or the 1 week before the race. The GIT S group, however, covered on average significantly less running distance per week during the 15 weeks prior to the race than the GIT AS group (P=0.032 and P=0.016 when co-varied for age). Interestingly, there was no significant difference between these two groups in their running distance during the 1 week immediately before the race. The total hours worked in the 15 weeks preceding the race was also similar in both groups.

Similarly, the triathletes who developed symptoms during the run leg of the race (37.6 ± 15.1km/wk, N=20, P=0.018), or developed only lower GIT symptoms during the race (38.9 ± 14.9km/wk, N=15, P=0.046), also covered on average significantly less running distance per week during the 15 weeks prior to the race than the asymptomatic (50.1 ± 16.2km/wk, N=19) group (P=0.018). There were no significant differences in any of the other training variables between the various sub-groups (Appendix G Tables G.5 and G.6).

Table 3.4: The swimming, cycling, running and/or total training frequency, distances and durations for the 1 and 15 week period before the triathlon and the total hours worked in the 15 week period before the triathlon of the GIT symptomatic and asymptomatic triathletes

		GIT S GROUP (N=35)	GIT AS GROUP (N=24)	P-value	Co-varied P-value [a]
Training Frequency (days/wk)		5.6 ± 0.9 (24)	5.9 ± 0.6 (16)	0.236	n.d.
15 week Working Time (hrs/wk)		45.7 ± 14.2 (20)	41,2 ± 19.3 (18)	0.423	n.d.
15 week Training Time	**Swim** (hrs/wk)	2.5 ± 1.0 (26)	3.0 ± 1.1 (19)	0.164	0.128
	Cycle (hrs/wk)	7.1 ± 2.6 (26)	7.5 ± 2.6 (19)	0.632	0.317
	Run (hrs/wk)	4.0 ± 1.5 (26)	4.7 ± 1.5 (19)	0.129	0.071
	Total (hrs/wk) [b]	13.7 ± 4.6 (26)	15.2 ± 3.9 (19)	0.246	0.104
15 week Training Distance	**Swim** (km/wk)	5.7 ± 2.5 (27)	6.7 ± 2.4 (19)	0.181	0.114
	Cycle (km/wk)	198.4 ± 98.2 (27)	204.2 ± 71.7 (19)	0.827	0.380
	Run (km/wk)	39.3 ± 15.8 (26)	50.1 ± 16.2 (19)	0.032	0.016
	Total (km/wk) [b]	245.4 ± 110.3 (26)	261.0 ± 79.0 (19)	0.602	0.232
1 week Training Time	**Swim** (hrs)	1.2 ± 0.9 (25)	1.4 ± 1.0 (18)	0.559	0.642
	Cycle (hrs)	3.9 ± 6.9 (24)	3.0 ± 4.3 (18)	0.621	0.566
	Run (hrs)	2.6 ± 7.0 (24)	1.0 ± 0.8 (18)	0.347	0.432
	Total (hrs) [b]	7.8 ± 14.4 (23)	4.5 ± 2.7 (17)	0.351	0.434
1 week Training Distance	**Swim** (km)	2.9 ± 1.9 (25)	2.7 ± 1.8 (19)	0.719	0.653
	Cycle (km)	55.6 ± 48.4 (24)	41.8 ± 34.6 (19)	0.302	0.363
	Run (km)	10.6 ± 6.4 (23)	9.8 ± 7.8 (18)	0.725	0.718
	Total (km) [b]	72.3 ± 54.4 (22)	50.1 ± 37.5 (18)	0.149	0.093

Values are expressed as average ± standard deviation, with the number of subjects (N) in parentheses. n.d., not determined.
[a] Co-varied for age. [b] The totals are the sum of the swim, cycle and run disciplines.

Table 3.5 depicts the triathletes' career and recent personal best performances in triathlons (standard and Ironman) and running distances (10km, 21.1km and 42.2km). There were no significant differences in the career personal best times for the

triathlon and road running events between the GIT S and GIT AS groups. Similarly, when co-varied for age, there were no significant differences between the previous 12 months and 15 weeks personal best times for triathlons or running events, respectively, of the two GIT groups. There were also no significant differences between the career and recent personal best performances in triathlons (standard and Ironman) and running distances (10km, 21.1km and 42.2km) between the GIT run symptomatic and asymptomatic sub-groups (Appendix G Table G.7), as well as between the lower GIT symptomatic and asymptomatic sub-groups (Appendix G Table G.8).

Table 3.5: Triathlon (standard and Ironman) and running (10km, 21.1km and 42.2km) career personal best times (PB) and best times achieved over the last 12 months or 15 weeks before the race of the GIT symptomatic and asymptomatic triathletes

		GIT S GROUP (N=35)	GIT AS GROUP (N=24)	P-value	Co-varied P-value [a]
Triathlon Career PB	**Standard** (min)	170.0 ± 73.7 (14)	147.3 ± 28.4 (12)	0.327	n.d.
	Ironman (min)	765.5 ± 94.3 (15)	759.4 ± 80.3 (14)	0.853	n.d.
Triathlon 12 Months PB	**Standard** (min)	165.9 ± 75.8 (13)	155.5 ± 31.0 (8)	0.717	0.711
	Ironman (min)	724.0 ± 133.2 (12)	774.7 ± 75.1 (10)	0.298	0.443
Running Career PB	**10km** (min)	43.9 ± 7.9 (20)	41.8 ± 6.5 (16)	0.400	n.d.
	21.1km (min)	94.7 ± 15.0 (20)	100.7 ± 25.3 (18)	0.371	n.d.
	42.2km (min)	200.1 ± 36.6 (15)	215.5 ± 28.6 (17)	0.194	n.d.
Running 15 Weeks PB	**10km** (min)	48.0 ± 7.3 (12)	50.3 ± 7.2 (8)	0.505	0.776
	21.1km (min)	105.2 ± 15.2 (10)	118.3 ± 24.1 (9)	0.170	0.406
	42.2km (min)	233.1 ± 38.7 (7)	248.8 ± 19.7 (5)	0.429	0.477

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.
[a] Co-varied for age.
PB, personal best time; n.d., not determined.

When a sub-group of the triathletes' actual run time during the 2007 South African Ironman Triathlon was expressed, relative to their recent 15 week 21.1km personal best times, there was a tendency (P=0.060) for the GIT S group (2.8 ± 0.4, N=10) to run at a lower intensity (i.e. slower relative to their recent personal best time) than the GIT AS group (2.4 ± 0.3, N=9).

There were no significant differences between the two groups with respect to:

- The number of standard and Ironman Triathlons competed in during their careers or the previous 2 years
- The year in which they started competing in standard and Ironman Triathlons.
- The number of 10km, 21.1km and 42.2km running races competed in during their careers
- The year in which they started competing in these running events (Appendix G Table G.9)

There was no significant difference in the race speeds of the GIT S (30.5 ± 3.1km/hour N=17) and GIT AS (31.1 ± 2.6km/hour N=11) groups when the personal best times in a cycle race between 80 and 120km during the 15 weeks prior to the race were compared (P=0.589)(Appendix G Table G.10). Similarly, there were no significant differences in the race speeds when the triathletes who developed GIT symptoms during the run (P=0.604), or developed only lower GIT symptoms (P=0.640) during the race, were analysed (Appendix G Tables G.11 and G.12).

3.3.4 Personal general medical history

Table 3.6 shows past and current medical history in the GIT symptomatic and asymptomatic triathlete groups. A history of previous GIT symptoms associated with exercise was not found to be a significant predictor of GIT symptoms during the race (P=0.629), GIT symptoms during the run leg (P=0.783) nor lower GIT symptoms during the race (P=1.000). A previous history of a specific GIT symptom as shown in Table 3.6 was not found to be a significant predictor of GIT symptoms during the race.

Medication use during any triathlon and/or the week prior to the race was also not found to be significantly associated with GIT symptoms (P=0.789). Similarly, medication use during the 2007 South African Ironman Triathlon was also not associated with GIT symptoms (P=0.349). Of the triathletes (N=59) who took medication during the race, 4 took GIT prophylactics which included Loperomide HCl (Imodium) (N=2), Diphenoxylate HCl / atropine sulphate (Lomotil), Hyoscine-N-butylbromide (Buscopan) (N=1) and Procholorperazine (Stemetil) (N=1). NSAIDS were taken by 17.1% of the GIT symptomatic group and 33.3% of the asymptomatic group and were not found to be significantly associated with GIT symptoms (P=0.214).

There was, however, a tendency for the GIT asymptomatic group to have a history of previous collapse associated with exercise (P=0.072). Two of the triathletes reported

previous abdominal surgery and both these triathletes experienced GIT symptoms during the race (P=0.498).

Table 3.6: Past and current medical history of the GIT symptomatic and asymptomatic triathletes

	GIT S GROUP (N=35)	GIT AS GROUP (N=24)	P-value
History of GIT Symptoms	61.5 (26)	50.0 (20)	0.629
History of Nausea	0 (0)	0 (0)	1.000
History of Vomit	11.4 (4)	4.2 (1)	0.639
History of Abdominal Cramps	22.9 (8)	20.8 (5)	1.000
History of Diarrhoea	11.4 (4)	16.7 (4)	0.704
History of Urge	5.7 (2)	4.2 (1)	1.000
History of Bloat	8.6 (3)	4.2 (1)	0.639
Medication Use during Triathlon Career [a]	30.1 (26)	30.0 (20)	0.789
Medication Use during 2007 Ironman Triathlon	34.3 (35)	50.0 (24)	0.349
GIT prophylactics	5.7 (35)	8.3 (24)	1.000
NSAIDS	17.1 (35)	33.3 (24)	0.214
History of Collapse	3.9 (26)	25.0 (20)	0.072
History of Abdominal Surgery	7.7 (26)	0.0 (20)	0.498

Values are expressed as a frequency (%) with the maximum number of subjects (N) is in parentheses.
[a] during the event and/or 1 week prior to the race.

3.3.5 Pre- and post-race heart rate and blood pressure (systolic and diastolic)

Figure 3.1A shows the change in pre- and post-race heart rates in the GIT symptomatic and asymptomatic groups. There was a significant increase in post-race compared with the pre-race heart rate (P<0.001) but there was no significant difference between the two groups. The pre- and post-race systolic and diastolic

blood pressures in the two groups are shown in Figures 3.1B and 3.1C respectively. Although both the systolic and diastolic blood pressures significantly decreased from pre- to post-race ($P<0.001$), there were no significant differences in blood pressure between the GIT S and the GIT AS groups. Similar heart rate and blood pressure results were obtained for the two subgroups: i) only those who reported GIT symptoms during the run leg of the race and ii) the subgroup reporting only lower GIT symptoms ($P<0.001$ for all analyses) (Appendix G Figures G.1 and G.2).

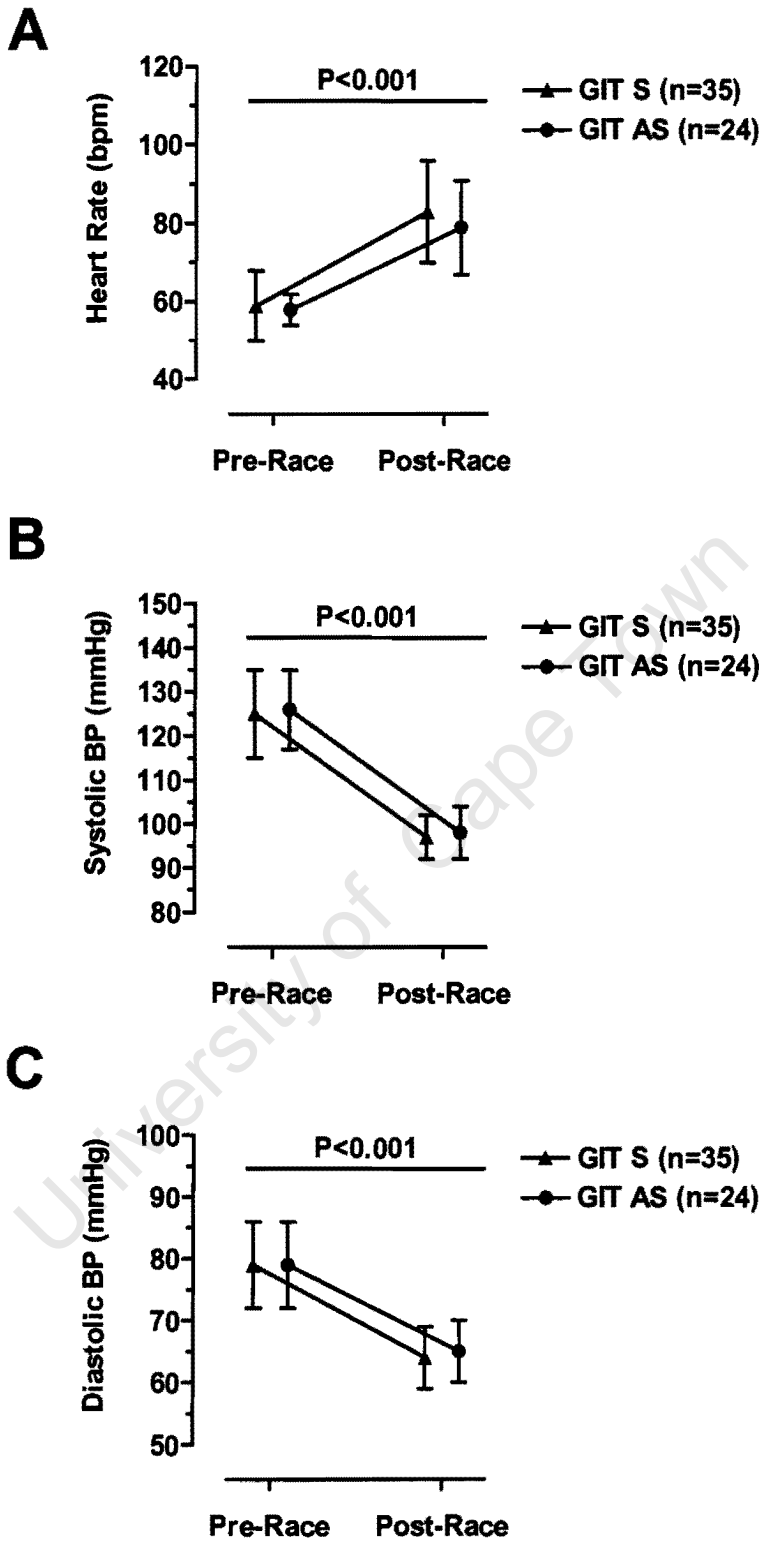

Figure 3.1 Pre- and post-race (A) heart rate, as well as, (B) systolic and (C) diastolic blood pressures of the triathletes in the GIT symptomatic and asymptomatic groups

3.3.6 Haemodynamic assessment of the SMA and the coeliac artery

The pre- and post-race duplex Doppler ultrasound measurements, reflecting the haemodynamic changes in the SMA and coeliac artery, for the GIT S and the GIT AS groups are depicted in Figures 3.2 and 3.3 respectively.

3.3.6.1. Blood vessel diameter

There was a significant reduction in the post-race diameter of the SMA compared to pre-race diameter (P=0.003) (Figure 3.2A). This reduction in SMA diameter was similar in both the GIT S and GIT AS groups. Similarly, there was a significant decrease in the post-race SMA diameter when only the run (P=0.005) and lower (P=0.021) GIT symptomatic sub-groups were analysed (Appendix G Figures G.3A and G.4A).

3.3.6.2. Systolic velocity

There was a significant decrease in post-race systolic velocity within the SMA (P<0.001) (Figure 3.2B), but not the coeliac artery (P=0.779) (Figure 3.3A), in both the GIT S and the GIT AS groups, with no difference between the two groups. Similar systolic velocity measurements were obtained when only the triathletes who reported GIT symptoms during the run leg and triathletes with lower GIT symptoms during the race were included in the analysis (Appendix G Figures G.3B, G.4B, G.5A and G.6A).

3.3.6.3. Diastolic velocity

There was a significant post-race increase in the diastolic velocity within both the SMA (P=0.017) (Figure 3.2C) and the coeliac artery (P=0.005) (Figure 3.3B) in both the GIT S and the GIT AS groups, with no differences between the two groups. Except for the changes in diastolic velocity within the SMA (P=0.059) (Appendix G Figure G4C), a similar post-race increase in diastolic velocity within the coeliac artery (P=0.007) was obtained when only the triathletes who reported lower GIT symptoms during the event were analysed (Appendix G Figure G6B). Similar results were, however, obtained within the SMA when only the triathletes with lower GIT symptoms during the race were included in the analysis (Appendix G Figures G.3C, G.4C, G.5B and G.6B)

3.3.6.4. Resistance Index (RI)

The post-race RI within both the SMA (P<0.001) (Figure 3.2D) and coeliac artery (P<0.001) (Figure 3.3C) decreased significantly in both the GIT S and the GIT AS groups, with no significant difference between the groups. Similar RI results were obtained when only the triathletes who reported GIT symptoms during the run leg and triathletes with lower GIT symptoms during the race were included in the analysis (Appendix G Figures G.3D, G.4D, G.5C and G.6C).

Of the triathletes (N=59) who took medication during the race, 4 took GIT prophylactic medication. When these 4 triathletes were removed from the analysis, haemodynamic findings remained unchanged (Appendix G Tables G13, 14 and 15).

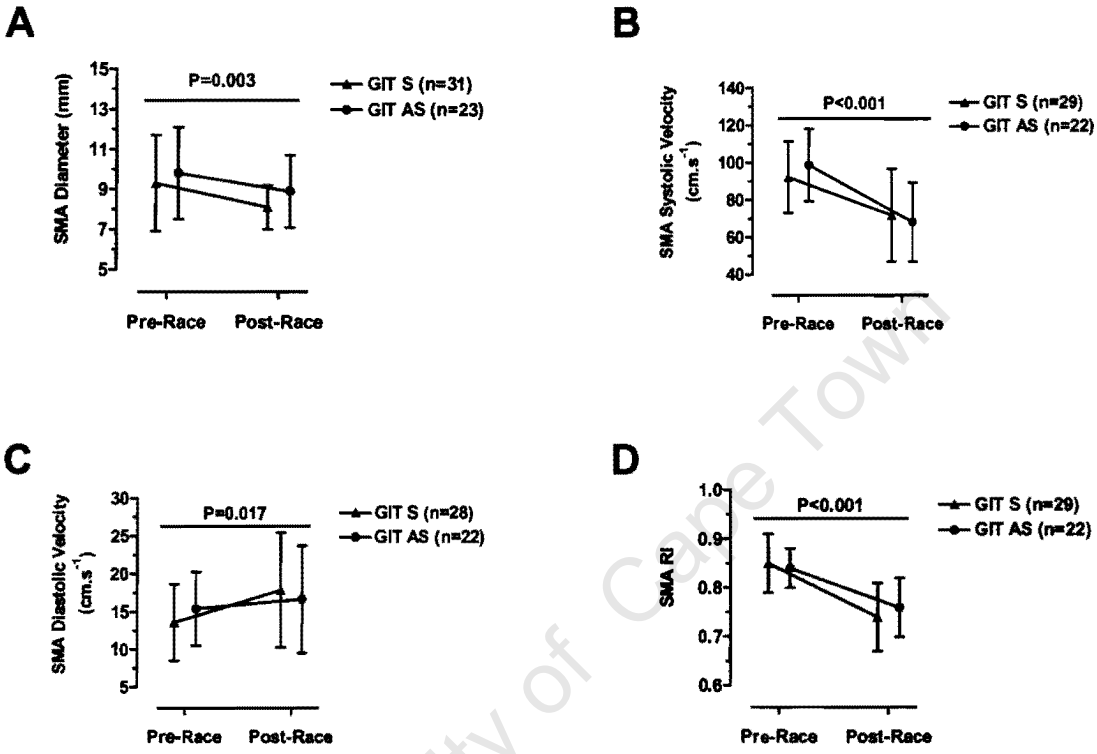

Figure 3.2 Pre- and post-race (A) diameter, (B) systolic velocity, (C) diastolic velocity, and (D) RI of the superior mesenteric artery (SMA) in the GIT symptomatic and asymptomatic groups

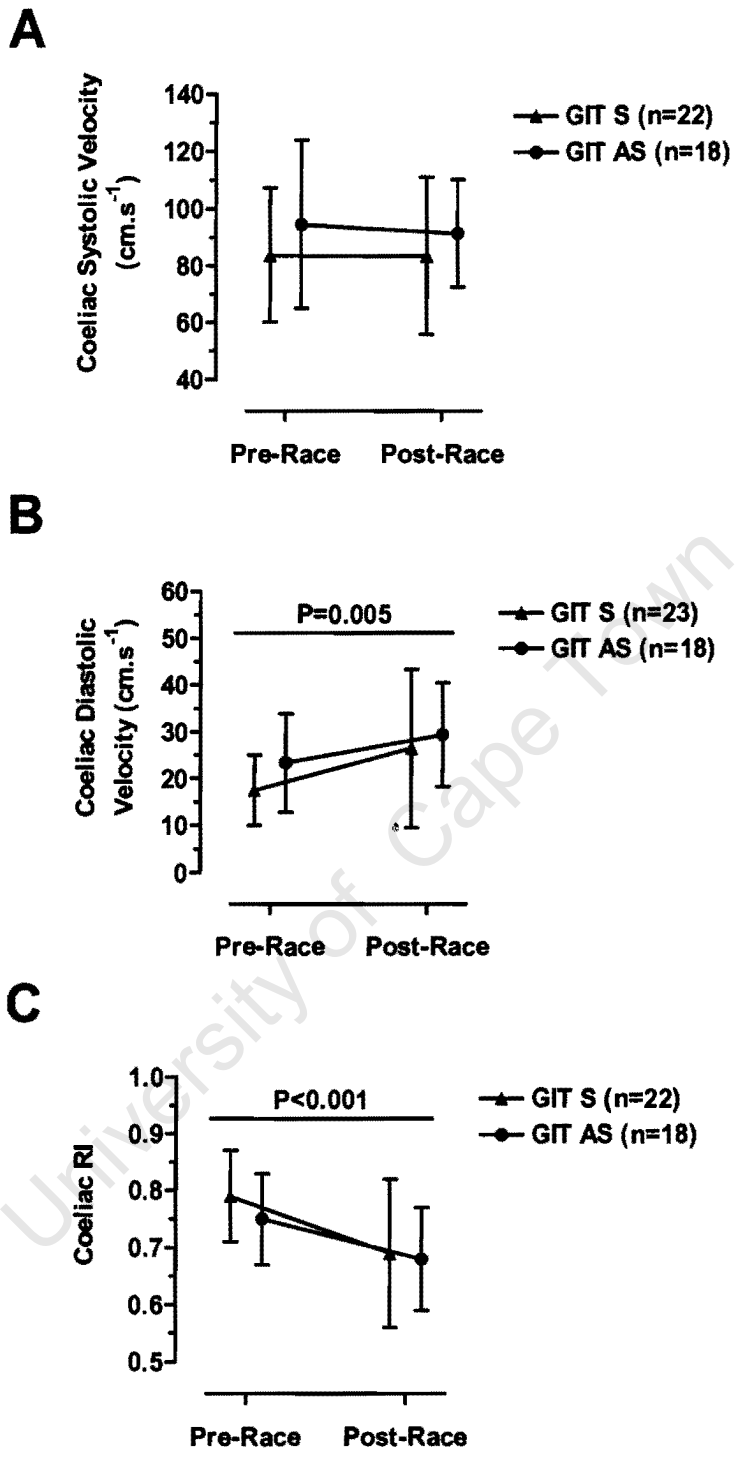

Figure 3.3 Pre- and post-race (A) systolic velocity, (B) diastolic velocity, and (C) RI of the coeliac artery in the GIT symptomatic and asymptomatic groups

3.3.7 Time delay from finishing the race to post-race haemodynamic assessment

The time delay between finishing the race and the post-race haemodynamic assessment was 1.4 ± 0.5 hours (N=35) for the GIT symptomatic group and 1.5 ± 0.5 hours (N= 24) for the asymptomatic group (P=0.402). Post-race haemodynamic measurements were not affected by the time delay and this is shown in Figures 3.4 and 3.5. In addition, the time between last ingestion of fluid or food and the pre-race Doppler ultrasound in the GIT symptomatic group and the asymptomatic group was not significant (P=0.172).

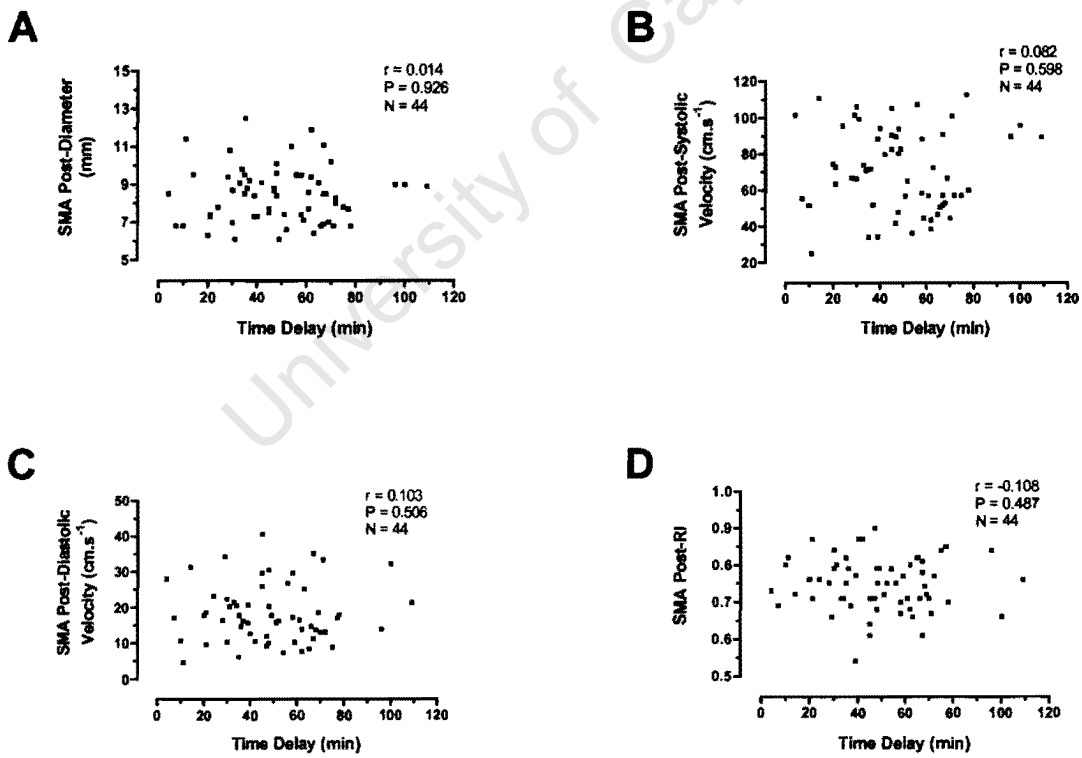

Figure 3.4 Correlation matrices describing the relationship between the time delay after the Ironman Triathlon and the SMA (A) diameter, (B) systolic velocity, (C) diastolic velocity and (D) RI measurements

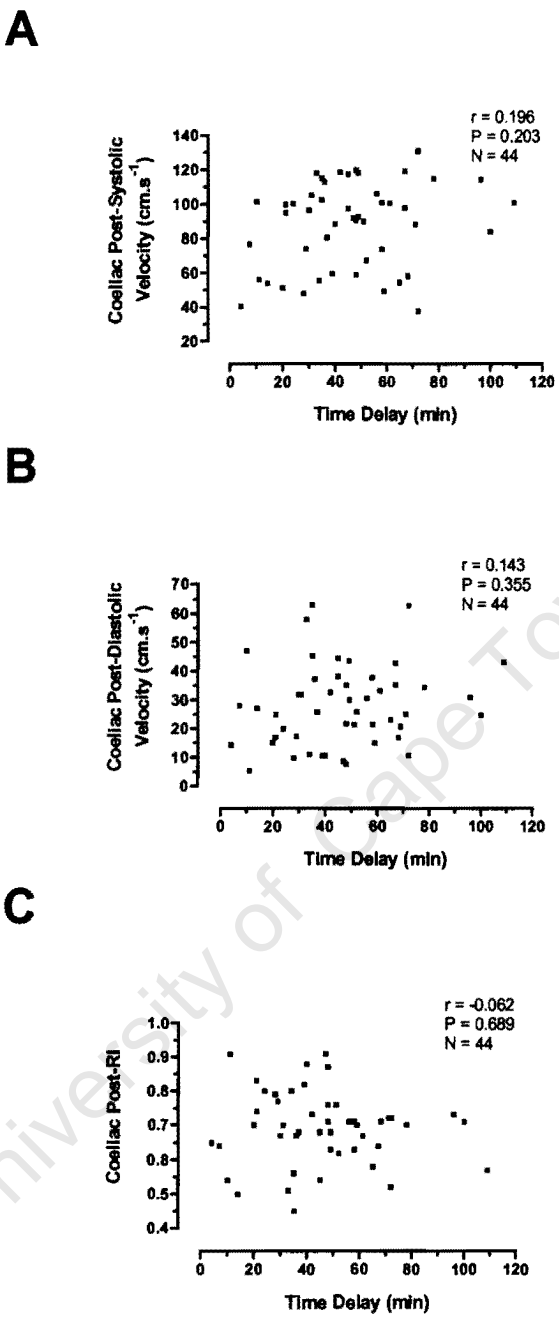

Figure 3.5 Correlation matrices describing the relationship between the time delay after the Ironman Triathlon and the coeliac artery (A) systolic velocity, (B) diastolic velocity and (C) RI measurements

3.4 DISCUSSION

The main aims of this prospective cohort study were 1) to determine if the splanchnic blood flow measured before and after an Ironman Triathlon are different in GIT symptomatic and asymptomatic triathletes, and 2) to identify the risk factors for developing GIT symptoms during an Ironman Triathlon.

The first finding of this prospective cohort study was that there were significant changes in the splanchnic haemodynamics after an Ironman Triathlon (notably a significant decrease in the post-race SMA diameter, and a significant post-race decrease in the RI of the SMA and the coeliac artery). Secondly, changes in the splanchnic haemodynamic measurements (including SMA diameter, SMA and coeliac artery systolic velocity, diastolic velocity and RI) were not significantly different between the triathletes who experienced GIT symptoms during the race compared with those who did not.

The third finding of this study was that in this group of triathletes, younger age was the only independent risk factor for developing GIT symptoms during an Ironman Triathlon. Other previously postulated risk factors for the development of GIT symptoms during exercise, such as gender, high intensity exercise, poorly conditioned athlete, medication use and previous abdominal surgery, were not associated with the development of GIT symptoms in this group of triathletes.

In this study, duplex Doppler ultrasound was used to assess the haemodynamic changes in the SMA and coeliac artery before and after an Ironman Triathlon. This was

a field study and, to our knowledge, the first study where measurements of splanchnic heamodynamics were undertaken in this field setting. The strengths of using this study design and setting were that 1) triathletes that were likely to develop GIT symptoms could be recruited and assessed before the event, 2) portable, non-invasive methodology could be used to measure splanchnic haemodynamics, 3) a large group of athletes could be recruited, 4) a number of potential risk factors for GIT symptoms could be assessed and 5) a competition setting during which GIT symptoms are more likely to occur existed. However, the main limitation of this field study design was the practical difficulty in minimising and, therefore, standardising the time delay between finishing the race and the post-race haemodynamic assessment. This problem was anticipated and therefore the splanchnic haemodynamic measurements were analysed according to the duration between finishing the race and the time of the post-race haemodynamic assessment. As indicated in the results, there was no relationship between time delay (finishing time to post-race haemodynamic assessment) and the changes in any of the splanchnic haemodynamic measurements. This indicated that the time delay did not influence the changes observed in the pre- to post-race splanchnic haemodynamic measurements in this study. However, it must also be noted that in previous studies the timing of post-exercise measurements were within a few minutes (2-30min) after exercise [97, 98], whereas, in this field study, the time delay from finishing the race to haemodynamic assessment varied from 54-120 minutes. Therefore interpretation of the post-race splanchnic haemodynamic measurements reported in this study has to take the time delay from finishing the race to haemodynamic measurement into account.

It is also important to point out that other limitations of this field study were:

1) fluid intake, hydration status as well as food intake during the race could not be recorded accurately, 2) a number of different GIT symptoms were reported and could be analysed separately for lower and upper GIT symptoms only, 3) differences in severity of GIT symptoms were not accurately reported by the triathletes, and 4) splanchnic haemodynamic measurements were not necessarily performed at the time of development of the GIT symptoms in the GIT symptomatic group.

Bearing these strengths and limitations in mind, the results of this study showed that there was a significant decrease in the diameter of the SMA post-race, compared with pre-race diameter. This finding supports previous observations in other prospective cohort studies that splanchnic vasoconstriction occurs during exercise, which results in redistribution of blood away from the GIT [12, 88, 104].

RI has been used to assess blood flow in the SMA in other studies [110]. It has been suggested that the RI is the most accurate and the most precise measurement of mesenteric hyperaemia [110]. In our study, RI was significantly decreased in the SMA and coeliac artery in Ironman triathletes after the race, and this reduced RI suggests mesenteric hyperaemia (an increase in blood flow). This is to our knowledge, the first study using RI as a measure of blood flow following prolonged exercise and, therefore, our findings cannot be compared to those from other similar studies. The precise reason/s for the decrease in vessel diameter, but yet an apparent increase in blood flow (reduced RI) are not clear. RI is calculated as

$$RI = \frac{\text{Systolic velocity} - \text{Diastolic velocity}}{\text{Systolic velocity}}$$

The observed reduction in RI in this study could, therefore, be as a result of reduced systolic velocity, increased diastolic velocity or both. In our study it appears that the observed decrease in RI was as a result of both a reduced systolic velocity as well as an increased diastolic velocity. However, the precise mechanisms underlying these changes are not clear but are most likely to reflect the post-exercise reduction in the sympathetic nervous system response to exercise. We postulated that the decrease in RI might be attributed to the reduction in systolic and diastolic blood pressures recorded in our study. Other studies using RI as a measure of flow did not report blood pressure change [110]. In our study of prolonged exercise duration, systolic and diastolic blood pressures were shown to be significantly reduced after the Ironman Triathlon. Systolic blood pressure was more markedly decreased than diastolic blood pressure. Thus the changes in blood pressure may have resulted in the alteration in systolic and diastolic velocities and hence RI. This suggestion emphasises the dynamic nature of haemodynamics and that blood flow cannot be considered as a static model. Other possible mechanisms that may have contributed to a reduced RI are the response to food or fluid intake, and variations in other neurotransmitter concentrations such as 5-hydroxytryptamine [110]. Our study was not designed to measure these possible mechanisms, and further studies are required to determine the mechanisms underlying these observations. However, the results from our study do appear to support the observations from other prospective cohort studies, which showed the physiological

vasoconstriction of the SMA, which occurs during exercise. In addition, if the decrease in RI can be explained by other factors, including the postulated influence of change in systolic and diastolic blood pressure, flow may indeed decrease and RI is an unsuitable measure of blood flow when other haemodynamic variables are not static. However, this hypothesis does not alter our finding that there was no significant difference in haemodynamic measurements between the GIT symptomatic and asymptomatic triathletes.

This study was primarily designed to determine whether the blood flow in the SMA and coeliac artery was significantly different between triathletes who experienced GIT symptoms during the Ironman Triathlon and those triathletes who were asymptomatic. Although changes in splanchnic haemodynamic measurements from pre-race to post-race differed, there were no significant differences in splanchnic haemodynamic measurements between the GIT symptomatic and asymptomatic groups. Therefore the results of our study do not support the hypothesis that the altered splanchnic haemodynamics, which were observed post-exercise, are associated with the development of GIT symptoms during an Ironman Triathlon. This is, to our knowledge, the first study where haemodynamic measurements were measured pre- and post-exercise in athletes who were GIT symptomatic and those who were not.

Another novel element to this study is the prolonged time period over which the exercise took place. Most previously published studies that have measured splanchnic blood flow during exercise were laboratory based and were of much shorter exercise duration [97, 98]. In a case control study, 16 subjects underwent a

duplex Doppler ultrasound of the SMA following a 30 minute rest period and then following a 15-minute exercise session (treadmill walking at 5km/hr at a 20% incline) [97]. Post-exercise measurements were taken immediately on cessation of exercise and then at 5-, 10-, 15- and 30-minutes post-exercise. In another study, 19 subjects underwent duplex Doppler ultrasound measurement of SMA blood flow while cycling at 75% VO_{2max} for 30 minutes [98]. The ultrasound was recorded and 5 measurements were taken on the video between the 15- and 30-minute mark of cycling. In comparison, triathletes in our study exercised for between 10 hours and 17 hours. Due to the field nature of this study, haemodynamic measurement during exercise was practically not feasible. Post-exercise haemodynamic assessment was used to represent blood flow during exercise as used by other investigators [97]. We were unable to demonstrate a difference in the post-race splanchnic haemodynamic measurements between GIT symptomatic and asymptomatic triathletes. This finding suggests that the pathophysiology of GIT symptoms associated with exercise is not related to alteration in post-race blood flow measurements. As mentioned, the nature of this field study did not allow us to measure splanchnic haemodynamics during exercise or to measure splanchnic haemodynamics at the precise time of the development of GIT symptoms. As previously mentioned, the time delay between finishing the race and the post-race haemodynamic assessment should also be considered. The results, therefore, have to be interpreted with these limitations in mind. However, it is likely that the splanchnic haemodynamic changes (such as decreased vessel diameter) that were shown post-exercise, were also present during exercise as the changes we observed post-exercise are in keeping with that of other studies where changes were measured immediately post-exercise (and up to 30min post-exercise) [97].

As already mentioned, the purpose of this study was not to investigate possible mechanism/s for altered post-exercise splanchnic haemodynamics. However, it is known that splanchnic haemodynamics are mainly influenced by the autonomic nervous system but may also be altered by other factors including dehydration and blood hormone concentrations. Future studies would need to be conducted to determine the possible mechanisms for the changes we observed post-exercise in the triathletes.

This study was also designed to determine possible risk factors that could be associated with the development of GIT symptoms in Ironman triathletes. The main finding of this component of the study was that younger age was an independent risk factor for the development of GIT symptoms in triathletes. Younger age as an intrinsic risk factor has been shown to be a significant predictor of the development of GIT symptoms in other cross-sectional studies (marathon runners and in six other endurance sports) [7, 15, 18]. Once again, the precise reasons for this finding are not known, and have not been investigated in this study. However, as mentioned previously (Chapter 2), the postulated explanations for this are that younger athletes 1) may perform exercise at a higher relative intensity than older athletes [18], 2) have a poorly "conditioned" GIT compared to older athletes [18], or 3) may be more prone to dehydration due to lack of experience [6].

Vertical impact sports, such as running, have been suggested to be associated with GIT symptoms [8, 39]. The results of our study showed that most GIT symptoms occurred during the run leg of the triathlon. Other studies including cross-sectional

and case-control studies have also shown that running is associated with more GIT symptoms than other non-impact sports such as cycling [7, 39]. It should, however, be noted that the run leg of the triathlon occurs at the end of the race and therefore the role of increased sympathetic drive associated with fatigue, dehydration, and other factors - other than running itself - should also be considered as possible reasons for the observation that GIT symptoms were more commonly reported in the running leg of the triathlon.

Other factors which have been proposed as potential risk factors for the development of GIT symptoms were also analysed in our study. These factors include female gender, high intensity exercise, poorly conditioned athlete, medication use and previous abdominal surgery.

Female gender was not shown to be a significant intrinsic risk factor in this prospective cohort study and is supported by the findings from another prospective cohort study where a group of subjects were studied while training for 18 months for a marathon [31]. Other cross-sectional studies have found female gender to be a risk factor but these studies had limitations and are not considered as strong evidence-based research [18, 19] (Chapter 2).

In this study, we found intensity of exercise (as measured by finishing times) was not a significant risk factor in the development of GIT symptoms. Actual performance times of the overall race and of each leg of the race were compared with the predicted times for each. It was found that the GIT symptomatic group ran slower during the race than they had predicted they would. Similarly, when a triathlete's run

times were expressed relative to their personal best time for a 21.1km race during the 15 weeks preceding the Ironman Triathlon, it was found that the GIT symptomatic triathletes ran at a lower intensity than the asymptomatic group. Both these findings are likely to be as a result of the GIT symptoms that the triathletes were experiencing during the run leg of the race.

Triathletes reported the distance and the finishing time of a cycle race in which they participated during the 15 weeks prior to the Ironman Triathlon. Speed was calculated and this was compared to the actual cycling speed during the race. This relative speed was then used as an indicator of intensity. There was no significant difference demonstrated between the GIT symptomatic and asymptomatic groups. Other prospective cohort studies have shown varied results with regard to the relationship between intensity of exercise and the development of GIT symptoms during exercise [30, 31, 34]. The greatest limitation in these studies is that there is no standardised measure of exercise intensity that was used in all the studies. An objective measure of exercise intensity in a field study is particularly challenging and therefore use of finishing times and self reported performance times in the 15 weeks prior to the race were chosen as the most representative measure of exercise intensity in this study.

In this study, training history was not found to be a significant predictor of GIT symptoms associated with exercise in the Ironman triathletes. Training histories were similar in the GIT symptomatic and asymptomatic groups. However, the GIT symptomatic group was found to have a lower training distance in the 15 weeks preceding the race, but the same duration of running compared with the

asymptomatic group. This difference was not significant in the 1 week prior to the race. There are anecdotal reports that untrained subjects appear to experience more GIT symptoms than trained athletes [6]. However, studies where this factor has been investigated in trained runners participating in marathon events have not shown less training to be a significant risk factor for GIT symptoms [18, 19]. However the marathon runners and our triathletes were all well conditioned for their events but further research comparing sedentary subjects with athletes may be more prudent in addressing this risk factor.

In our study, the use of medication, in particular NSAIDS was not a significant extrinsic risk factor in the development of GIT symptoms. Other prospective cohort studies have also not found an association between the use of NSAIDS and GIT symptoms associated with marathon running [30, 42]. In our cohort, 4 triathletes reported using some form of GIT prophylactic medication. Out of the 4 triathletes, 2 experienced GIT symptoms and the other 2 were asymptomatic. These 4 triathletes were excluded from the cohort and the data re-analysed. There was still no significant difference with regard the splanchnic haemodynamic measurements between the two groups.

In a previous cross-sectional study a history of abdominal surgery was found to be a predictor of GIT symptoms associated with exercise [7]. Our study did not show this to be a significant risk factor in Ironman triathletes.

GIT symptoms during triathlon and endurance running have been shown to be common [7, 15, 18]. In our study, the incidence of GIT symptoms in the cohort of Ironman

triathletes was 59%. The sample of triathletes in our study was not random, and selection bias cannot be excluded. Therefore the incidence of 59% of triathletes experiencing GIT symptoms during the Ironman Triathlon is likely to be an overestimate. However, in another cross-sectional study of 110 triathletes a prevalence of 50% of GIT symptoms was reported [2]. The study design of these two studies differs considerably, which makes the interpretation of the results difficult.

In our study, lower GIT symptoms were more commonly reported than upper GIT symptoms. This finding is in keeping with the findings from a number of other cross-sectional studies in marathon runners and athletes participating in 6 different endurance sports [7, 15, 18]. In our study, triathletes experienced lower GIT symptoms most commonly during the run leg of the Ironman Triathlon. Vomiting was shown to be the most common upper GIT symptom occurring mainly in the swim leg of the race. This may be related to motion sickness as the swim leg took place in the sea and sea conditions on race day were rough. The most common GIT symptom during the race was abdominal cramps, which was experienced equally during cycling and running. Blood in the stool was not reported by any triathlete after the race. This may be due to the fact that triathletes were not asked directly about this symptom and privacy was limited. Also, triathletes reported GIT symptoms as soon as they had finished the race at the post-race assessment and therefore it may have been too soon for the symptom of GIT bleeding to become evident to the triathlete. The occult nature of GIT bleeding also may influence subjective reporting of this GIT symptom.

As previously mentioned, in a cohort study of this nature, subjects are self- selected and therefore it is possible that triathletes with a history of GIT symptoms associated with exercise were more likely to volunteer for the study. However, this study relied upon subjects experiencing GIT symptoms in order to compare symptomatic to asymptomatic groups and, therefore, may have been beneficial. This possible selection bias would not have influenced the main results of this study, which were related to changes in blood flow before and after the Ironman Triathlon between the two groups. Of importance, is that a past history of GIT symptoms was not found to be a significant predictor of GIT symptoms during the Ironman Triathlon and therefore selection bias was not of importance in this study. The cohort was also shown to be matched with the rest of the field competing in the race with regard age and gender.

This prospective cohort study is a novel field study investigating triathletes over a prolonged period of exercise and a study of this kind is, to our knowledge, original. The splanchnic haemodynamic measurements used (diameter, systolic velocity, diastolic velocity and thus RI) are objective assessments and are reproducible in future studies.

In summary, the data presented in this study showed that there is a significant change in splanchnic haemodynamic measurements post-exercise compared with pre-exercise. However, there is no difference in splanchnic haemodynamic measurements in triathletes who experience GIT symptoms and those who do not during an Ironman Triathlon. These findings indicate that the underlying pathophysiology for the development of GIT symptoms associated with exercise may not be related to blood flow. Other hypotheses of pathophysiology should therefore

be investigated in future research studies in order to explain the underlying mechanism for GIT symptoms associated with exercise.

Chapter 4

Summary and conclusion

GIT symptoms are common in endurance athletes such as the Ironman triathletes investigated in this study. Training sessions and racing events can be disrupted and performance can be compromised by GIT symptoms, which range from mild to severe in nature. Therefore knowledge of the risk factors, underlying pathophysiology and possible preventative measures are essential for future management of this common problem. Research of GIT symptoms associated with exercise is, to date, still limited.

In this study, a cohort of triathletes was recruited prior to an Ironman Triathlon. In this cohort, pre- and post-race duplex Doppler ultrasound was used to measure splanchnic haemodynamics. Pre-race questionnaire surveys were also collected, and GIT symptoms and medication use were reported post-race.

There were four main findings in this study. Firstly, there was a significant change in splanchnic haemodynamics from pre- to post-race (decreased SMA diameter, decreased SMA and coeliac artery RI).

Secondly, there was no significant difference in these haemodynamic measurements between the GIT symptomatic and asymptomatic triathletes. These data do not support the hypothesis that altered blood flow to the GIT is a cause of GIT symptoms during exercise, as previously suggested.

The third finding confirms the findings of other investigators that younger age is a significant risk factor for the development of GIT symptoms. Finally, the results of this study show that other proposed risk factors, including female gender, previous abdominal surgery, high intensity exercise, a poorly conditioned athlete and medication use, were not associated with the development of GIT symptoms during the Ironman Triathlon.

Future research should be directed at investigating other possible pathophysiological mechanisms to determine the possible causes of GIT symptoms associated with exercise. Further prospective cohort and case control studies investigating intrinsic and extrinsic risk factors, especially the effect of dietary factors on GIT symptoms, are necessary.

The clinical implications determined in this study include the following:

- GIT symptoms are common in triathletes and were observed in 59% of triathletes competing in an Ironman Triathlon
- A younger age has been shown to be a significant risk factor for developing GIT symptoms during exercise
- From a review of the available evidence, dehydration may be a predisposing factor for the development of GIT symptoms during exercise, although this was not assessed in this study
- Participation in an Ironman Triathlon is associated with significant post-exercise changes in blood flow to the GIT, but findings from this study do not confirm that altered blood flow was associated with the development of GIT symptoms during exercise.

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Appendices

Appendix A

Invitation to participate in the Medical Research at Ironman 2007

Once again, the medical research team will conduct studies at the 2007 Ironman in Port Elizabeth. We anticipate that the findings ultimately will assist you in improving your performance and improving the standard of your medical treatment at future triathlons and other endurance events:

Research results from Ironman 2006

Attached is a summary of the main results from the research we conducted last year at the Ironman 2006 (please download the attachment). A number of the research projects are ongoing, and the same or similar questions will again be examined this year.

What are the research questions the team wishes to answer?

The following research questions have been identified and will be investigated:

1. What is the best treatment of a collapsed triathlete?
2. Does training affect the risk of developing Exercise Associated Muscle Cramping in Ironman triathletes?
3. Why can Ironman triathletes cope so well with pain and discomfort during training and competition?
4. How does your genetic make-up affect your performance and possible medical complications during an Ironman triathlon?
5. Does your brain become exhausted during an Ironman event – what is the evidence?
6. What are the causes of gastro-intestinal (GIT) distress in Ironman triathletes ? (It was very evident from the research findings of 2006, that this is a very common problem)

How can you volunteer to participate in the research studies in 2007?

As a participant in the Port Elizabeth IRONMAN 2007 triathlon, you will be given the unique opportunity to participate in this research effort. The following are very important:

- Please understand that your participation is entirely voluntary
- You will be given the opportunity to participate in any number, or all components of the study
- Brief information of each component is given below, but more details of the research studies and precise instructions on how to participate in the research are attached
- Please download and read the following documents:
    1. Subject information sheet (this will give you detailed information about each component of the research)
    2. Informed consent form (If you wish to participate, this document needs to be signed in the presence of a member of the research team – at the time of registration in Port Elizabeth)
    3. Medical and training questionnaire (Please complete this questionnaire in the 2-3 weeks before registration, and bring it with you to the research stand at the registration area – this questionnaire can be completed even if you do not wish to participate in all the research studies)
- We acknowledge that the questionnaire is long, and we therefore suggest that you complete it over a few days and perhaps section by section. Your assistance is MUCH appreciated.

Brief information on each component of the research study

1. Treatment of the collapsed triathlete
In this study we wish to determine which of two commonly used forms of treatment (drinking fluids, or receiving fluids into you vein through a "drip") are most effective in the treatment of collapsed athletes. Under the expert care of the medical team in the medical tent, you will be able to voluntarily participate in this study (either before, or on admission to the medical tent).

2. Exercise associated muscle cramping
In this study, we wish to determine whether there is a training-related factor that may play a role in the risk of developing cramping. Information for this study will be obtained by completing the medical questionnaire and by getting your "effort rating" during the race (this will be explained to you). Further information will also be obtained from those of you that have your own recording and down-loadable type heart rate monitor. If you are interested in participating in this study, please start (or continue if you already do this) monitor your heart rate during training in the 4-6 weeks before the race and during the race. It will be necessary to download the heart rate data and then to submit this to us via email, or you can bring the data on your flash-drive to registration. We could even get this information from you after the event!

3. Pain coping strategies in Ironman triathletes
As you are all well aware, intense training and competing in an extreme endurance event such as the Ironman is associated with discomfort and physical pain. In this study, we wish to identify strategies used by triathletes to cope with pain experienced during extreme physical exercise. This information will be obtained by a questionnaire (completed before the race), and by testing your level of concentration, heart rate variability and your pain threshold before the race (20-30 min test). This information will be determined 1-4 weeks before the race at a research centre in Cape Town or it can be done at registration before the race. Some of these tests will be repeated after the race.

4. Genetic make-up and performance, physiological responses and medical complications during an Ironman triathlon
In this study, we wish to determine whether genetic markers are associated with performance and medical complications during an Ironman triathlon. Information for this study will be obtained by completing a questionnaire. In addition, we will need volunteers to donate a small blood sample (1 teaspoon) from which your genetic material (DNA) will be extracted for the identification of gene variants. This information and the blood sample will be obtained at registration before the race.

5. Brain "exhaustion" after an Ironman Triathlon
In this study, we wish to measure the effect of the Ironman on brain and nerve processing and the nerve activity that, for instance, controls your heart rate. Using an electroencephalogram (EEG) machine (measured through a cap, similar to a swim cap, that has electrodes that only record nerve activity) we will be measuring brainwave patterns and heart rate variability during a simple mental test before and immediately after (within 60min of completing) the Ironman. This test is not painful, and takes about 20-30 min. It will be conducted 1-4 weeks before the race at the Sports Science Institute in Cape Town, or at the registration area before the race.

6. Possible causes of gastro-intestinal (GIT) distress in Ironman Triathletes
In this study we wish to find out why such a large percentage of triathletes suffer from stomach and other abdominal upsets during training and racing. Volunteers for this component of the study will be asked to complete the questionnaire. In addition, in a smaller group of volunteers, we wish to measure the blood flow to the intestines using an ultrasound machine (such as used in scans during pregnancy or when we scan the tendons) before the race (during registration in Port Elizabeth) and then again immediately after the race (particularly in those triathletes who regularly develop abdominal problems). This scan is not painful, and will take about 10 minutes.

A final word from the medical team and the research team

One of the main components of the projects is the completion of a detailed medical questionnaire. The information obtained form this questionnaire will be very useful for the medical team and can lead to improvements in medical care if you need it. We therefore encourage all of you to complete the questionnaire, and also consider participating in some (or all) of these other tests.

Medical Research Director	Chief Medical Officer	Race Director
Prof Martin Schwellnus	Dr Peter Schwartz	Mr Paul Wolff

Appendix B

SUBJECT INFORMATION SHEET

Dear Tri-athlete

We have the privilege to inform you that scientific research at the Port Elizabeth Spec-Savers Ironman South Africa triathlon has been planned in collaboration with the MRC/UCT Research Unit for Exercise Science and Sports Medicine based at the Sports Science Institute of South Africa. This will provide a unique opportunity for a research programme to address important medical and physiological problems associated with the Ironman triathlon. Each participant will be able to access a summary of the findings of the study, once it has been completed. The research study will concentrate on the following 6 main components that will ultimately lead to an **improvement in medical and physiological knowledge which may improve training strategies and medical treatment** at future triathlons and other endurance events:

- Management of the collapsed tri-athlete
- Causes of exercise associated muscle cramping (EAMC) in Ironman triathletes
- Pain coping strategies in Ironman Triathletes
- Genetic basis for performance, physiological responses and medical complications during an Ironman Triathlon
- Neural fatigue following an Ironman Triathlon

As a participant in the Port Elizabeth Spec-Savers Ironman South Africa triathlon, you will be given the choice to participate in this research effort. Your participation is entirely voluntary. Please read through the details of the following six components of the study. You will be

given the opportunity to participate in one or more components of the study. The details of each component are explained in this document, and if you wish to participate in one or more components of the study, please read through and sign the INFORMED CONSENT FORMS that relate to each component of the study. Please feel free to contact members of the research team should you have any questions related to the study (or any component of the study). Contact details of the research team are as follows: Ironman@sports.uct.ac.za or (021) 650 4567

SUBJECT INFORMATION SHEET:

COMPONENTS OF THE RESEARCH STUDY TO BE CONDUCTED AT THE 2007 IRONMAN TRIATHLON IN PORT ELIZABETH

The research study at the 2007 Spec-Savers Ironman South Africa triathlon, comprise of six components. The detailed information on each of these components of the study is as follows:

Component 1: Management of the collapsed Tri-athlete

General information:

The aim of this study is to evaluate the optimum treatment strategies for which to treat collapsed tri-athletes, after an Ironman race. Although intravenous (fluid that is infused through a needle into one of your veins – also referred to as IV fluid) fluid replacement is a common practice in the treatment of collapsed tri-athletes, medical personnel need to be advised of a treatment method that will prevent possible fluid overload, which can cause hyponatraemia. Hyponatraemia can be a very severe condition. Your participation in this trial will aid in the understanding and management of how best to correct any fluid imbalance following this race.

If you collapse during or after the Ironman Triathlon and are brought into the medical tent, you will be evaluated and treated according to the current best standard of care principles. Your legs will be elevated and your heart rate, blood pressure, mental status and serum sodium concentration will be measured. If you are confused and your sodium level is normal, other laboratory tests will be performed such as an evaluation of your body temperature and blood sugar levels. If your body temperature is normal and do not have evidence for another treatable medical condition, a small needle and tube will be placed into a vein in your arm. The appropriate fluid (into your vein or drinking normally by mouth) (ad libitum – you chose how much you wish to drink) – will be given to you until you recover and can leave the medical tent without assistance. Your discharge will be at the discretion of the supervising medical officer. If your condition deteriorates at any time, you will be immediately removed from the trial, treated appropriately and transported to the nearest hospital. At all stages of the research study and medical care, the highest standard of safety and medical country as practised in this country will be adhered to.

The risk of adverse affects of placement of an intravenous line include: infection, delayed healing, bruising, physical pain, mental discomfort and possible injury to a nerve or vessel. The risk of these adverse effects are rare and every attempt to minimize these risks will be undertaken by the use of sterile technique and use of disposable, single use, material. Your blood will be used for evaluation of serum sodium or blood glucose concentration only. No other tests will be performed on your blood and your blood samples will be appropriately discarded after these tests are performed.

We will obey the strict practices of confidentiality and anonymity. Each subject's identity will be known only to the researchers and numbers will be assigned to each sample in lieu of names. No results will be publicly available and the scientific publication of results will never disclose subject identity. Upon specific request, data such as electrolyte analyses will be made available to subjects.

Potential risks of this component of the study

- The completion of personal details, racing, training, equipment use, medical, supplement use, fluid use and lifestyle history questionnaires are not associated with any risk. Completion of self-rated behavioural questionnaires has not previously been shown to be associated with risk. A potential risk is that people who have experienced significant past trauma will find questionnaires on this uncomfortable. The questions within the behavioural questionnaires are asking are about temperament and none of the scales are directed at picking up psychopathology. Questionnaire and other clinical data (paper and electronic) will be kept confidential, will be kept secure, and will not be made available to any party other than the research team without the consent of the individual subjects.
- The risks associated with participation in this component of the study do not exceed the risks associated with competing in the Ironman competition. The administration of fluid into your vein will involve an invasive placement of an intravenous line (a small needle and tube). The risks associated with the placement of an intravenous line include: infection, delayed healing, hematoma, physical pain, mental discomfort and injury to a nerve or vessel. These risks will be minimized by the use of trained phlebotomists, sterile technique and disposable, single use materials. If at any time the condition of a collapsed tri-athlete deteriorates, the most appropriate treatment will be initiated, the trial terminated and the patient will be transported to the local hospital if necessary. The support form the local hospital is part of the normal standard medical care associated with this event.

Potential benefits of this component of the study

- The data collected in this component of the study will aid in the development of optimal treatment strategies for collapsed tri-athletes. Although fluid replacement directly into your vein is a common practice in the treatment of collapsed tri-athletes, medical personnel need to be advised of a more judicious approach to treatment as to avoid the deleterious effects of fluid overload (hyponatraemia). This information will aid in the

understanding and management of serum sodium disorders in collapsed tri-athletes by scientifically 1) evaluating the efficacy of fluid replacement directly into your vein versus oral rehydration and 2) assessing if the normalization of serum sodium levels are important in the recovery of collapsed tri-athletes.

Component 2: Causes of Exercise Associated Muscle Cramping (EAMC) in Ironman Triathletes

General information

The purpose of this component of the study is to determine the possible cause of exercise associated muscle cramping (EAMC) in endurance athletes. Tri-athletes will be contacted as soon as possible and given the opportunity to volunteer to participate in this component of the study. Anyone who owns a recording heart rate monitor will be eligible to participate. Details of the study are as follows:

- A questionnaire detailing personal particulars, training and racing history, psychological and behavioural, medical information, and history of muscle cramping will be completed.
- Each triathlete will be asked to send a file via email to the Sports Science Institute of their weekly heart rate data as recorded during their training and racing using their personal recording heart rate monitors.
- You will be asked to complete a questionnaire on your training habits for swimming, cycling and running in preparation for the Ironman and your personal best times for the 3 disciplines.
- You will be familiarised with the subjective scores for "*perception of effort rating*" before the race. During the race researchers will be allocated to about 12 stages throughout the race. As you swim, run or cycle past these researchers they will hold up a board with the

scores for "*perception of effort rating*". You will be asked to shout out your score as you go past them and they will record these scores against your race number.

Potential risks of this component of the study

- The completion of personal details, racing, training, equipment use, medical, supplement use, fluid use and lifestyle history questionnaires are not associated with any risk. Completion of self-rated behavioural questionnaires has not previously been shown to be associated with risk. A potential risk is that people who have experienced significant past trauma will find questionnaires on this uncomfortable. The questions within the behavioural questionnaires are asking are about temperament and none of the scales are directed at picking up psychopathology. Questionnaire and other clinical data (paper and electronic) will be kept confidential, will be kept secure, and will not be made available to any party other than the research team without the consent of the individual subjects.
- Data for this component of the study will involve contact with subjects during the race. There is a potential risk that in the process of data collection, the performance of subjects in the race will be interfered with. This risk will be minimal, as the nature of the data collection is such that subjects will only be asked to shout out a number as they pass members of the research team at designated points in the race. However, should tri-athletes feel that this affects their performance during the race, they will be free to withdraw from this component of the study during the race. There will be no interference with other race participants during this data collection process.

Potential benefits of this component of the study

- The anticipated benefits of this component of the study are that the results will further our understanding of the possible cause/s of EAMC in endurance athletes. In particular, once the aetiology of EAMC is better understood, this will improve our ability to prevent this condition.

Component 3: Pain coping strategies in Ironman Triathletes

General information

The purpose of this component of the research study is to determine if athletes participating in an endurance event (such as the Ironman) use a common coping strategy to endure pain that is related to exercise.

- Before the race you will be required to visit a centre, designated to your area (either in Cape Town, Port Elisabeth, Durban, Bloemfontein or Johannesburg), where you will be asked to complete a questionnaire with personal details, training details, past injury, pain and medical details, details about family history and a psychological questionnaire. You will also be asked to perform a stroop test. The stroop test is a simple, computer based test. The mental concentration that is required for the test is relevant for the data collection and not the outcome of the test. During the test your heart rate variability will be recorded. This procedure entails wearing a heart rate monitor strapped around your chest. This procedure is not associated with any discomfort. While the EEG recordings themselves are completely painless, a slight (1) measure of discomfort may be experienced when the electro-cap is pulled (2) over the scalp - similar to pulling a swimming cap over the scalp. (3) When the electro gel is applied it may feel cold and sludgy - cleaning towels and water will be available to freshen up afterwards. In addition, your pain threshold will be assessed with a digital probe. As the onset of pain will be assessed, this procedure is associated with minimal discomfort. You will also be familiarised with the subjective scores for *"perception of effort rating" and "pain assessment"* before the race.
- During the three days of registration before the event and immediately after the event, the Stroop test and the concomitant recording of the heart rate variability will be repeated.

- The assessment of the pain threshold level will be repeated immediately before and after the race, together with a recording of the athletes' feelings/mood.
- During the race researchers will be allocated to about 12 stages throughout the race. As you swim, run or cycle past these researchers they will hold up two boards with the scores for *"perception of effort rating"* and *"pain assessment"*. You will be asked to shout out their respective scores as they go pass.

Potential risks of this component of the study

- The completion of personal details, racing, training, equipment use, medical, supplement use, fluid use and lifestyle history questionnaires are not associated with any risk. Completion of self-rated behavioural questionnaires has not previously been shown to be associated with risk. A potential risk is that people who have experienced significant past trauma will find questionnaires on this uncomfortable. The questions within the behavioural questionnaires are asking are about temperament and none of the scales are directed at picking up psychopathology. Questionnaire and other clinical data (paper and electronic) will be kept confidential, will be kept secure, and will not be made available to any party other than the research team without the consent of the individual subjects.
- There is no risk associated with the recording of the heart rate variability.
- There is no risk associated with the assessment of the pain threshold with the digital pain probe. As the onset of pain is determined, the discomfort is minimal.
- During the race researchers will be allocated to about 12 stages throughout the race. As the athletes swim, run or cycle past these researchers they will hold up two boards with the scores for *"perception of effort rating"* and *"pain assessment"*. The athletes will be asked to shout out their respective scores as they go past them and these scores will be recorded against the athlete's race number. Data for this component of the study will involve contact with subjects during the race. There is a potential risk that in the process of data collection, the performance of subjects in the race will interfere with. This risk will

be minimal, as the nature of the data collection is such that subjects will only be asked to shout out two numbers as they pass members of the research team at designated points in the race. However, should tri-athletes feel that this affects their performance during the race; they will be free to withdraw from this component of the study. There will be no interference with other race participants during this data collection process.

Potential benefits of this component of the study

- The identification of coping strategies in athletes with regards to pain will help to teach similar coping strategies to patients with chronic pain conditions in order to improve their quality of life.

Component 4: Genetic basis for performance, physiological responses and medical complications during an Ironman Triathlon

This study will be conducted by the UCT/MRC Research Unit for Exercise Science and Sports Medicine at the University of Cape Town in Cape Town, South Africa, in conjunction with the Molecular Genetics Department B and Laboratory of Forensic Genetics of the Cyprus Institute of Neurology and Genetics in Nicosia, Cyprus.

The study involves donate ten millilitres (2 teaspoons) of venous blood and this will be done at one of the pre-race facilities (either in Cape Town, Port Elisabeth, Durban, Bloemfontein or Johannesburg) or at race registration. The sample will be used for the extraction and analysis of genetic material (DNA).

The DNA will only be used for scientific research purposes relating to the genetic basis of (1) athletic ability, (2) physiological response to and (3) medical complaints during ultra-

endurance events. Personal particulars and sporting and medical questionnaires will have to be completed and this information will be treated with the strictest confidentiality and will only be used for scientific research purposes. All data will be analysed anonymously and DNA samples will be destroyed on completion of the study.

Part of the DNA extracted form the donated blood sample will be sent to the Cyprus Institute of Neurology and Genetics in Cyprus for analysis. DNA samples will be shipped to and analysed in Cyprus anonymously. DNA will be genotyped (analysed) for variations (polymorphisms) within genes relating to the genetic basis of athletic ability, physiological response to and (3) medical complaints during ultra-endurance events.

Potential risks of this component of the study

- The completion of personal details, racing, training, equipment use, medical, supplement use, fluid use and lifestyle history questionnaires are not associated with any risk. Completion of self-rated behavioural questionnaires has not previously been shown to be associated with risk. A potential risk is that people who have experienced significant past trauma will find questionnaires on this uncomfortable. The questions within the behavioural questionnaires are asking are about temperament and none of the scales are directed at picking up psychopathology. Questionnaire and other clinical data (paper and electronic) will be kept confidential, will be kept secure, and will not be made available to any party other than the research team without the consent of the individual subjects.
- The potential risks to you during blood collection are minimal and are related to 1) blood sample collection technique, and 2) the volume of blood collected prior to racing and the potential risk of a decreased performance in the race. The potential risks associated with blood collection technique from the ante-cubital veins are: infection, delayed healing, haematoma, physical pain, mental discomfort and injury to a nerve or a vessel. These risks are small and will be minimized by the use of trained phlebotomists, use of sterile

techniques and the use of disposable, single use materials. The risk of decreased performance as a result of blood collection will be reduced by not subjecting any participant to the collection of a blood volume exceeding 15ml prior to the race.

Potential benefits of this component of the study

- There is not direct benefit in participating in this component of the study. The long term anticipated benefits of this component of the research study are to identify genetic factors that may predispose to 1) improved performance or 2) increased risk of medical consequences (such as abnormal electrolyte imbalances). This information will eventually assist tri-athletes in predicting and improving their performance, and decrease their risk of medical complications during participation in triathlon.

Component 5: Neural fatigue following an Ironman Triathlon

The aim of this study is to increase our understanding of the extent of neural processing slowdown/changes and arousal changes that occur in tri-athletes having just completed an exhaustive Ironman Triathlon. Since this component of the study requires completion of a familiarisation test 6 weeks prior to the event, in Newlands, Cape Town, only Cape Town based competitors will be considered for this component.

The way we will test for neural processing changes is by way of a repetitive reaction time cognitive test – a computer generated Stroop test – whereby participants have to respond to the colour of 4 different colour words presented in the centre of the laptop screen. The 4 colour words, red, blue, green and yellow will be presented on the screen in a different colour to what the word says, e.g. red written in blue ink, or green written in yellow. To ensure that participants read the words, 20% of the 4 colour words will be presented in grey – in this case participants have to respond to the word (i.e. not the colour).

Arousal changes will be determined from heart rate variability (HRV) and the electroencephalogram (EEG) power spectrum.

A familiarisation test will be conducted 6 weeks prior to the Ironman in the EEG room at the MRC/UCT Research Unit for Exercise Science and Sports Medicine, which is located at the Sports Science Institute of South Africa. A further pre-event test will be conducted the day before the Ironman during registration in a separate tent; and finally a post-event test will be done within 30 min of completing the Ironman in the same tent.

We will be using a portable Biopac MP150 W System to record the EEG and HRV data. The measurements are completely non-invasive and harmless and will be collected by way of a neoprene scull cap containing 20 electrodes for the EEG data and 3 electrodes attached to both wrists and the left ankle to record HRV data.

The anticipated benefits of this component of the study are that the results will further our understanding of the deterioration of neural processing in athletes completing extreme endurance exercise. If significant deterioration in brain processing is indeed found, strategies can be implemented to combat this, whether by dietary, training or psychological means.

Potential risks of this component of the study

- The completion of a questionnaire is not associated with any risk. Completion of self-rated behavioural questionnaires has not previously been shown to be associated with risk. A potential risk is that people who have experienced significant past trauma will find questionnaires on this uncomfortable. The questions within the behavioural questionnaires are asking are about temperament and none of the scales are directed at picking up psychopathology. Questionnaire and other clinical data (paper and electronic)

will be kept confidential, will be kept secure, and will not be made available to any party other than the research team without the consent of the individual subjects.

- There is no risk associated with the recording of the heart rate variability.
- There is no risk associated with the recording of the Stroop test
- There is no risk associated with the recording of an EEG

Potential benefits of this component of the study

- There is not direct benefit in participating in this component of the study. The long term anticipated benefits of this component of the research study are to identify genetic factors that may predispose to 1) improved performance or 2) increased risk of medical consequences (such as abnormal electrolyte imbalances). This information will eventually assist tri-athletes in predicting and improving their performance, and decrease their risk of medical complications during participation in triathlon.

Component 6: Factors associated with gastro-intestinal (GIT) distress in Ironman triathletes

It is well established that gastrointestinal (GIT) symptoms (nausea, vomiting, abdominal cramps, urge to defecate (passing a stool), diarrhoea or blood in the stool) are common amongst endurance athletes. In a study conducted by our Unit during the 2006 Ironman triathlon about 40% of athletes indicated that they suffered from GIT symptoms. Furthermore, most of the symptoms were lower GIT symptoms (urge to defecate, diarrhoea or blood in the stool). However, we do not yet know the precise causes of these symptoms It is believed that lower GIT symptoms could be related to a decrease in blood flow to the small and large bowel, because blood flow is diverted from the GIT to the working muscle during exercise. Furthermore, dehydration may add to this problem. Other possible mechanisms are dietary

(increased fibre intake), psychological stress, mechanical movement of the bowel (mainly during running) and hormonal (increased secretion of hormones affecting gastro-intestinal motility). In this component of the research project, we wish to identify some of the possible mechanism for these symptoms, so that medical care can be improved.

The main aims of this study is to identify possible aetiological factors that are associated with GIT complaints experienced by the triathletes. More specifically, the following will be measured:

- To establish an association between the development of GIT symptoms during the race and pre-race dietary habits, pre-race emotional stress factors and other medical conditions (past history of surgery, past history of GIT disease, age, gender, training etc.) (obtained through a pre-race questionnaire)
- To establish whether there is a significant difference in the blood flow to the small and large bowel (celiac artery and superior mesenteric artery blood flow immediately pre- and post-exercise and between triathletes who developed GIT symptoms and those who did not develop any GIT symptoms during the race
- To establish whether the athletes with GIT complaints during the race have a higher risk of blood in a post-race stool sample
- To ascertain whether GIT symptoms are associated with dehydration (as measured by changes in pre- post-race body weight)

This study involves the following. You will be contacted prior to the event via email or will be given information at the time of registration. Once you have volunteered, and have given consent to participate, you will be asked to complete a Medical Questionnaire (Appendix). You will also be contacted again two weeks after the race via email and asked to answer another brief medical questionnaire.

At either a designated research centre, or at registration in Port Elizabeth, you will have a Doppler abdominal ultrasound to determine blood flow in your celiac artery (CA) and superior mesenteric artery (SMA) (prior to the race during the registration). This procedure is similar to the ultrasound done in pregnant women to screen for abnormalities in the baby. You will be asked to lie on an examination couch on your back with the abdomen (rib cage to the pubic bone exposed). A gel will be applied to your skin, and the radiologist will move the scanning probe across the skin. This is not associated with any pain or discomfort and the procedure lasts about 5-10 minutes. Your heart rate and brachial artery blood pressure will be obtained at the same time as the ultrasound.

After the race you will be asked to have a repeat ultrasound, immediately on completing the event. Heart rate and brachial artery blood pressure will again be obtained at the same time as the ultrasound.

Stool samples will be obtained from you (should you agree to this part) after the race. This involves collecting a sample from you after the race, in a designated container, which you can hand to the research staff for analysis for traces of blood.

Potential risks of this component of the study

- The completion of the medical questionnaire is not associated with any risk. Questionnaire and other clinical data (paper and electronic) will be kept confidential, will be kept secure, and will not be made available to any party other than the research team without the consent of the individual subjects.
- Abdominal ultrasound: There are no known risks of an abdominal ultrasound in healthy individuals.

Potential benefits of this component of the study

- There is not direct benefit in participating in this component of the study. The long term anticipated benefits of this component of the research study are to identify factors that may cause gastrointestinal symptoms in triathletes. This information may lead to 1) lower risk of developing these symptoms and 2) improved medical care of triathletes that develop these symptoms.

Appendix C

INFORMED CONSENT FORM

I, _____, agree voluntarily to participate in the following components **(DELETE THOSE COMPONENTS YOU DO NOT AGREE TO PARTICIPATE IN)** of the UCT/MRC Research Unit for Exercise Science and Sports Medicine's, University of Cape Town, research project titled:-

1. "A study on the management of the collapsed tri-athlete",
2. "A study to determine the cause of Exercise Associated Muscle Cramping (EAMC)"
3. "A study on the management of pain in triathlon athletes",
4. "A study to determine the genetic basis for performance, physiological responses and medical complications during an Ironman Triathlon"
5. "A study to determine the extent of neural fatigue in athletes immediately post Ironman triathlon"
6. "Factors associated with gastro-intestinal (GIT) distress in Ironman triathletes"

I understand that my participation in this research project has no direct benefits to me during the Ironman 2007 competition. However, I understand that my participation in the research project will advance the medical and scientific knowledge related to endurance sports. Therefore, information gathered through my participation in this project could advance the future medical care, training advice and performance of endurance athletes.

I have read the subject information sheets and the following procedures and concepts have been explained to me in full:

(DELETE THOSE COMPONENTS YOU DO NOT AGREE TO PARTICIPATE IN)

1. **<u>Completion of a questionnaire:</u> (all components)**

   The completion of personal details, racing, training, equipment use, medical, supplement use, fluid use and lifestyle history questionnaires are not associated with any risk. Completion of self-rated behavioural questionnaires has not previously been shown to be associated with risk. A potential risk is that people who have experienced significant past trauma will find questionnaires on this uncomfortable. The questions within the behavioural questionnaires are asking are about temperament and none of the scales are directed at picking up psychopathology. Any personal identification of subjects (names and surnames), questionnaire data and other clinical data (paper and electronic) will be kept confidential, will be kept secure, and will not be made available to any party other than the research team without the consent of the individual subjects.

   I agree that the all the questionnaire information, my performance during the Ironman triathlon, together with all the other data collected from the various components of this trial may be used to answer scientific questions about the medical conditions, physiological responses and measures of performance associated with the participation in and completion of an Ironman triathlon.

2. **<u>Treatment if I collapse after the race:</u> (only for the collapsed athlete component)**

   If I collapse during or after the race I might receive either fluid replacement directly into your vein or oral fluids ad libitum (as much as I want) but according to my post-race blood sodium level. Optimum care will be provided to me according to the current standard of care. Treatment will cease when my laboratory values have returned to normal and I am alert and oriented. I will be transported to the local hospital if my condition requires more urgent medical attention.

3. **<u>Pre- and post-race serum electrolyte (salt) levels and weights</u> (only for the collapsed athlete component)**

I have agreed to donate 5 milliliters (1 teaspoons) of venous blood during registration and immediately after completing the race in the medical facility. The sample will be used to measure my serum electrolyte (blood salt) levels. The potential risks to subjects of blood collection ar I have agreed to donate ten milliliters (2 teaspoons) of venous blood. The sample will be used for the extraction and analysis of genetic material (DNA). mal and are related to 1) blood sample collection technique, and 2) the volume of blood collected prior to racing and the potential risk of a decreased performance in the race. The potential risks associated with blood collection technique from the ante-cubital veins are: infection, delayed healing, haematoma, physical pain, mental discomfort and injury to a nerve or a vessel. These risks are small and will be minimized by the use of trained phlebotomists, use of sterile techniques and the use of disposable, single use materials. The risk of decreased performance as a result of blood collection will be reduced by not subjecting any participant to the collection of a blood volume exceeding 15 ml prior to the race.

Body weight will be measured on the morning before the start of the race and immediately after completing the race in the medical facility using a standard electronic scale, and there is no risk associated with this procedure.

4. **<u>Measurement of heart rate data:</u> (only for the cramps component)**

   This will be done with the subjects own heart rate monitor used during training and racing. The stored files will be emailed to the researcher at the Sports Science Institute, and will be kept confidential.

5. **<u>Score of perceived exertion during the race:</u> (only for the cramps and the management of pain components)**

   During the race researchers will be allocated to about 12 stages throughout the race. As you swim, run or cycle past these researchers they will hold up two boards with the scores for "*perception of effort rating*". You will be asked to shout out your respective scores as you go past them and they will record these scores against your race number. Data for this component of the study will involve contact with subjects during the race. There is a potential risk that in the process of data collection, the performance of subjects in the race will interfere with. This risk will be minimal, as the nature of the data collection is such that subjects will only be asked to shout out two numbers as they pass members of the research team at designated points in the race. However, should tri-athletes feel that this affects their performance during the race; they will be free to withdraw from this component of the study during the race. There will be no interference with other race participants during this data collection process.

6. **<u>Pain during the race:</u> (only for the management of pain components)**

   During the race researchers will be allocated to about 12 stages throughout the race. As you swim, run or cycle past these researchers they will hold up two boards with the scores for *"pain assessment"*. You will be asked to shout out your respective scores as you go past them and they will record these scores against your race number. Data for this component of the study will involve contact with subjects during the race. There is a potential risk that in the process of data collection, the performance of subjects in the race will interfere with. This risk will be minimal, as the nature of the data collection is

such that subjects will only be asked to shout out two numbers as they pass members of the research team at designated points in the race. However, should tri-athletes feel that this affects their performance during the race; they will be free to withdraw from this component of the study during the race. There will be no interference with other race participants during this data collection process.

7. **Recording of heart rate variability during stroop test: (only for the management of pain components)**

   The stroop test is a simple, computer based test. The mental concentration that is required for the test is relevant for the data collection and not the outcome of the test. There is no risk associated with the recording of the heart rate variability

8. **Pain threshold with a digital pain probe: (only for the management of pain components)**

   There is no risk associated with the assessment of the pain threshold with the digital pain probe. As the onset of pain is determined, the discomfort is minimal.

9. **Brain wave measurements: (only for the neural fatigue)**

   There are no potential risks associated with brain wave measurements, since we are merely recording the underlying electric activity generated by the brain and not stimulating the brain in any way. Similarly, there are also no potential risks associated with measuring the electrical activity generated by the heart. There may be some discomfort experienced by the EEG gel needed to increase the conductivity of the electric signal, but no more so than what would be experienced by applyingbhair gel to flatten your hair.

10. **<u>Blood sample collection for genetic studies:</u> (only for the genetics component)**

At one of the pre-race facilities or at race registration, I have agreed to donate ten milliliters (2 teaspoons) of venous blood. The sample will be used for the extraction and analysis of genetic material (DNA).

The potential risks to subjects of blood collection are minimal and are related to 1) blood sample collection technique, and 2) the volume of blood collected prior to racing and the potential risk of a decreased performance in the race. The potential risks associated with blood collection technique from the ante-cubital veins are: infection, delayed healing, haematoma, physical pain, mental discomfort and injury to a nerve or a vessel. These risks are small and will be minimized by the use of trained phlebotomists, use of sterile techniques and the use of disposable, single use materials. The risk of decreased performance as a result of blood collection will be reduced by not subjecting any participant to the collection of a blood volume exceeding 15 ml prior to the race.

The DNA will only be used for scientific research purposes relating to the genetic basis of (1) athletic ability, (2) physiological response to (3) medical complications during ultra-endurance events. I have also agreed to complete personal particulars, training, sporting, measures of behavioural endophenotypes and medical questionnaires and understand that all the information that is collected during the study will be treated with the strictest confidentiality and will only be used for scientific research purposes. Questionnaire and other clinical data (paper and electronic) will be kept confidential, will be kept secure, and will not be made available to any party other than the research team without the consent of the individual subjects. I also understand that all data will be analysed anonymously and my DNA sample will be destroyed on completion of the study.

I understand that some of the DNA extracted form the donated blood sample will be sent to the Cyprus Institute of Neurology and Genetics in Cyprus for analysis. I understand that the DNA samples will be shipped to and analysed in Cyprus anonymously. I understand that the DNA will be genotyped (analysed) for variations (polymorphisms) within genes relating to the genetic basis of athletic ability, tendon and ligament overuse injuries and dysnatraemia during ultra-endurance events only.

I understand that whilst there is no direct benefit to myself, if a genetic predisposition for (1) athletic ability, (2) physiological response to and (3) medical complications during ultra-endurance events can be established, then future generations will be able to establish their risk for this condition. This may allow better prevention and treatment options in the future. I understand that I will receive the overall results of the study.

I have read (or, where appropriate, have had read to me) and understood the information about this study, and any questions I have asked have been answered to my satisfaction. I agree to participate in the study, realising that I have the right to request that my DNA sample be destroyed at anytime. I agree that research data provided by me or with my permission during the project may be included in a thesis, presented at conferences and published in journals on the condition that neither my name nor any other identifying information is used.

11. <u>Abdominal ultrasound to determine blood flow to the abdominal organs</u> (only for the GIT component)

I agree to having a pre-and post-race abdominal ultrasound to measure the blood flow to my abdominal organs.

I have read the preceding subject information sheet and understand the testing procedures outlined therein. I understand any accompanying risks and discomforts. Knowing these risks

and discomforts and having had the opportunity to pose questions answered to my satisfaction, I hereby consent to participate in this study. I understand that I may withdraw from this study at any time without further question. I have been informed that the individual data derived from my participation in these protocols will remain confidential. I understand that the medical staff and the research team have professional medical insurance.

Name of the tri-athlete: _____

Signature of tri-athlete _____

Date: _____

Name of investigator: _____Prof Martin Schwellnus____

Signature of Investigator: _____

Date: _____ _____

Appendix D

Department of Human Biology

UCT/MRC Research Unit for Exercise Science & Sports Medicine
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2006 IRONMAN – MEDICAL AND TRAINING QUESTIONNAIRES

These questionnaires have been constructed by the Medical Research team, in conjunction with the Medical Director of the Ironman 2006. The information obtained from these questionnaires is essential for the planning of medical care during events such as the Ironman 2006. We acknowledge that the questionnaires are long, but we are asking about 20 minutes of your valuable time to complete them. The completion of the questionnaires is voluntary, all the information will be kept confidential and will only be used for research and medical care planning purposes. We suggest that you consider completing this before the event, or at the time of registration.

Prof Martin Schwellnus (Chairman, Research Team)
Dr Peter Schwartz (Medical Director, Ironman 2006)

Instructions

You can either complete the questionnaires electronically using Microsoft word or print the questionnaires and complete them manually. Please answer each question by filling in the details in the allocated space or checking one or more of the option boxes.

If you complete the questionnaire electronically using Microsoft word, please e-mail the completed forms to ironman@sports.uct.ac.za and bring the signed consent form to the research table at race registration.

If you complete the questionnaire manually, please bring the completed forms together with the signed consent form to the research table at race registration.

Please complete sections A, B, C, D and E

Please complete only the relevant questions in the following section

TPQ / TCI (96 shared items)		
1. I usually am confident that everything will go ell, even in situations that worry most people.	True☐	False☐
2. I often try new things just for fun or thrills, even if most people think it is a waste of time.	True☐	False☐
3. I like to discuss my experiences and feelings openly with friends instead of keeping them to myself.	True☐	False☐
4. When nothing new is happening, I usually start looking for something that is thrilling or exciting.	True☐	False☐
5. Usually I am more worried about that most people that something might go wrong in the future.	True☐	False☐
6. I don't mind discussing my personal problems with people whom I have known briefly or slightly.	True☐	False☐
7. I would like to have warm and close friends with me most of the time.	True☐	False☐
8. I nearly always stay relaxed and carefree even when nearly everyone else is fearful.	True☐	False☐
9. I usually demand very good practical reasons before I am willing to change my old ways of doing things.	True☐	False☐
10. I often have to stop what I am doing because I start worrying that something might go wrong.	True☐	False☐
11. I hate to change the way I do things, even if many people tell me there is a new and better way to do it.	True☐	False☐
12. My friends find it hard to know my feelings because I seldom tell them about my private thoughts.	True☐	False☐
13. I like it when people can do exactly what they want without strict rules and regulations.	True☐	False☐
14. I often stop what I am doing because I get worried, even when my friends tell me everything will go well.	True☐	False☐
15. It wouldn't bother me to be alone all the time.	True☐	False☐
16. I like to be very organized and set up rules for people whenever I can.	True☐	False☐
17. I usually do things my own way, rather than giving in to the wishes of other people.	True☐	False☐
18. I usually feel tense and worried when I have to do something new and unfamiliar.	True☐	False☐
19. I often feel tense and worried in familiar situations, even when others feel there is little to worry about.	True☐	False☐
20. Other people often think that I am too independent because I won't so what they want.	True☐	False☐
21. Even when most people feel it is not important, I often insist on things being done in a strict and orderly way.	True☐	False☐
22. I often do things based on how I feel at the moment, without thinking about how they are done in the past.	True☐	False☐
23. I often feel tense and worried in unfamiliar situations, even when others feel there is no danger at all.	True☐	False☐
24. I often brake rules and regulations when I think I can get away with it.	True☐	False☐
25. I don't care very much whether other people like me or the way I do things.	True☐	False☐
26. I usually stay calm and secure in situations that most people would find physically dangerous.	True☐	False☐
27. I feel it is more important to be sympathetic and understanding of other people than to be practical and tough- minded.	True☐	False☐
28. I lose my temper more quickly than most people.	True☐	False☐
29. I am usually confident that I can easily do things that most people would consider dangerous (such as driving as automobile fast on a wet or icy road).	True☐	False☐

30. I often react so strongly to unexpected news that I say or do things that I regret.	True☐	False☐
31. People find it easy to come to me for help, sympathy, and warm understanding.	True☐	False☐
32. I am much more reserved and controlled than most people.	True☐	False☐
33. When I have to meet a group of strangers, I am more shy than most people.	True☐	False☐
34. I am strongly moved by sentimental appeals (like when asked to helped crippled people).	True☐	False☐
35. I almost never get so excited that I lose control of myself.	True☐	False☐
36. I have a reputation as someone who is practical and does not act on emotion.	True☐	False☐
37. I often avoid meeting strangers because I lack confidence with people I do not know.	True☐	False☐
38. I usually stay away from social situations where I would have to meet strangers, even if I am assured that they will be friendly.	True☐	False☐
39. I usually push myself harder than most people do because I want to do as well as I possibly can.	True☐	False☐
40. I often push myself to the point of exhaustion or try to do more than I really can.	True☐	False☐
41. I would probably stay relaxed and outgoing when meeting a group of strangers, even if I were told they were unfriendly.	True☐	False☐
42. It is difficult for me to keep the same interests for a long time because my attention often shifts to something else.	True☐	False☐
43. I think I would stay confident and relaxed when meeting strangers, even if I were told they are angry with me.	True☐	False☐
44. I could probably accomplish more than I do, but I don't see the point of pushing myself harder than is necessary to get by.	True☐	False☐
45. I like to think about things for a long time before I make a decision.	True☐	False☐
46. Most of the time I would prefer to do something a little risky (like riding in an automobile over steep hills and sharp turns), rather than having to stay quiet and inactive for a few hours.	True☐	False☐
47. I often follow my instincts, hunches, or intuition without thinking through all the details.	True☐	False☐
48. I try to do as little work as possible, even when other people expect more of me.	True☐	False☐
49. I often have to change my decisions because I had a wrong hunch or mistaken first impression.	True☐	False☐
50. Most of the time I would prefer to so something risky (like hang-gliding or parachute jumping(, rather than having to stay quiet and inactive for a few hours.	True☐	False☐
51. I am satisfied with my accomplishments and have little desire to do better.	True☐	False☐
52. I see no point in continuing to work on something unless there is a good chance of success.	True☐	False☐
53. I have less energy and get tired more quickly than most people.	True☐	False☐
54. I usually think about all the facts in detail before I make a decision.	True☐	False☐
55. I nearly always think about all the facts in detail before I make a decision, even when other people demand a quick decision.	True☐	False☐
56. I often need naps or extra rest periods because I get tired so easily.	True☐	False☐
57. I don't go out of my way to please other people.	True☐	False☐
58. I am more energetic and tire less quickly than most people.	True☐	False☐
59. I am usually able to get other people to believe me, even when I know that what I am saying is exaggerated or untrue.	True☐	False☐
60. I can usually do a good job of stretching the truth to tell a funnier story or to play a joke on someone.	True☐	False☐
61. I usually can stay "on the go" all day without having to push myself.	True☐	False☐

62. I am usually more upset than most people by the loss of a close friend.	True ☐	False ☐
63. I have trouble telling a lie, even when it is meant to spare someone else's feelings.	True ☐	False ☐
64. I am better at saving money than most people.	True ☐	False ☐
65. Even after there are problems in a friendship, I nearly always try to keep it going anyway.	True ☐	False ☐
66. I recover more slowly than most people from minor illnesses or stress.	True ☐	False ☐
67. I need much extra rest, support, or reassurance to recover from minor illnesses or stress.	True ☐	False ☐
68. I often spend money until I run out of cash or get into debt from using too much credit.	True ☐	False ☐
69. Because I so often spend too much money on impulse, it is hard for me to save money, even for special plans like a vacation.	True ☐	False ☐
70. It is extremely difficult for me to adjust to changes in my usual way of doing things because I get so tense, tired or worried.	True ☐	False ☐
71. If I am feeling upset, I usually feel better around friends than when left alone.	True ☐	False ☐
72. I usually feel much more confident and energetic than most people, even after minor illnesses or stress.	True ☐	False ☐
73. Some people think I am too stingy or tight with my money.	True ☐	False ☐
74. I often keep trying the same thing over and over again, even when I have not had success in a long time.	True ☐	False ☐
75. It is hard for me to enjoy spending money on myself, even when I have saved plenty of money.	True ☐	False ☐
76. I recover more quickly than most people from minor illnesses or stress.	True ☐	False ☐
77. I hate to make decisions based only on my first impressions.	True ☐	False ☐
78. I think I will have very good luck in the future.	True ☐	False ☐
79. I am most often moved deeply by fine speech or poetry.	True ☐	False ☐
80. If I am embarassed or humiliated, I get over it very quickly.	True ☐	False ☐
81. I like old "tried and true" ways of doing things according to their priority of importance to me because of lack of time.	True ☐	False ☐
82. I like to keep my problems to myself.	True ☐	False ☐
83. I enjoy saving money more than spending it on entertainment or thrills.	True ☐	False ☐
84. Even when I am with friends, I prefer not to "open up" very much.	True ☐	False ☐
85. I feel very confident and sure of myself in almost all social situations.	True ☐	False ☐
86. I usually like to stay cool and detached from other people.	True ☐	False ☐
87. I never worry about terrible things that might happen in the future.	True ☐	False ☐
88. I am more hard-working than most people.	True ☐	False ☐
89. In conversations I am much better as a listener than as a talker.	True ☐	False ☐
90. I like to please other people as much as I can.	True ☐	False ☐
91. Regardless of any temporary problem that I have to overcome, I always think it will turn out well.	True ☐	False ☐
92. I like to stay at home better than to travel and explore new places.	True ☐	False ☐
93. I am usually so determined that I continue to work long after other people have given up.	True ☐	False ☐
94. I usually have good luck in whatever I try to do.	True ☐	False ☐
95. I like to pay close attention to details in everything I do.	True ☐	False ☐
96. It is easy for me to organize my thoughts while talking to someone.	True ☐	False ☐

K10					
Instructions: The following questions ask about how you have been feeling during the **past four weeks**. For each question, please circle the number that best describes how often you have had this feeling. Your answers will be kept confidential.					
In the past four weeks:	**None of the time**	**A little of the time**	**Sometime of the time**	**Most of the time**	**All of the time**
1. About how often did you feel tired of for no good reason?	1	2	3	4	5
2. About how often did you feel nervous?	1	2	3	4	5
3.About how often did you feel so nervous that nothing could calm you down?	1	2	3	4	5
4. About how often did you feel hopeless?	1	2	3	4	5
5. About how often did you feel restless or fidgety?	1	2	3	4	5
6. About how often did you feel restless you could not sit still?	1	2	3	4	5
7. About how often did you feel depressed?	1	2	3	4	5
8. About how often did you feel that everything is an effort?	1	2	3	4	5
9. About how often did you feel so sad that nothing could cheer you up?	1	2	3	4	5
10. About how often did you feel worthless?	1	2	3	4	5

Section E. Family medical history		
Have any of your blood (biological) relatives ever had the following? Please tick yes or no. If yes, please tick the relationship of that person to you (You may tick more than one of the relationship blocks).		
Description		**If Yes, please indicate the relationship**
Exercise associated muscle cramps	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Night muscle cramps	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Chronic Achilles tendon injury	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Achilles tendon rupture	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Any ligament injury	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Asthma	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Allergies (in general)	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Heart Disease	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Diabetes	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Depression, Anxiety attacks, Personality disorder	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother
Gastro-intestinal (GIT) disease	Yes ☐ No ☐	☐ Father ☐ Mother ☐ Brother ☐ Sister ☐ Child ☐ Grandfather ☐ Grandmother

Section F. Personal general medical history	
In this section, you are asked to read through 14 questions about your personal general medical history. If you answer "yes" to any of questions 1 to 12, please complete the additional questions at the end of the section (section G on page 18).	
1. In the **6 weeks before this race** (from 1st February) did you suffer from any **symptoms of flu** (fever, sore throat, blocked or runny nose, cough, wheeze, muscle aches and pains)?	Yes ☐ No ☐
2. Have you **ever** in triathlon career suffered from **muscle cramping** (painful, spontaneous, sustained spasm of a muscle) during or immediately (within 6 hours) after exercise (in training or competition)?	Yes ☐ No ☐
3. Have you **ever** in your triathlon career suffered from **a tendon or ligament injury** (pain, swelling, stiffness) in any tendon (including Achilles tendon, knee tendons, and shoulder tendons) or ligaments (partial or complete tear)?	Yes ☐ No ☐
4. Have you **ever** in your triathlon career **used medicines to treat injuries** in the week **before or during a race** – including anti-inflammatory drugs, cortisone (pills, or injection), or pain killers?	Yes ☐ No ☐
5. Have you **ever** in your triathlon career suffered **gastrointestinal** symptoms **during exercise** including heartburn, nausea, vomiting, abdominal pain, urge to defecate (pass a stool), diarrhoea, or blood in the stools?	Yes ☐ No ☐
6. Have you **ever** in your triathlon career suffered from symptoms of the **nervous system** including exercise induced headaches, nerve tingling or loss of sensation?	Yes ☐ No ☐
7. Have you **ever** in your triathlon or cycling career (in particular with **cycling**) suffered from **injury to the genital area** including genital numbness after cycling, genital pain after cycling, genital swelling or altered sexual function after cycling?	Yes ☐ No ☐
8. Have you **ever** in your triathlon career suffered from **symptoms of allergies** including nose allergies (hay fever), allergic sinusitis, allergic asthma, skin allergies, a past history of allergies to medication, plant material or animal material?	Yes ☐ No ☐
9. Do you **currently suffer from asthma** including exercise induced asthma, or symptoms of asthma such as shortness of breath, wheezing, or chronic coughing?	Yes ☐ No ☐
10. Have you ever **collapsed** (fell down **not because of an accident**, needing medical attention) during, at the finish or after a race or training session?	Yes ☐ No ☐
11. Do you **currently** suffer from any **symptoms of injury** in the muscles, tendons, bones, ligaments or joints?	Yes ☐ No ☐
12. Do you **currently**, or did you **in the last year**, suffer from any symptoms of **exercise related skin disease**?	Sunburn: Yes ☐ No ☐ Skin cancer: Yes ☐ No ☐ Other skin damage resulting sun exposure: Yes ☐ No ☐

13. Please tick in which anatomical area you ever had **surgery** performed.	☐ Gastric (stomach) ☐ Oesophageal (swallowing pipe) ☐ Small bowel ☐ Large bowel (colon) ☐ Rectum ☐ Gallbladder ☐ Pancreas ☐ Liver ☐ Abdomen (general) ☐ Wrist ☐ Head ☐ Finger ☐ Neck ☐ Lower back ☐ Face ☐ Hip ☐ Front chest ☐ Thigh ☐ Back chest ☐ Knee ☐ Shoulder ☐ Lower leg ☐ Upper arm ☐ Achilles ☐ Elbow ☐ Ankle ☐ Forearm ☐ Foot ☐ Other (Specify: _____)
14 Management of pain during the last 3 months	
14a. Did you alter or stop your training schedule due to pain in any part of your body?	Yes ☐ No ☐
If yes: For how long	_____ days
Did you adapt your training schedule for a while when your injury/illness was healed?	Yes ☐ No ☐
14b. How do you feel when you experience pain? (you can tick more than one option)	☐ It does not bother me much ☐ Angry ☐ Frustrated ☐ Depressed ☐ Resentful ☐ Overwhelmed
14c. When you experience pain, do you? (you can tick more than one option)	☐ Adjust your training schedule ☐ Stop training ☐ Slowly get "back on track" of your training schedule ☐ Train harder to make up for the missed training sessions ☐ Ignore the pain and continue to train ☐ Feel scared to do anything that could aggravate the pain ☐ Think that the pain means that you have a severe injury ☐ Tell everybody about it
15. **Female athletes only:** Please complete the following questions (14a. to 14g.) related to your menstrual cycle and other gynaecological history	
15a. At what age did you start your periods (menstruating)?	(years)
15b. In the last 12 months, how many menstrual cycles did you have?	
15c. Have you ever had irregular menstrual periods in the past? (excluding pregnancy)?	Yes ☐ No ☐

15d. Have you had a hysterectomy/ovarectomy?	Yes ☐ No ☐
15e. How many times have you been pregnant?	(times)
15f. What form of contraception are you currently using?	☐ None ☐ Oral contraceptive pill ☐ Injection ☐ Intra-uterine device ☐ Sterilization (tubes tied) ☐ Other: _____
15g. If yes to question 15f. above, for oral contraceptive pill, for what reason was the pill prescribed?	☐ Not applicable ☐ Dermatological ☐ Contraception ☐ Regulate period ☐ Other: _____

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE

If you have answered **YES** to any of the first 11 questions of the Personal General Medical History questionnaire (section F) please complete the relevant additional questions that follow in section G.

Please bring the completed forms together with the signed consent form to the pre-race facility or the research table at race registration.

Section G. Additional detailed medical history

(Please complete all the sections to which you answered "Yes" in the Personal general medical history)

1. Flu symptoms in the last 6 weeks

If you answered **YES** to **question 1** in section F, please complete the following two questions related to flu symptoms in the last 6 weeks.

(1a) Please tick which of these flu symptoms you suffered from **in the last 6 weeks**.	☐ Fever ☐ Cough ☐ Joint pains ☐ Blocked nose ☐ Wheezing ☐ Sore Throat ☐ Runny nose ☐ Muscle aches ☐ Any other flu symptoms (Specify: _____)
(1b) Please tick which of these flu symptoms you suffered from **in the last 7 days**.	☐ Fever ☐ Cough ☐ Joint pains ☐ Blocked nose ☐ Wheezing ☐ Sore Throat ☐ Runny nose ☐ Muscle aches ☐ Any other flu symptoms (Specify: _____)

2. Muscle cramping

If you answered **YES** to **question 2** in section F, please complete the following questions (2a. to 2m.) related to your cramping.

(2a) For how many years have you suffered from cramping?	(years)
(2b) Did you suffer from cramping during or after exercise in the **last 12 months**?	Yes ☐ No ☐
(2c) With what **type of exercise** is your cramping associated (You can tick more than one form of exercise)?	☐ Swimming ☐ Cycling ☐ Running
(2d) In the **last 10 races or training sessions**, how many times have you experienced cramping?	Races: ____/10 Training sessions: ____/10
(2e) What treatment/s have you had that **successfully relieved** an acute cramp? (can tick more than one)	☐ Stretching ☐ Resting ☐ Drinking fluid ☐ Ice application ☐ Massage ☐ Magnesium ☐ Salt (tablets or solution) ☐ Other (Specify: _____)
(2f) At **what point in the race or training run** do you usually first experience cramping?	☐ First quarter ☐ Second quarter ☐ Third quarter ☐ Fourth quarter ☐ After the race ☐ No pattern
(2g) In which **muscles** do you usually cramp (please list the muscle by the one which cramps most frequently (as 1) and the others after that (2-4)?	☐ Calves ☐ Hamstrings ☐ Quadriceps (thigh) ☐ Foot muscles ☐ Other (Specify: _____)
(2h) Have you **ever** suffered from cramping in your **whole body** (arms and legs)?	Yes ☐ No ☐
(2i) Have you **ever** been **admitted to hospital** following cramping?	Yes ☐ No ☐
(2j) Have you **ever** been **confused or in a coma** during or after a cramping episode?	Yes ☐ No ☐
(2k) Have you ever had **"dark urine"** in the 3 days following a cramping episode?	Yes ☐ No ☐
(2l) If you cramp, **how long** does the cramp usually last for (min)?	(minutes)
(2m) If you cramp, how **severe** is the cramp usually? (please tick)	☐ Mild: < 5 minutes and you are able to continue exercising ☐ Moderate: 5-15 minutes and you are able to continue exercising ☐ Severe: >15 minutes or if you have to STOP exercising

3. Past Tendon and Ligament Injury History

If you answered **YES** to **question 3** in section F, please complete the following questions (3a. to 3d.) related to your past history of tendon/ligament injury/ies.

(3a) Please tick which **tendon/s** you have injured? (next column on the tright)

Also indicate (tick) if your injured tendon was longsatnding pain (tendinopathy) or an acute tear/rupture

Tendon		Longstanding Pain (Tendinopathy)	Acute Tear/ Rupture
Foot and ankle:	☐ Achilles tendon	☐	☐
	☐ Tibialis posterior	☐	☐
	☐ Plantar fascia	☐	☐
Knee:	☐ Patellar tendon	☐	☐
Elbow and wrist:	☐ Wrist extensor tendon	☐	☐
Shoulder:	☐ Rotator cuff	☐	☐
Other _____		☐	☐

(3b) Please tick which **ligament/s** you have injured? (next column on the tright)

Also indicate if your sprained or completely tore the ligamant

Ligament	Sprain	Complete Tear
☐ Shoulder ligaments	☐	☐
☐ Elbow ligaments	☐	☐
☐ Wrist ligaments	☐	☐
☐ Finger ligaments	☐	☐
☐ Knee (ACL)	☐	☐
☐ Knee (MCL)	☐	☐
☐ Knee (PCL)	☐	☐
☐ Knee (LCL)	☐	☐
☐ Ankle lateral ligaments	☐	☐
☐ Ankle medial ligaments	☐	☐
☐ Spinal ligaments	☐	☐
☐ Other:	☐	☐

(3c) Please tick if you have you ever suffered from any of the following **joint capsule** injuries?

☐ Acute shoulder dislocation
☐ Chronic shoulder instability
☐ Other: _____

(3d) Do you suffer from any other **connective tissue or rheumatological diseases** or disorders? (If yes, please specify which one)

Yes ☐ No ☐ (refer to the list on the next page)
(If yes, specify: _____)

List of some Connective Tissue and/or Rheumatic Diseases and Disorders

Ankylosing Spondylitis	Lipid Storage Diseases	Pseudogout
Aspartylglycosaminuria (AGU)	Marfan Syndrome	Reactive Arthritis
Behcet's Syndrome	Menkes Kinky Hair Syndrome	Reiter's Syndrome
Crohn's Disease	Mucopolysaccharidoses	Relapsing Polychrondritis
Discoid Lupus Erythematosus	Myopathies and Dystrophies	Scleroderma
Ehlers-Danlos syndrome (EDS)	Ochronosis (Homocystinuria)	Sjogren's Syndrome
Eosinophilic Fascitis	Osteogenesis imperfecta (OI)	Systemic Lupus Erythematosus (SLE)
Giant Cell (Temporal) Arthritis	Polyarteritis Nodosa	Systemic Sclerosis
Gout	Polymyalgia Rheumatica	Wegener's Granulomatosis
Hypersentive Vasulatis	Polymyositis & Dermatomyositis	

4. Use of medicines to treat an injury before or during participation If you answered **YES** to **question 4** in section F, please complete the following two questions related to medicine use for injuries before or during races.	
(4a) Which of the following medicines have you used in the past to treat an injury **in the week just before** a race?	☐ Paracetamol (e.g. Panado, Tylenol) ☐ Non-steroidal anti-inflammatories (e.g. Voltaren, Cataflam) ☐ Cortisone (pills) ☐ Cortisone injection ☐ Codeine ☐ Anti-inflammatory gels/creams/patches ☐ Any other pain killers (Specify: _____)
(4b) Which of the following medicines have you used in the past to treat an injury **during a race**?	☐ Paracetamol (e.g. Panado, Tylenol) ☐ Non-steroidal anti-inflammatories (e.g. Voltaren, Cataflam) ☐ Cortisone (pills) ☐ Cortisone injection ☐ Codeine ☐ Anti-inflammatory gels/creams/patches ☐ Any other pain killers (Specify: _____)

5. Gastrointestinal symptoms during exercise

If you answered **YES** to **question 5** in section F, please indicate which gastrointestinal symptoms you have ever suffered from **during exercise** and, how frequently (in the last 12 months and in the last 10 races), and in which type of exercise.

Symptom	Number of times you experienced the GIT symptom in the last 12 months **(during exercise)**	Number of times you experienced the GIT symptom in the last 10 races **(during races)**	Please indicate which **type of exercise** is mostly associated with the GIT symptom	Please indicate the "**severity**" **of the GIT symptom** during exercise
Nausea			☐ Swimming ☐ Cycling ☐ Running	☐ Does not affect training or racing ☐ Affects training/racing (slow down or reduce time) ☐ Prevents training/racing
Vomiting			☐ Swimming ☐ Cycling ☐ Running	☐ Does not affect training or racing ☐ Affects training/racing (slow down or reduce time) ☐ Prevents training/racing
Heartburn			☐ Swimming ☐ Cycling ☐ Running	☐ Does not affect training or racing ☐ Affects training/racing (slow down or reduce time) ☐ Prevents training/racing
Abdominal pain			☐ Swimming ☐ Cycling ☐ Running	☐ Does not affect training or racing ☐ Affects training/racing (slow down or reduce time) ☐ Prevents training/racing
Urge to pass a stool (defecate)			☐ Swimming ☐ Cycling ☐ Running	☐ Does not affect training or racing ☐ Affects training/racing (slow down or reduce time) ☐ Prevents training/racing
Diarrhoea			☐ Swimming ☐ Cycling ☐ Running	☐ Does not affect training or racing ☐ Affects training/racing (slow down or reduce time) ☐ Prevents training/racing
Passing blood in the stool			☐ Swimming ☐ Cycling ☐ Running	☐ Does not affect training or racing ☐ Affects training/racing (slow down or reduce time) ☐ Prevents training/racing
Please indicate if you previously suffered from or had any of the following (you may tick more than one)?				☐ History of heartburn ☐ Gastroscopy ☐ Ulcer (gastric, duodenal) ☐ Irritable bowel syndrome ☐ Allergy to milk products ☐ Other past history of GIT disease

6. Diseases of the nervous system

If you answered **YES** to **question 6** in section F, please indicate which nervous disease symptoms you have ever suffered from **during exercise** and, how frequently (in the last 12 months and in the last 10 races), and in which type of exercise.

Symptom	Number of times in the last 12 months **(during exercise)**	Number of times in last 10 races **(during races)**	Tick type of exercise
Headaches			☐ Swimming, ☐ Cycling, ☐ Running
Nerve tingling in the hands			☐ Swimming, ☐ Cycling, ☐ Running
Loss of sensation in the hands			☐ Swimming, ☐ Cycling, ☐ Running

7. Genital tract injury during cycling

If you answered **YES** to **question 7** in section F, please indicate which symptoms of genital tract injury have you suffered from **during or after cycling**, how frequently (in the last 10 sessions), how long symptoms last, and what factors prevent or relieve symptoms?

Symptom	Number of times in the last 10 cycling sessions	Please indicate when the symptoms occur	Please indicate if any of the following reduce or prevent the symptoms (can tick more than one)
Genital numbness		☐ Only during cycling ☐ During and up to 1 hour after cycling ☐ During and 1-24 hours after cycling ☐ During and > 24 hours after cycling	☐ Changing the saddle type ☐ Changing the saddle position ☐ Using padded cycling shorts ☐ Wearing no underwear ☐ Wearing additional underwear ☐ Other (Specify: _____)
Genital pain		☐ Only during cycling ☐ During and up to 1 hour after cycling ☐ During and 1-24 hours after cycling ☐ During and > 24 hours after cycling	☐ Changing the saddle type ☐ Changing the saddle position ☐ Using padded cycling shorts ☐ Wearing no underwear ☐ Wearing additional underwear ☐ Other (Specify: _____)
Genital bruising		☐ Only during cycling ☐ During and up to 1 hour after cycling ☐ During and 1-24 hours after cycling ☐ During and > 24 hours after cycling	☐ Changing the saddle type ☐ Changing the saddle position ☐ Using padded cycling shorts ☐ Wearing no underwear ☐ Wearing additional underwear ☐ Other (Specify: _____)
Altered sexual function following a cycling session		☐ Up to 1 hour after cycling ☐ 1-24 hours after cycling ☐ > 24 hours after cycling	☐ Changing the saddle type ☐ Changing the saddle position ☐ Using padded cycling shorts ☐ Wearing no underwear ☐ Wearing additional underwear ☐ Other (Specify: _____)

8. Allergy history

If you answered **YES** to **question 8** in section F, please complete the following questions (8a. to 8e.) related to your current and past history of allergies.

(8a) Please indicate how long (years) have you been suffering from allergies?					years
(8b) Please tick which type of allergy do you currently suffer from					
Nose (hay fever)	Yes ☐ No ☐	Sinusitis	Yes ☐ No ☐	Asthma (allergic)	Yes ☐ No ☐
Skin allergies	Yes ☐ No ☐	Eye allergies	Yes ☐ No ☐	Allergy to plant material	Yes ☐ No ☐
Allergy to foods	Yes ☐ No ☐	Allergy to animals	Yes ☐ No ☐	Allergy to medication	Yes ☐ No ☐
(8c) Please tick which type of allergy do you currently take medication for					
Nose (hay fever)	Yes ☐ No ☐	Sinusitis	Yes ☐ No ☐	Asthma (allergic)	Yes ☐ No ☐
Skin allergies	Yes ☐ No ☐	Eye allergies	Yes ☐ No ☐	Allergy to plant material	Yes ☐ No ☐
Allergy to foods	Yes ☐ No ☐	Allergy to animals	Yes ☐ No ☐	Allergy to medication	Yes ☐ No ☐
(8d) Please tick which type of medication do you currently take					
Cortisone nose spray	Yes ☐ No ☐	Cortisone nose inhaler	Yes ☐ No ☐	Anti-histamine tablets	Yes ☐ No ☐
Cortisone cream	Yes ☐ No ☐	Anti-histamine cream	Yes ☐ No ☐	Other inhaler / tablets or cream	Yes ☐ No ☐
(8e) Please tick which symptoms of allergy do you currently suffer from					
Sneezing	Yes ☐ No ☐	Itchy runny nose	Yes ☐ No ☐	Headache	Yes ☐ No ☐
Itchy palate	Yes ☐ No ☐	Streaming eyes	Yes ☐ No ☐	Fatigue	Yes ☐ No ☐
Itchy eyes	Yes ☐ No ☐	Blocked nose	Yes ☐ No ☐	Poor sleep	Yes ☐ No ☐
Post nasal drip	Yes ☐ No ☐	Coughing	Yes ☐ No ☐	Wheezing	Yes ☐ No ☐
In which months of the year do you currently have symptoms of allergies? (You tick more than one)	☐ Jan ☐ Feb ☐ March ☐ April ☐ May ☐ June ☐ July ☐ Aug ☐ Sept ☐ Oct ☐ Nov ☐ Dec				
(8f) Please tick which type of allergy did you suffer from in the past (NOT currently)					
Nose (hay fever)	Yes ☐ No ☐	Sinusitis	Yes ☐ No ☐	Asthma (allergic)	Yes ☐ No ☐
Skin allergies	Yes ☐ No ☐	Eye allergies	Yes ☐ No ☐	Allergy to plant material	Yes ☐ No ☐
Allergy to foods	Yes ☐ No ☐	Allergy to animals	Yes ☐ No ☐	Allergy to medication	Yes ☐ No ☐

9. Asthma history

If you answered **YES** to **question 9** in section F, please complete the following questions (9a. to 9k.) related to your current history of asthma

(9a) Do you currently suffer from asthma?	Yes ☐ No ☐
(9b) How many years have you suffered from asthma?	(years)
(9c) How was your asthma diagnosed?	☐ A doctor taking a history and performing an examination ☐ Lung function test (blow test) but no exercise ☐ Lung function test (blow test) before and after exercise ☐ Metacholine challenge test ☐ Eucapnic hyperventilation test (rebreathing test) ☐ Other test (Specify: _____)
(9d) Which **type of asthma** do you currently suffer from?	☐ Asthma that occurs at any time but not during exercise ☐ Asthma that occurs at any time including during exercise ☐ Asthma that only occurs during exercise
(9e) Please indicate **how frequently do you currently experience the symptoms** of asthma (shortness of breath, wheezing, coughing or coughing after exercise)?	**Daytime symptoms (per week)** ☐ < 2 / week ☐ 2-4 / week ☐ >4 / week ☐ All the time **Night time symptoms (per month)** ☐ < 1 / month ☐ 2-3 / month ☐ ≥4 / month ☐ All the time **Exercise related symptoms (per 10 exercise sessions)** ☐ <1 per 10 sessions ☐ 2-3 per 10 sessions ☐ ≥4 per 10 sessions
(9f) Please indicate if you had symptoms of asthma that were severe enough to necessitate **hospital admission in the last 12 months**	☐ No hospital admission for asthma in the last 12 months ☐ 1-2 hospital admissions for asthma in the last 12 months ☐ 3-4 hospital admissions for asthma in the last 12 months ☐ >4 hospital admissions for asthma in the last 12 months
(9g) Which **symptoms of asthma** do you currently suffer from?	☐ Wheezing ☐ Dry cough ☐ Shortness of breath ☐ Tight chest ☐ Chest pain ☐ Other (Specify: _____)

(9h) What **medication do you currently use** for your asthma? (you may tick more than one option)	☐ Cortisone inhaler (e.g. Beclate, Becloforte, Becodisks, Becotide, Budeflam, Flixotide, Inflammide, Pulmicort, Qvar, etc) ☐ Salbutamol (bronchodilator) inhaler (e.g. Ventolin, Venteze, Vomax, Airomir, Asthavent etc.) ☐ Salmeterol (bronchodilator) inhaler (Serevent) ☐ Fenoterol (bronchodilator) inhaler (Berotec) ☐ Terbutaline (bronchodilator) inhaler (Bricanyl) ☐ Formoterol (bronchodilator) inhaler (e.g. Foradil, Foratec, Oxis) ☐ Ipratropium (bronchodilator) inhaler (Atrovent) ☐ Tiotropium (bronchodilator) inhaler (Spiriva) ☐ Combined cortisone and bronchodilator inhaler (e.g. Atrovent, Berodual, Combivent, Duolin, Duovent, Seretide, Symbicord) ☐ Cortisone tablets ☐ Bronchodilator tablets ☐ Leukotriene receptor antagonist tablets (e.g. Acccolate, Singulair) ☐ Other inhaler ☐ Other medication (Specify: _____)
(9i) **When do you use your medication** for your asthma?	☐ Daily (irrespective of exercise) ☐ Only before exercise ☐ Other (Specify: _____)
(9j) **How long before an exercise session** do you use your medication for asthma?	min
(9k) Have you obtained **TUE (therapeutic use exemption forms)** for your asthma medication?	Yes ☐ No ☐

10. History of previous collapse If you answered **YES** to **question 10** in section F, please complete the following questions (10a. to 10d.) related to your current history of asthma	
(10a) Have you ever collapsed during training or racing?	☐ Training ☐ Racing ☐ Training and racing
(10b) How many times have you collapsed in training session or races during the last **five years**?	_____ training session _____ races
(10c) How many times have you collapsed in training session or races during the last **12 months** (1 year)?	
(10d) When you collapse, does it mostly occur before of after the finish line / completion of the training session?	☐ Before the finish ☐ After the finish
(10e) What is the cause of you collapse?	☐ Dehydration ☐ Heat illness ☐ Hyponatremia ☐ Low blood pressure ☐ Low blood sugar ☐ Other condition (Specify: _____)

11. History of any current injury that you suffer from

If you answered **YES** to **question 11** in section F, please complete the following questions (11a. to 11g.) related to each of your current injury/ies (Space is provided for two injuries)

Injury 1			
(11a) What was the approximate date when you first became aware of the injury?	Month	Year	
(11b) Please indicate which side of your body is injured (if applicable)	☐ Right	☐ Left	
(11c) Please indicate which anatomical area is currently injured	☐ Head ☐ Neck ☐ Face ☐ Front chest ☐ Back chest ☐ Shoulder ☐ Upper arm	☐ Elbow ☐ Forearm ☐ Wrist ☐ Finger ☐ Lower back ☐ Hip ☐ Thigh	☐ Hamstring ☐ Quadriceps ☐ Knee ☐ Shin ☐ Achilles ☐ Ankle ☐ Foot
	Other (Specify: _____)		
(11d) Please indicate the type of structure that was injured	☐ Muscle ☐ Tendon ☐ Bone	☐ Ligament ☐ Joint	
	Other (Specify: _____)		
(11e) Please indicate in which sport (discipline) the injury occurred	☐ Running ☐ Swimming	☐ Cycling	
	Other (Specify: _____)		
(11f) Please indicate the severity of the injury (tick one box please)	☐ I only experience symptoms after exercise - Grade 1 ☐ I experience symptoms during exercise, but it does not interfere with exercise - Grade 2 ☐ I experience symptoms during exercise that may interfere with my training/ competition - Grade 3 ☐ I am so painful that I may not be able to train or compete - Grade 4		
(11g) Please indicate how your injury was treated to date (you can tick more than one)?	☐ Rest ☐ Stretches ☐ Physiotherapy ☐ Surgery ☐ Strengthening exercises ☐ Equipment change	☐ Tablets ☐ Cortisone injection ☐ Other injection ☐ Orthotics	
	Other (Specify: _____)		

Injury 2			
(11a) What was the approximate date when you first became aware of the injury?	Month		Year
(11b) Please indicate which side of your body is injured (if applicable)	☐ Right	☐ Left	
(11c) Please indicate which anatomical area is currently injured	☐ Head ☐ Neck ☐ Face ☐ Front chest ☐ Back chest ☐ Shoulder ☐ Upper arm	☐ Elbow ☐ Forearm ☐ Wrist ☐ Finger ☐ Lower back ☐ Hip ☐ Thigh	☐ Hamstring ☐ Quadriceps ☐ Knee ☐ Shin ☐ Achilles ☐ Ankle ☐ Foot
	Other (Specify: _____)		
(11d) Please indicate the type of structure that was injured	☐ Muscle ☐ Tendon ☐ Bone	☐ Ligament ☐ Joint	
	Other (Specify: _____)		
(11e) Please indicate in which sport (discipline) the injury occurred	☐ Running ☐ Swimming	☐ Cycling	
	Other (Specify: _____)		
(11f) Please indicate the severity of the injury (tick one box please)	☐ I only experience symptoms after exercise - Grade 1 ☐ I experience symptoms during exercise, but it does not interfere with exercise - Grade 2 ☐ I experience symptoms during exercise that may interfere with my training/ competition - Grade 3 ☐ I am so painful that I may not be able to train or compete - Grade 4		
(11g) Please indicate how your injury was treated to date (you can tick more than one)?	☐ Rest ☐ Stretches ☐ Physiotherapy ☐ Surgery ☐ Strengthening exercises ☐ Equipment change	☐ Tablets ☐ Cortisone injection ☐ Other injection ☐ Orthotics	
	Other (Specify: _____)		

Appendix E

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Research Ethics Committee
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09 February 2007

REC REF: 002/2007

Prof M Schwellnus
Human Biology

Dear Prof Schwellnus

PROJECT TITLE: THE PORT ELIZABETH IRONMAN TRIATHLON 2007: MEDICAL CONSEQUENCES FOLLOWING ENDURANCE SPORTS

Thank you for your letter to the Research Ethics Committee dated 07 February 2007.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study.

Your comments to the queries raised are noted with thanks.

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Please note that ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

lcmjedi

Appendix F1

GASTROINTESTINAL RESEARCH PRE-RACE

ULTRASOUND

DATE

RACE NUMBER

NAME

AGE

DOB

SEX M F

GIT function past 3 days and GIT symptoms associated with exercise:

Medication : What

When

Time since last meal :

O/E: BP

HR

Abdominal examination:

Ultrasound: SMA Coeliac artery

Diameter

Systolic velocity

Diastolic velocity

RI

Table G.3: The predicted, as reported in the pre-race questionnaire, and actual performance times of the GIT Run symptomatic and asymptomatic triathletes

		GIT RUN S SUB-GROUP (N=26)	GIT AS GROUP (N=24)	P-value
Predicted Times	**Overall** (min)	756.0 ± 83.5 (20)	756.6 ± 110.7(19)	0.985
	Swim (min)	86.3 ± 15.9 (20)	83.7 ± 16.7 (19)	0.625
	Cycle (min)	389.8 ± 41.3 (20)	389.5 ± 49.4 (19)	0.985
	Run (min)	270.8 ± 43.2 (20)	278.7 ± 49.6 (19)	0.597
Actual Times	**Overall** (min)	808.0 ± 101.5 (26)	784.1 ± 96.0 (24)	0.399
	Swim (min)	96.1 ± 16.5 (26)	93.8 ± 15.6 (24)	0.611
	Cycle (min)	398.0 ± 41.0 (26)	392.4 ± 41.2 (24)	0.634
	Run (min)	294.8 ± 51.3 (26)	279.3 ± 41.8 (24)	0.249
% Predicted Times	**Overall** (%) [a]	106.3 ± 8.6 (20)	104.2 ± 7.7 (19)	n.d.
	Swim (%) [a]	114.3 ± 14.0 (20)	114.0 ± 13.7 (19)	n.d.
	Cycle (%) [a]	100.8 ± 5.3 (20)	100.3 ± 6.4 (19)	n.d.
	Run (%) [a]	108.8 ± 13.7 (20)	101.9 ± 10.8 (19)	n.d.

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.
[a] Actual times expresses relative to the predicted split and overall times.
n.d., not determined.

Table G.4: The predicted, as reported in the pre-race questionnaire, and actual performance times of the Lower GIT symptomatic and asymptomatic triathletes

		LOWER GIT S SUB-GROUP (N=22)	GIT AS GROUP (N=24)	P-value
Predicted Times	**Overall** (min)	738.3 ± 52.3 (15)	756.6 ± 110.7(19)	0.561
	Swim (min)	85.7 ± 15.9 (15)	83.7 ± 16.7 (19)	0.728
	Cycle (min)	380.3 ± 32.0 (15)	389.5 ± 49.4 (19)	0.539
	Run (min)	264.0 ± 27.3 (15)	278.7 ± 49.6 (19)	0.312
Actual Times	**Overall** (min)	803.6 ± 98.3 (22)	784.1 ± 96.0 (24)	0.501
	Swim (min)	97.0 ± 18.4 (22)	93.8 ± 15.6 (24)	0.529
	Cycle (min)	395.5 ± 42.3 (22)	392.4 ± 41.2 (24)	0.800
	Run (min)	292.1 ± 50.0 (22)	279.3 ± 41.8 (24)	0.348
% Predicted Times	**Overall** (%) [a]	107.5 ± 9.7 (15)	104.2 ± 7.7 (19)	n.d.
	Swim (%) [a]	116.8 ± 14.0 (15)	114.0 ± 13.7 (19)	n.d.
	Cycle (%) [a]	101.8 ± 4.4 (15)	100.3 ± 6.4 (19)	n.d.
	Run (%) [a]	109.1 ± 15.4 (15)	101.9 ± 10.8 (19)	n.d.

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.
[a] Actual times expresses relative to the predicted split and overall times.
n.d., not determined.

Table G.5: The swimming, cycling, running and/or total training frequency, distances and durations for the 1 and 15 week period before the triathlon and the total hours worked in the 15 week period before the triathlon of the GIT Run symptomatic and asymptomatic triathletes

		GIT RUN S SUB- GROUP (N=26)	GIT AS GROUP (N=24)	P-value
Training Frequency (days/wk)		5.5 ± 1.0 (18)	5.9 ± 0.6 (16)	0.166
15 week Working Time (hrs/wk)		45.7 ± 15.7 (15)	41,2 ± 19.3 (18)	0.473
15 week Training Time	**Swim** (hrs/wk)	2.5 ± 0.9 (20)	3.0 ± 1.1 (19)	0.167
	Cycle (hrs/wk)	6.8 ± 2.4 (20)	7.5 ± 2.6 (19)	0.388
	Run (hrs/wk)	3.9 ± 1.4 (20)	4.7 ± 1.5 (19)	0.076
	Total (hrs/wk) [a]	13.2 ± 4.1 (20)	15.2 ± 3.9 (19)	0.128
15 week Training Distance	**Swim** (km/wk)	5.7 ± 2.6 (21)	6.7 ± 2.4 (19)	0.216
	Cycle (km/wk)	182.0 ± 78.2 (21)	204.2 ± 71.7 (19)	0.357
	Run (km/wk)	37.6 ± 15.1 (20)	50.1 ± 16.2 (19)	0.018
	Total (km/wk) [a]	227.0 ± 89.7 (20)	261.0 ± 79.0 (19)	0.218
1 week Training Time	**Swim** (hrs)	1.1 ± 0.7 (19)	1.4 ± 1.0 (18)	0.246
	Cycle (hrs)	3.9 ± 7.8 (19)	3.0 ± 4.3 (18)	0.646
	Run (hrs)	2.8 ± 7.8 (19)	1.0 ± 0.8 (18)	0.346
	Total (hrs) [a]	7.9 ± 16.2 (18)	4.5 ± 2.7 (17)	0.394
1 week Training Distance	**Swim** (km)	2.6 ± 1.8 (19)	2.7 ± 1.8 (19)	0.858
	Cycle (km)	50.8 ± 49.9 (19)	41.8 ± 34.6 (19)	0.525
	Run (km)	8.7 ± 5.1 (18)	9.8 ± 7.8 (18)	0.635
	Total (km) [a]	65.5 ± 56.0 (17)	50.1 ± 37.5 (18)	0.343

Values are expressed as average ± standard deviation, with the number of subjects (N) in parentheses.
[a] The totals are the sum of the swim, cycle and run disciplines.

Table G.6: The swimming, cycling, running and/or total training frequency, distances and durations for the 1 and 15 week period before the triathlon and the total hours worked in the 15 week period before the triathlon of the Lower GIT symptomatic and asymptomatic triathletes

		LOWER GIT S SUB-GROUP (N=22)	GIT AS GROUP (N=24)	P-value
Training Frequency (days/wk)		5.6 ± 1.0 (16)	5.9 ± 0.6 (16)	0.219
15 week Working Time (hrs/wk)		45.9 ± 17.6 (12)	41,2 ± 19.3 (18)	0.118
15 week Training Time	**Swim** (hrs/wk)	2.4 ± 0.8 (15)	3.0 ± 1.1 (19)	0.081
	Cycle (hrs/wk)	6.8 ± 1.9(15)	7.5 ± 2.6 (19)	0.373
	Run (hrs/wk)	3.9 ± 1.5 (15)	4.7 ± 1.5 (19)	0.137
	Total (hrs/wk) [a]	13.1 ± 3.7 (15)	15.2 ± 3.9 (19)	0.118
15 week Training Distance	**Swim** (km/wk)	5.4 ± 2.6 (16)	6.7 ± 2.4 (19)	0.142
	Cycle (km/wk)	186.6 ± 79.1 (16)	204.2 ± 71.7 (19)	0.486
	Run (km/wk)	38.9 ± 14.9 (15)	50.1 ± 16.2 (19)	0.046
	Total (km/wk) [a]	233.1 ± 88.6 (15)	261.0 ± 79.0 (19)	0.339
1 week Training Time	**Swim** (hrs)	1.0 ± 0.6 (14)	1.4 ± 1.0 (18)	0.246
	Cycle (hrs)	2.6 ± 2.0 (15)	3.0 ± 4.3 (18)	0.755
	Run (hrs)	1.2 ± 0.9 (14)	1.0 ± 0.8 (18)	0.537
	Total (hrs) [a]	4.7 ± 2.6 (14)	4.5 ± 2.7 (17)	0.837
1 week Training Distance	**Swim** (km)	3.0 ± 1.9 (14)	2.7 ± 1.8 (19)	0.681
	Cycle (km)	64.7 ± 57.1 (15)	41.8 ± 34.6 (19)	0.159
	Run (km)	10.2 ± 6.2 (13)	9.8 ± 7.8 (18)	0.864
	Total (km) [a]	84.3 ± 63.8 (13)	50.1 ± 37.5 (18)	0.071

Values are expressed as average ± standard deviation, with the number of subjects (N) in parentheses.
[a] The totals are the sum of the swim, cycle and run disciplines.

Table G.7: Triathlon (standard and Ironman) and running (10km, 21.1km and 42.2km) career personal best times (PB) and best times achieved over the last 12 months or 15 weeks before the race of the GIT Run symptomatic and asymptomatic triathletes

		GIT RUN S SUB-GROUP (N=26)	GIT AS GROUP (N=24)	P-value
Triathlon Career PB	**Standard** (min)	171.0 ± 78.2 (12)	147.3 ± 28.4 (12)	0.335
	Ironman (min)	777.3 ± 101.5 (11)	759.4 ± 80.3 (14)	0.628
Triathlon 12 Months PB	**Standard** (min)	169.5 ± 78.0 (12)	155.5 ± 31.0 (8)	0.638
	Ironman (min)	727.8 ± 151.6 (9)	774.7 ± 75.1 (10)	0.397
Running Career PB	**10km** (min)	44.7 ± 78.2 (16)	41.8 ± 6.5 (16)	0.281
	21.1km (min)	94.2 ± 14.3 (15)	100.7 ± 25.3 (18)	0.380
	42.2km (min)	201.2 ± 37.8 (12)	215.5 ± 28.6 (17)	0.256
Running 15 Weeks PB	**10km** (min)	48..3 ± 7.6 (11)	50.3 ± 7.2 (8)	0.574
	21.1km (min)	106.3 ± 15.4 (7)	118.3 ± 24.1 (9)	0.271
	42.2km (min)	241.5 ± 34.8 (6)	248.8 ± 19.7 (5)	0.688

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.
PB, personal best time;

Table G.8: Triathlon (standard and Ironman) and running (10km, 21.1km and 42.2km) career personal best times (PB) and best times achieved over the last 12 months or 15 weeks before the race of the Lower GIT symptomatic and asymptomatic triathletes

		LOWER GIT S SUB-GROUP (N=22)	GIT AS GROUP (N=24)	P-value
Triathlon Career PB	**Standard** (min)	183.2 ± 84.2 (10)	147.3 ± 28.4 (12)	0.180
	Ironman (min)	792.5 ± 83.6 (12)	759.4 ± 80.3 (14)	0.315
Triathlon 12 Months PB	**Standard** (min)	182.1 ± 94.5 (8)	155.5 ± 31.0 (8)	0.462
	Ironman (min)	746.8 ± 157.4 (8)	774.7 ± 75.1 (10)	0.625
Running Career PB	**10km** (min)	45.4 ± 8.0 (12)	41.8 ± 6.5 (16)	0.202
	21.1km (min)	96.9 ± 13.7 (13)	100.7 ± 25.3 (18)	0.624
	42.2km (min)	215.9 ± 30.8 (9)	215.5 ± 28.6 (17)	0.972
Running 15 Weeks PB	**10km** (min)	50.7 ± 8.3 (6)	50.3 ± 7.2 (8)	0.922
	21.1km (min)	112.3 ± 11.4 (7)	118.3 ± 24.1 (9)	0.552
	42.2km (min)	241.5 ± 34.8 (6)	248.8 ± 19.7 (5)	0.688

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.
PB, personal best time;

Table G.9: The number of triathlon (standard and Ironman) and running events (10km, 21.1km and 42.2km) competed in career and the past 2 years and the year in which competing began in the GIT symptomatic and asymptomatic triathletes

		GIT S GROUP (N=35)	GIT AS GROUP (N=24)	P-value
No. of triathlons in career	**Standard**			
	Ironman	3 ± 2 (25)	2. ± 2 (19)	0.384
No. of triathlons in 2 years	**Standard**			
	Ironman	2 ± 1 (24)	2 ± 1 (18)	0.123
Year started triathlon events	**Standard**			
	Ironman	2004 ± 3 (26)	2004 ± 2 (19)	0.740
No. of running events in career	**10km**	25 ± 30 ± (32)	32 ± 75 (28)	0.651
	21.1km	19 ± 23 (33)	27 ± 58 (26)	0.460
	42.2km	17 ± 26 (26)	27 ± 47 (28)	0.365
Year started running events	**10km**	1996 ± 8 (35)	1993 ± 11 (40)	0.226
	21.1km	1998 ± 7 (35)	1993 ± 9 (36)	0.025
	42.2km	1998 ± 7 (26)	1996 ± 8 (31)	0.228

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.

Table G.10: Personal best distance, time and speed in a cycle race between 80 and 120km during the 15 weeks prior to the race in the GIT symptomatic and asymptomatic triathletes

	GIT S GROUP (N=35)	GIT AS GROUP (N=24)	P-value
Distance (km)	105.1 ± 16.5 (17)	116.2 ± 23.0 (11)	0.151
Time (min)	209.8 ± 50.1 (17)	223.7 ± 37.1 (11)	0.435
Speed (km/hr)	30.5 ± 3.1 (17)	31.1 ± 2.6 (11)	0.589

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.

Table G.11: Personal best distance, time and speed in a cycle race between 80 and 120km during the 15 weeks prior to the race in the GIT Run symptomatic and asymptomatic triathletes

	GIT RUN S SUB-GROUP (N=26)	GIT AS GROUP (N=24)	P-value
Distance (km)	101.0 ± 6.9 (14)	116.2 ± 23.0 (11)	0.028
Time (min)	199.7 ± 20.1 (14)	223.7 ± 37.1 (11)	0.050
Speed (km/hr)	30 ± 2.9 (14)	31.1 ± 2.6 (11)	0.604

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.

Table G.12: Personal best distance, time and speed in a cycle race between 80 and 120km during the 15 weeks prior to the race in the Lower GIT symptomatic and asymptomatic triathletes

	LOWER GIT S SUB-GROUP (N=22)	**GIT AS GROUP** (N=24)	**P-value**
Distance (km)	101.3 ± 8.5 (10)	116.2 ± 23.0 (11)	0.070
Time (min)	192.5 ± 17.7 (10)	223.7 ± 37.1 (11)	0.026
Speed (km/hr)	31.7 ± 2.7 (10)	31.1 ± 2.6 (11)	0.640

Values are expressed as average ± standard deviation, with the number of subjects (n) in parentheses.

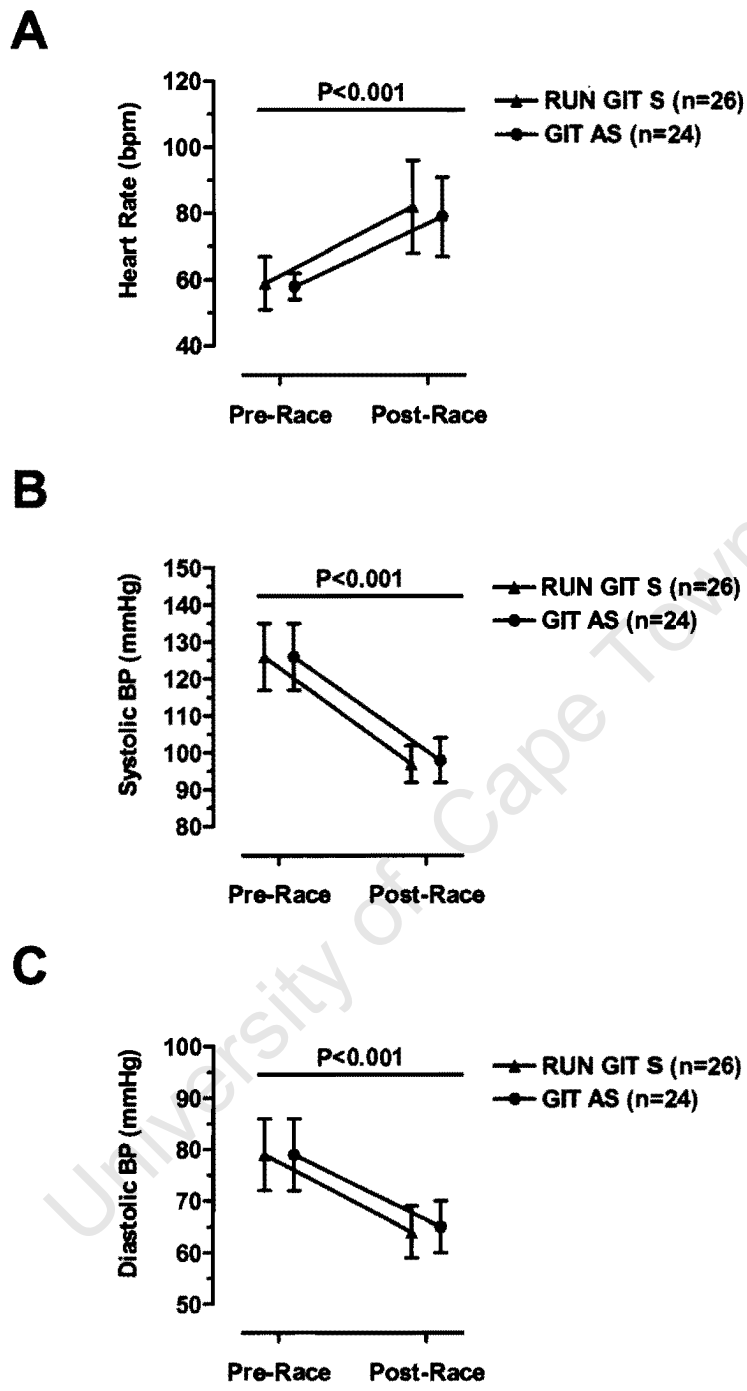

Figure G.1: Pre- and post-race (A) heart rate as well as, (B) systolic and (C) diastolic blood pressures of the triathletes in the GIT run symptomatic and asymptomatic sub-groups

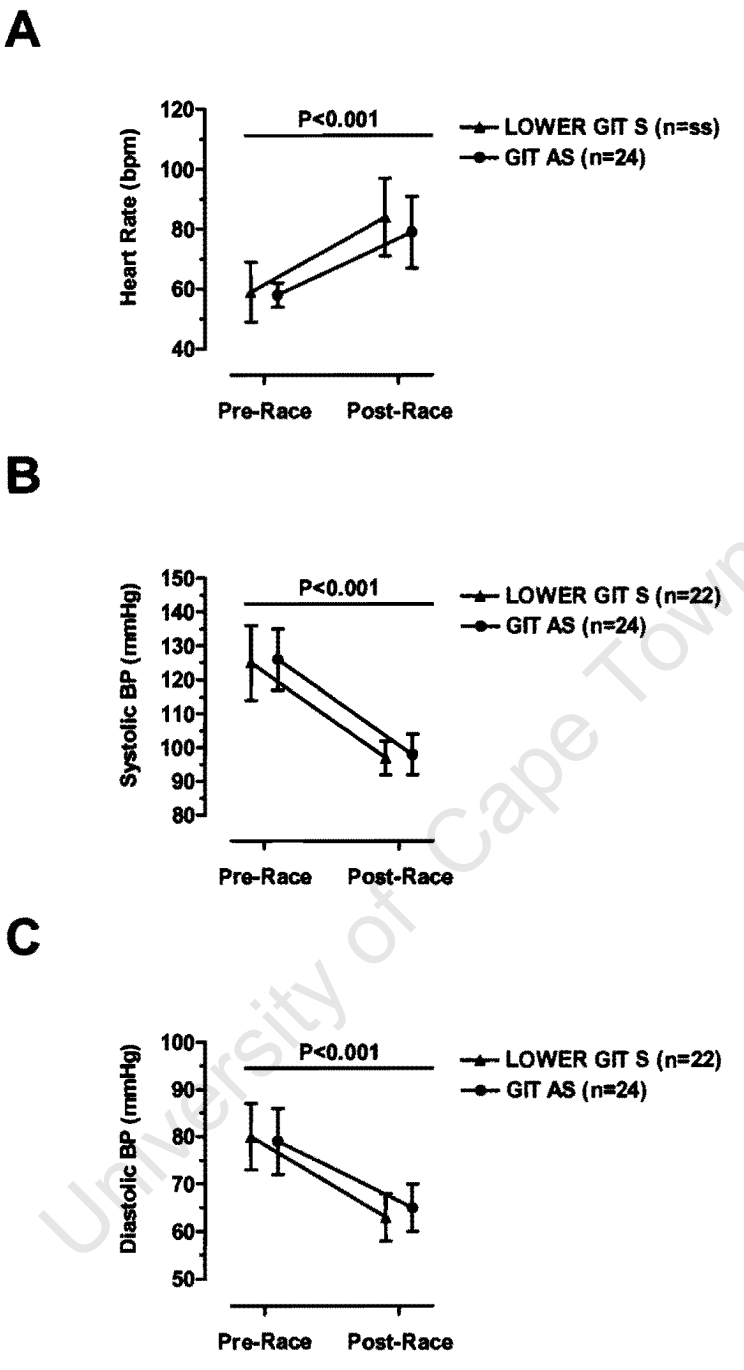

Figure G.2: Pre- and post-race (A) heart rate as well as, (B) systolic and (C) diastolic blood pressures of the triathletes in the Lower GIT symptomatic and asymptomatic groups

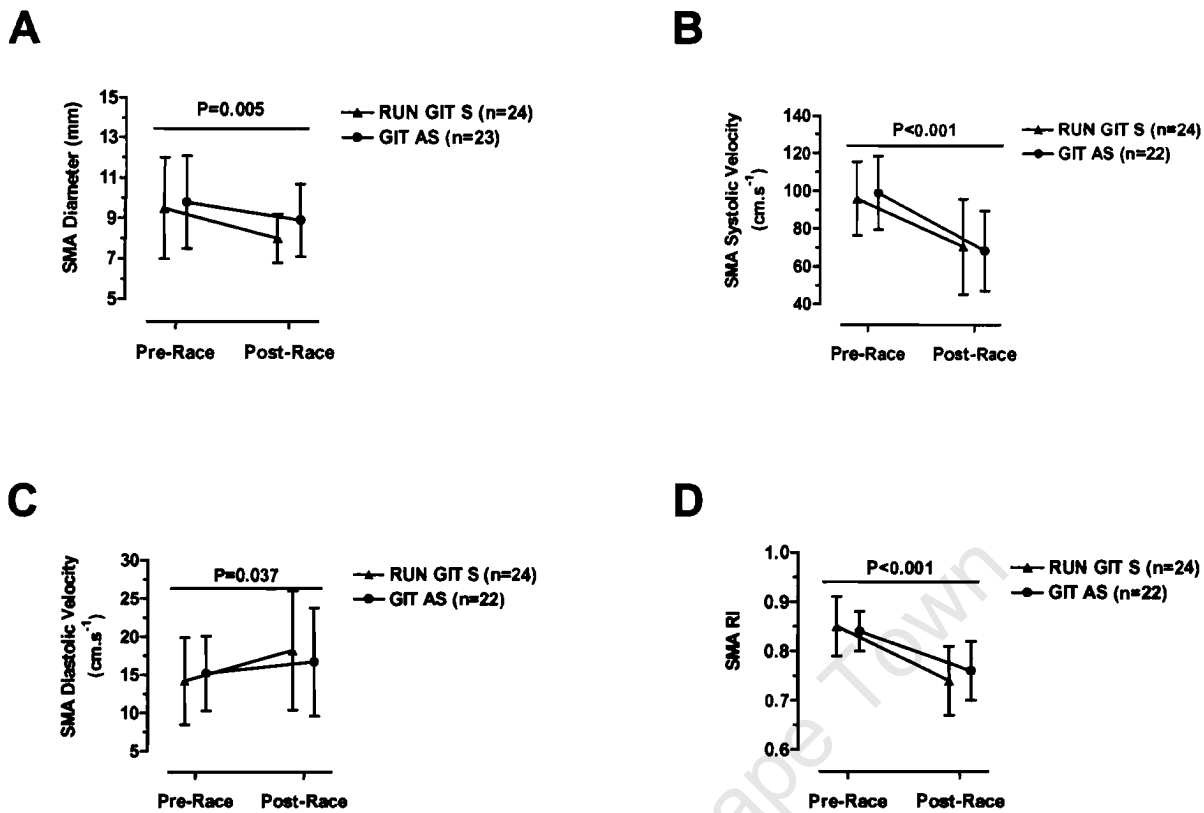

Figure G.3: Pre- and post-race (A) diameter, (B) systolic velocity, (C) diastolic velocity, and (D) RI of the SMA in the GIT Run symptomatic and asymptomatic groups

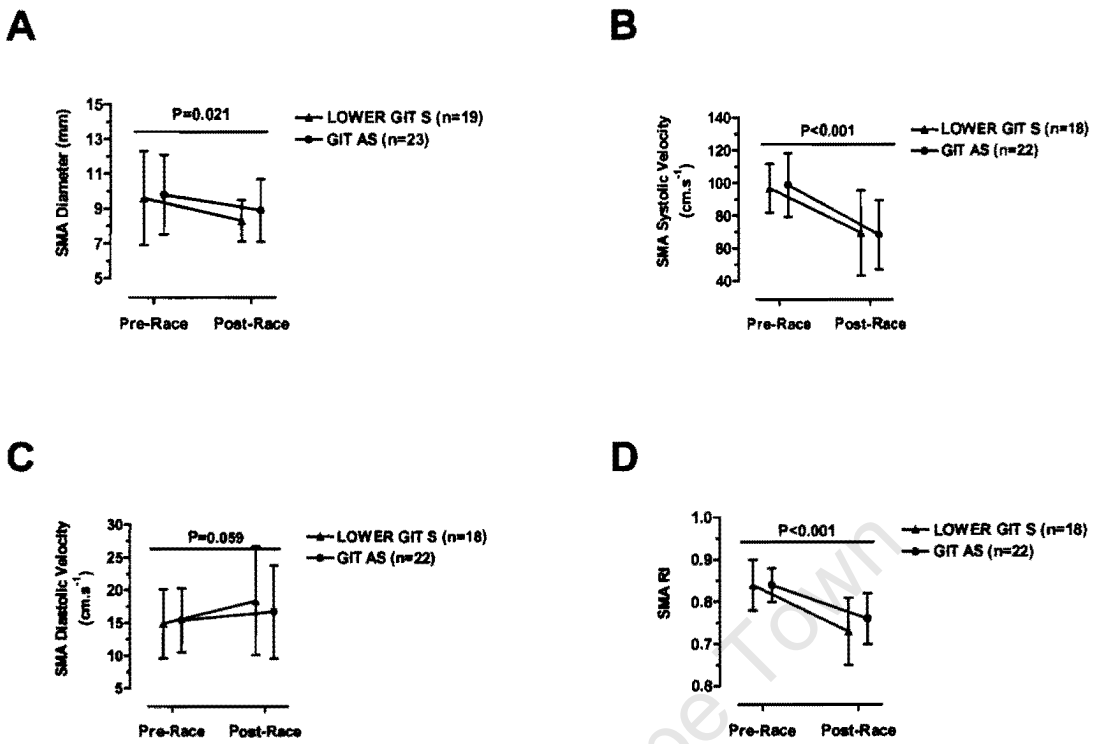

Figure G.4: Pre- and post-race (A) diameter, (B) systolic velocity, (C) diastolic velocity, and (D) RI of the SMA in the Lower GIT symptomatic and asymptomatic groups

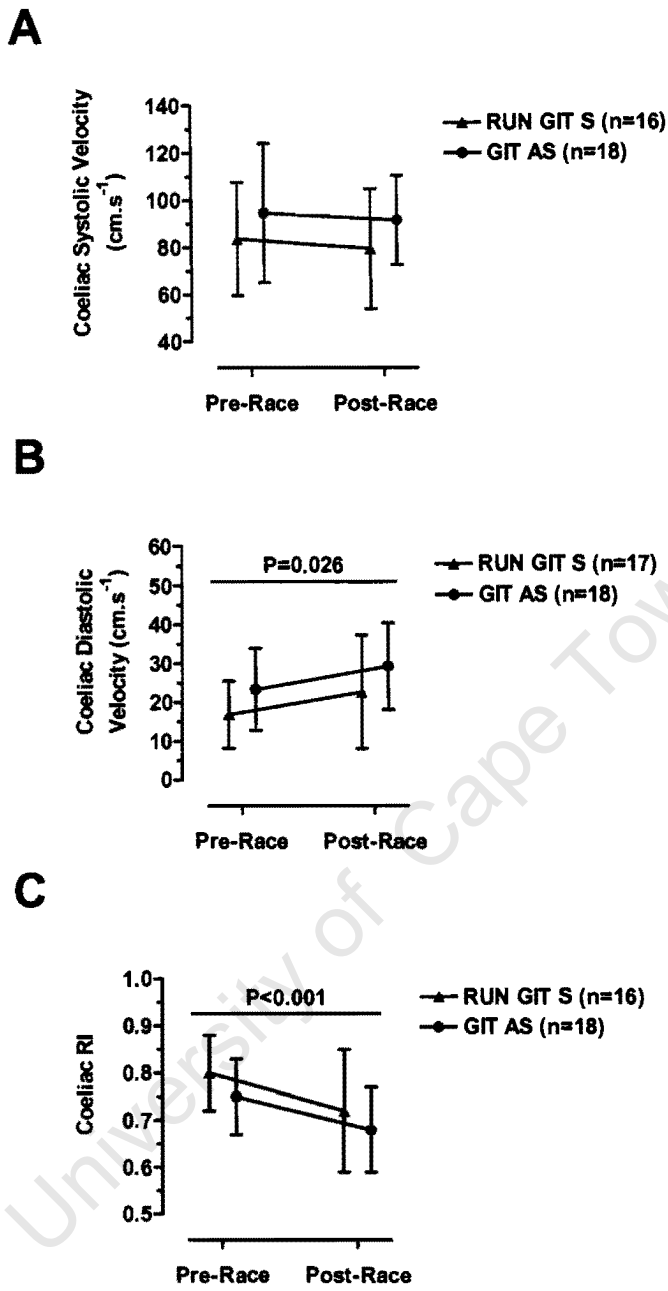

Figure G.5: Pre- and post-race (A) systolic velocity, (B) diastolic velocity, and (C) RI of the coeliac artery in the GIT Run symptomatic and asymptomatic groups

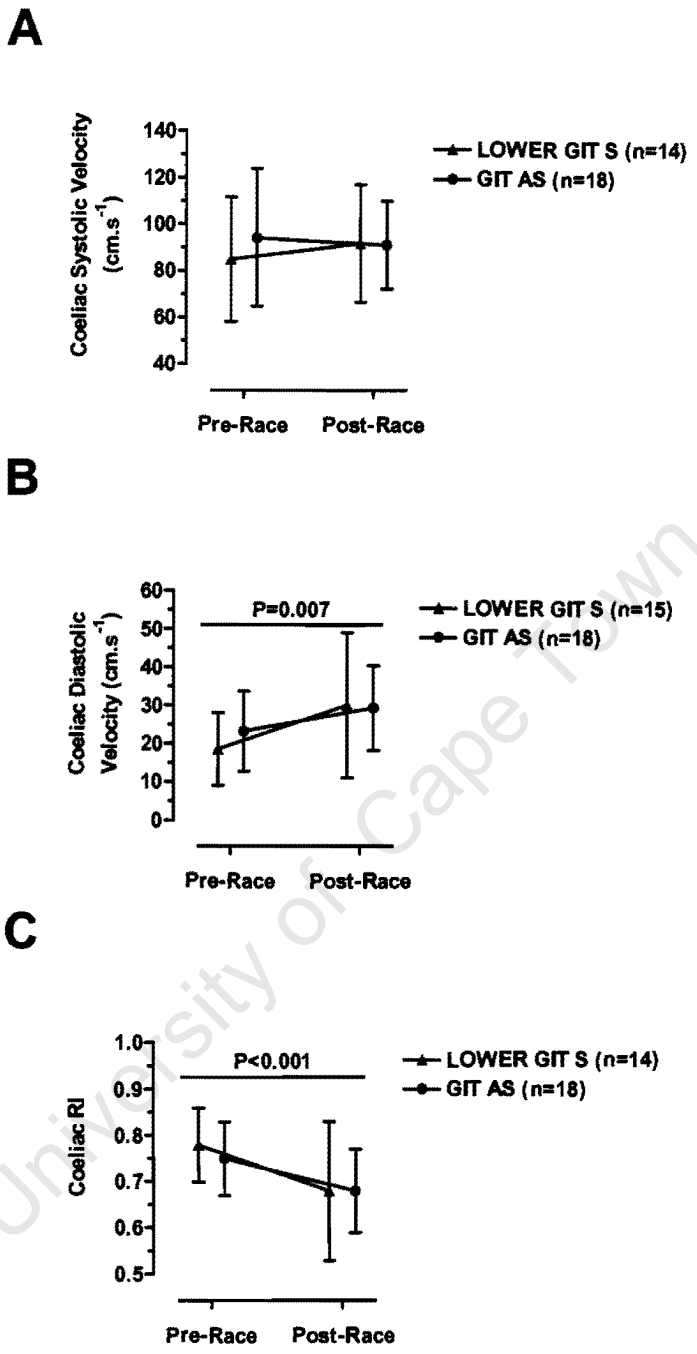

Figure G.6: Pre- and post-race (A) systolic velocity, (B) diastolic velocity, and (C) RI of the coeliac artery in the Lower GIT symptomatic and asymptomatic groups

Results from GENEPOP

Thu Nov 13 17:08:52 WST 2008

```
Genepop web version of 3.4 Option: Hardy-Weinberg test

File: 170852 (COL5A1    )

Number of populations detected: 4
Number of loci detected:       1


Estimation of exact P-values
by the Markov chain method
-------------------------------------------
Markov chain parameters for all tests
         Dememorization        : 1000
         Batches               : 100
         Iterations per batch  : 1000


Hardy Weinberg: Probability test

==================================================
 Results by locus
==================================================


Locus: DpnII-FMFM
-------------------------------------------------------------------
                                        Fis:
                                        ------------------------
POP                       P-val  S.E    W&C    R&H    Matr
------------------------  ------ ------ ------ ------ ------
ACL001                    0.1320 0.0021 -0.267 -0.270    -
ACL002                    0.7850 0.0017 -0.056 -0.056    -
ACL104                    0.4291 0.0038 -0.097 -0.098    -
ACL100                    0.4800 0.0040 -0.078 -0.078    -
All (Fisher's method) :
chi2 : 7.693882
Df : 8
Prob: 0.463929


Normal Ending.
```