Multiple Transportable Carbohydrates and Endurance Exercise: Addressing
Selected Issues in the Literature

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Dedication

I dedicate this dissertation to my mother, Margaret Wilson. Your memory continues to inspire and guide me throughout life. Without your love and guidance, this would not have been possible.

Abstract

Over the last two decades, numerous studies have shown that feeding multiple saccharides during exercise—compared to a single saccharide—increases exogenous carbohydrate oxidation, reduces gastrointestinal distress, and improves performance when carbohydrate intake exceeds 50-60 g·hr.$^{-1}$ Glucose and fructose utilize separate intestinal transporters and have therefore been referred to in the literature as multiple transportable carbohydrates (MTC). Despite the growing evidence, few studies have examined MTC during running, and none of the previous studies assessed their effects on running stride parameters. Moreover, no published study has quantified MTC use in a non-simulated setting, and previous studies largely failed to include women, as only 17 of 266 participants from 24 studies have been female. This dissertation attempted to address these limitations using observational and experimental approaches. The findings from Chapter 3 suggest that many athletes do not consume a balanced mix of saccharides during ultra-endurance competition. This is likely due, in part, to the saccharide profiles found in many foods and beverages sold as carbohydrate supplements. This suggests that competitors may need more education regarding MTC and should pay close attention to the saccharide composition of the products they consume during competition. The findings from Chapters 4 and 5 markedly add to the literature examining MTC during endurance running. The results showed that ingestion of a glucose-fructose beverage (1.3 g·min^{-1} carbohydrate)—compared to glucose-only—improved running performance and psychological affect, as well as reduced gastrointestinal distress. Performance benefits were apparent for men and women alike, and ranged from 1.6-2.6%. Additionally, ingestion of glucose-fructose better maintained stride frequency during 120 min of constant-velocity running. Thus, this dissertation contributes to the knowledge base of MTC in several ways. It contains the first data to show that MTC can enhance running performance, including for women. It also includes the first data to quantify MTC use during a "real-life" event. Finally, it provides a foundation for future studies attempting to examine the effects of MTC during running and under field-based environments.

Table of Contents

List of Tables

List of Figures

1

General Introduction

1.1   Introduction

The influence of carbohydrate intake on endurance exercise has been studied for decades, and the purported positive effects have influenced the nutritional intake of many athletes during training and competition. At present, an innumerous amount of carbohydrate supplements are marketed to athletes for use during prolonged exercise, and the influence of this marketing, as an example, has resulted in 6.7 billion liters of sport drinks sold in the United States alone (International Markets Bureau, 2011). Recently, experimental lab studies have pushed the envelope in terms of the tolerable amount of carbohydrate that can be consumed during exercise. Previous research noted that consuming >60 g·hr^{-1} of carbohydrate increased gastrointestinal (GI) distress without substantially improving performance (Rodriguez, DiMarco, & Langley, 2009). Emerging evidence, however, suggests that supplying a mix of saccharides—as opposed to a single saccharide—improves exogenous carbohydrate oxidation and reduces GI distress when carbohydrate is consumed at >50-60 g·hr^{-1} (Jeukendrup, 2010). Importantly, the ratio of glucose-to-fructose in a supplement or food appears to be a significant determinant of the effects, with several studies suggesting that a glucose-to-fructose ratio of 1.2:1 to 1:1 is optimal (Jentjens, Shaw, Birtles, Waring, Harding, & Jeukendrup, 2005; O'Brien & Rowlands, 2011; O'Brien, Stannard, Clarke, & Rowlands, 2013; Rowlands, Thorburn, Thorp, Broadbent, & Shi, 2008). These findings have been used by numerous manufacturers to market products as containing a superior blend of carbohydrate for performance and GI function (GU Pure Performance Energy, 2013; PowerBar, 2013). Despite the marketing of these products, much remains to be known about the ingestion of multiple saccharides during exercise, referred to in the literature previously as multiple transportable carbohydrates (MTC; Jeukendrup, 2010). The following gaps in the MTC literature will be addressed in this dissertation:

1. No published study has quantified the use of MTC during a non-simulated endurance event, and as a result, practically nothing is known about the use of

MTC outside of artificial laboratory settings. Research is needed to establish to what extent competitors follow the current guidelines regarding MTC and if the use of MTC is associated with performance and GI distress.

2. Of the studies that have examined MTC during exercise, only two used running as the exercise modality (Clarke et al., 2012; Pfeiffer, Cotterill, Grathwohl, Stellingwerff, & Jeukendrup, 2009). This is particularly interesting since GI distress is more common during running than cycling (Peters et al., 1993). Moreover, running is the most popular endurance sport in the United States, with approximately 500,000 individuals finishing a marathon in 2011 (Running USA, 2013). Furthermore, the two studies that utilized running were unlikely to find significant effects because the exercise duration was probably too short (Pfeiffer et al., 2009) and the rate of carbohydrate ingestion was too low (Clarke et al., 2012). Thus, further research is needed to clarify the effects of MTC on running metabolism, GI function, and performance.

3. Previous research has largely been isolated to men. Only 17 of 266 participants from 24 studies have been women (see **Table 2-4**, Chapter 2), clearly limiting recommendations for females regarding MTC. This imbalance of study populations is somewhat ironic since a majority of recreational runners today are women (Running USA, 2013).

4. Scarce research has examined the effects of carbohydrate intake on stride parameters during prolonged running (Rollo & Williams, 2009; Williams, Brewer, & Walker, 1992). Moreover, no published study has assessed what effect, if any, MTC have on running stride parameters. Stride changes, such as decreased stride frequency and increased contact time, are characteristic of running fatigue, and it has been hypothesized that these changes may result partially from a shift to fat metabolism with muscle glycogen depletion (Suriano, Edge, & Bishop, 2010). MTC better maintained carbohydrate oxidation than single-saccharides in some studies (Currell & Jeukendrup, 2008; Lecoultre et al., 2010), thus providing a theoretical basis for preservation of stride frequency with MTC ingestion.

1.2   Dissertation Aims

This dissertation aims to address the aforementioned limitations using both observational and experimental approaches, and three manuscripts have been drafted to accomplish this objective. The first manuscript descriptively quantifies the use of MTC during a non-simulated, ultra-endurance triathlon and also explores whether MTC are associated with GI distress. The second manuscript details an experimental crossover study that compares the metabolic, GI, psychological, and performance effects of two beverages containing different saccharides during running lasting ~2.5 hours. Finally, the third manuscript details an experimental crossover study that assessed the effects of MTC on stride parameters during prolonged running lasting ~2.5 hours. The following Specific Aims and Hypotheses are addressed in the three manuscripts.

Specific Aim 1: To provide saccharide profiles for foods and beverages used during an ultra-endurance triathlon, as well as quantify the saccharides consumed by participants and compare these quantities to recommendations from the MTC literature. MTC literature will be comprehensively reviewed and summary findings will be outlined. Given that this is the first observational study in this area, an exploratory analysis will be undertaken to test the following hypotheses:

Hypothesis 1: glucose intake will be positively associated with GI distress during the run among participants consuming ≥ 50 g·hr^{-1} carbohydrate during the swim and bicycle.

Hypothesis 2: fructose intake will be negatively associated with GI distress during the run among participants consuming ≥ 50 g·hr^{-1} carbohydrate during the swim and bicycle.

Specific Aim 2: To examine the effects of MTC on metabolism, psychological affect, GI distress, and performance during prolonged running. The following hypotheses will be tested:

Hypothesis 1: MTC will result in faster time trial (TT) performance after steady-state running compared to glucose-only.

Hypothesis 2: MTC will result in less GI distress compared to glucose-only.

Hypothesis 3: MTC will result in greater blood lactate concentrations compared to glucose-only.

Hypothesis 4: MTC will result in greater total carbohydrate oxidation at the end of exercise compared to glucose-only.

Hypothesis 5: MTC will result in better psychological affect compared to glucose-only.

Specific Aim 3: To examine the effects of MTC on stride parameters—stride time, stride frequency, contact time, and stride length—during prolonged running. The following hypothesis will be tested:

Hypothesis 1: MTC will result in higher stride frequency during steady-state running compared to glucose-only.

Hypothesis 2: MTC will result in lower contact time during steady-state running compared to glucose-only.

2

Literature Review

1.1 Introduction

Recent guidelines from the American College of Sports Medicine (ACSM) and American Dietetic Association (ADA) recommend 30-60 $g \cdot hr^{-1}$ of carbohydrate be consumed during exercise lasting longer than one hour (Rodriguez et al., 2009). Emerging evidence from the past two decades, however, demonstrates that higher rates of exogenous carbohydrate oxidation can be achieved if carbohydrate is supplied at >50-60 $g \cdot hr^{-1}$ and is comprised of multiple saccharides (mix of glucose and fructose; Jeukendrup, 2010). While the first of these studies focused on exogenous carbohydrate oxidation, subsequent work demonstrated improvements in performance (Jeukendrup, 2010), and further studies have shown the risk of GI distress is minimized when multiple saccharides are consumed (Jeukendrup et al., 2006; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Rowlands, Swift, Ros, & Green, 2012; Tarpey, Roberts, Kass, Tarpey, & Roberts, 2013). The use of products or foods containing multiple saccharides—referred to as MTC—has been one of the more exciting advances in the field of sport nutrition over the past several decades.

Despite a sizeable volume of research on MTC during exercise, numerous unanswered questions remain. This dissertation aims to address several shortcomings in the MTC literature, and the following literature review provides the foundation and justification for this work. First, historical research regarding the use of carbohydrate as a means to augment exercise performance is reviewed. Studies examining pre-exercise and during-exercise carbohydrate feeding are reviewed separately, as are the mechanisms believed to be responsible for the observed benefits. Studies specifically examining MTC are reviewed to identify methodological shortcomings and unanswered questions. Finally, field-based observational studies examining the link between carbohydrate, performance, and GI distress are outlined since one of this dissertation's manuscripts uses an observational, field-based approach.

2.2 Pre-exercise Carbohydrate

2.2.1 Historical perspective.

The relationship between carbohydrate and endurance performance has been studied for nearly a century. In the early 20th century, blood glucose was studied in relation to fatigue and cognitive symptoms at the Boston Marathon, which first implicated carbohydrate as a factor related to endurance running performance (Gordon et al., 1925; Levine, Gordon, & Derick, 1924). Levine et al. (1924) found that among five runners tested before and after the Boston Marathon, all experienced at least a 10% decrease in blood glucose and one experienced a 44% decline. The following year, 16 runners (12 of whom participated the previous year) consumed a high-carbohydrate diet prior to the marathon and/or consumed carbohydrate-rich candies during the race (Gordon et al., 1925). Eight of the 12 runners had better finishing times compared to the previous year and almost all exhibited fewer symptoms such as confusion, irritability, and pallor. Subsequent studies demonstrated strong relationships between muscle glycogen depletion and the onset of fatigue (Bergström, Hermansen, Hultman, & Saltin, 1967; Hermansen, Hultman, & Saltin, 1967; Hultman, 1967) and showed that feeding carbohydrate before prolonged exercise reduces fatigue (Bergstom et al., 1967; Karlsson & Saltin, 1971). An abundance of research on the effects of pre-exercise carbohydrate intake has been conducted in the years since, and while a review of every relevant study would be impractical, the seminal research will subsequently be discussed.

With the observation that muscle glycogen levels are closely linked to fatigue, investigators began developing pre-exercise dietary strategies to manipulate glycogen stores. Starting in the 1960s, relatively extreme regimens were employed, usually referred to as carbohydrate loading. One of the first carbohydrate loading studies relied on several days of high-dose exercise and dietary carbohydrate restriction to deplete glycogen stores, which was followed by several days of elevated carbohydrate intake accompanied by rest (Bergström et al., 1967). While this extended protocol was effective at elevating muscle glycogen, it was cumbersome, time-consuming, and caused negative symptoms

during the glycogen-depleting phase. Subsequently, several investigations have shown that muscle glycogen stores can be elevated by less demanding protocols (Sedlock, 2008). An innovative study demonstrated that as little as 24 hours of high carbohydrate intake (~10 g·kg^{-1} of body mass) accompanied by rest can elevate muscle glycogen similarly as lengthy protocols (Bussau, Fairchild, Rao, Steele, & Fournier, 2002). Furthermore, elevated muscle glycogen can be maintained for several days post-loading with a moderate carbohydrate diet and rest (Goforth, Arnall, Bennett, & Law, 1997). The effectiveness of pre-exercise carbohydrate loading on performance varies by the duration of the subsequent exercise task to be performed. Studies that have used exercise protocols ≤60 min have often found no performance benefit of increasing carbohydrate intake beyond habitual levels, while studies utilizing protocols ≥90 min have more consistently demonstrated benefits (Hawley, Palmer, & Noakes, 1997; Hawley, Schabort, Noakes, & Dennis, 1997; Kavouras, Troup, & Berning, 2004).

Numerous studies have also examined whether carbohydrate intake in the hours just prior to exercise can enhance performance. Consumption of 200-300 g of carbohydrate 3-4 hours prior to prolonged exercise can improve performance, especially after an overnight fast and when carbohydrate is not consumed during exercise (Hargreaves, Hawley, & Jeukendrup, 2004). Ingestion of carbohydrate within 15-90 min of exercise has been more controversial, as it can cause hypoglycemia during exercise in some individuals (Costill et al., 1977; Foster, Costill, & Fink, 1979). Ingestion of carbohydrate—most notably glucose—results in the release of insulin, which in combination with the accelerated muscular uptake of glucose at the onset of exercise, results in a drop in blood glucose. Subsequent studies, however, have demonstrated that the incidence of hypoglycemia is highly individual, resolves after a short time, and does not generally affect performance (Jeukendrup & Killer, 2010).

Beyond acute feeding studies, several chronic studies examining diet over a period of at least a week support the role of carbohydrate during high-load endurance training. Sherman, Doyle, Lamb, and Strauss (1993) randomized 18 runners and 18 cyclists to either high- or moderate-carbohydrate diets (10 vs. 5 g·kg^{-1} of weight per day)

during seven days of intense training consisting of one hour of exercise at 75% peak VO_2 followed by five 1-min sprints at 100% peak VO_2. Both the runners and cyclists on the high-carbohydrate diet maintained muscle glycogen levels in comparison to those on the moderate-carbohydrate diet. Despite this, performance on a time-to-exhaustion (TTE) test at 80% peak VO_2 did not differ between groups; however, given that the average time for the TTE trials was only ~10 min, it is possible that a longer performance test would have elicited performance differences (Sherman et al., 1993). Achten et al. (2004) conducted a similar study using a crossover design and examined the effects of different carbohydrate intakes in seven trained runners over a period of 11 days. The runners performed high-intensity running (~75% max heart rate [HR]) for 60-90 min on most days while consuming carbohydrate at 8.5 or 5.5 $g \cdot kg^{-1}$ of weight per day. Symptoms of fatigue were significantly higher after 11 days during the lower carbohydrate condition, and runners were better able to maintain speed during an 8-km TT on day 11 while on the high-carbohydrate diet.

Based on the aforementioned evidence, guidelines for endurance athletes almost unanimously recommend carbohydrate ingestion prior to endurance events lasting longer than 90 min. A summary of the current recommendations for pre-exercise carbohydrate intake from various sport and nutrition organizations is outlined in **Table 2-1** (Burke, Hawley, Wong, & Jeukendrup, 2011; Rodriguez et al., 2009). Recently, attention has been given to the strategy of training with low carbohydrate availability in an effort to increase training adaptations (Burke, 2010; Hawley & Burke, 2010). An example of this approach comes from Hansen et al. (2005), in which seven men performed knee extensor exercises for 10 weeks, with one leg completing two sessions daily and the other leg completing the two sessions spaced over two days. Thus, the leg completing two sessions daily completed the second session with low muscle glycogen. Overall, resting muscle glycogen and mitochondrial enzyme 3-hydroxyacyl-CoA dehydrogenase activity increased only in the twice-daily legs. Additionally, there was a larger increase in citrate synthase activity in the twice-daily legs compared to the once-daily legs. While several other studies have shown that training under carbohydrate-restriction can decrease the

utilization of carbohydrate during exercise and up-regulate markers of muscular adaptation, these strategies have not consistently led to improvements in performance (Burke, 2010). Therefore, it remains to be seen whether certain events—especially those lasting longer than 4-5 hours—would benefit from these dietary strategies. With little high-quality evidence currently available, however, most practitioners and researchers still advocate high-carbohydrate intakes prior to most endurance events.

Table 2-1. Recommendations for pre-exercise carbohydrate intake		
Organization	**Daily carbohydrate needs**	**Acute pre-exercise**
ADA, ACSM, & Dietitians of Canada (Rodriguez et al. 2009)	6-10 g·kg^{-1} of BM	200-300 g CHO 3-4 hr before exercise
IOC Consensus Conference (Burke et al., 2011)	3-12 g·kg^{-1} of BM depending on training intensity and duration	• 10-12 g·kg^{-1} of BM per day for 36-48 hr • 1-4 g·kg^{-1} of BM for meals 1-4 hr before exercise
Abbreviations: ACSM, American College of Sports Medicine; ADA, American Dietetic Association; BM, body mass; CHO, carbohydrate; IOC, International Olympic Committee.		

2.2.2 Mechanisms for improving performance.

Increased muscle glycogen content.

Early studies noted a strong relationship between muscle glycogen content and the point of volitional fatigue during prolonged exercise (Hermansen et al., 1967; Hultman, 1967). Additionally, it has been observed that blood glucose uptake into the muscle is still increasing at the point of fatigue, which indirectly suggests that muscle glycogen is a more important limiting substrate than blood-derived glucose (Angus, Febbraio, & Hargreaves, 2002). The rate with which muscle glycogen becomes depleted is primarily a function of exercise intensity. Exercise at 60-70% of VO_{2peak} depletes muscle glycogen within 2-3 hours while as little as 30-60 min of exercise at 80-100% VO_{2peak} can deplete muscle glycogen (Gollick, Piehl, & Saltin, 1974). The strong association between muscle glycogen depletion and the timing of fatigue does not

necessarily provide causal evidence for the role of muscle glycogen, and indeed, several other mechanisms contribute to fatigue during prolonged endurance exercise, including metabolic disturbances (Allen, Lamb, & Westerblad, 2008) and neural alterations (Noakes, St. Clair Gibson, & Lambert, 2005).

Increased liver glycogen content.

Liver-derived glucose—whether provided from glycogenolysis or gluconeogenesis—serves as substrate for energy production during prolonged exercise. Studies examining muscle glycogen during the 1960s used liver biopsies to directly assess liver glycogen levels, which were found to be significantly reduced following prolonged exercise (Hultman & Nilsson, 1971). While the use of liver biopsies for exercise performance research has rarely been used in the last half century, other less invasive techniques have confirmed that prolonged exercise significantly reduces liver glycogen (Casey et al., 2000). Compared to resting conditions, liver-derived glucose output increases several-fold during moderate-intensity (60% VO_{2peak}) exercise, of which approximately 75-85% is derived from liver glycogenolysis (Coggan, Swanson, Mendenhall, Habash, & Kien, 1995). Liver gluconeogenesis, however, increasingly supplies substrate for the working muscle as exercise duration increases; its relative contribution to the total liver glucose output increases from 25% to nearly 50% after four hours of exercise (Ahlborg, Felig, Hagenfeldt, Hendler, & Wahren, 1974).

Increased brain glycogen content.

While investigators have traditionally focused on muscle and liver glycogen, the role of brain glycogen in exercise-induced fatigue has recently been considered. Obviously, traditional techniques for measuring glycogen—such as biopsies—are not appropriate for measuring brain glycogen in humans, and consequently, animal studies have provided most of the relevant evidence regarding the role of brain glycogen in exercise-induced fatigue. Matsui et al. (2011), for example, showed brain glycogen levels in rats were reduced by 37–60% in five brain loci after prolonged exercise. Interestingly, super-compensation of brain glycogen in rats occurred after exhaustive exercise, similar

to what is seen in muscles (Matsui et al. 2012). Although the development of new imaging techniques such as noninvasive nuclear magnetic resonance spectroscopy should allow for the study of brain glycogen in relation to exercise, no studies in humans have been published (Tesfaye, Seaquist, & Oz, 2011).

2.3   During-exercise Carbohydrate

2.3.1 Historical perspective.

While much of the early research related to carbohydrate and endurance performance focused on pre-exercise strategies, studies in the 1980s began to examine the effects of feeding exogenous carbohydrate during exercise (Coggan & Coyle, 1989; Coggan & Coyle, 1991; Coyle et al., 1983; Fielding et al., 1985; Hargreaves, Costill, Coggan, Fink, & Nishibata, 1984). Coyle et al. (1983), for example, had ten male cyclists perform two trials while consuming either a glucose solution or a placebo. The subjects were asked to cycle until exercise intensity dropped below 50% VO_{2peak}, and compared to a mean exercise time of 126 min with placebo, subjects exercised for 159 min while consuming glucose. As in many studies to follow, subjects fasted for 12 hours before the tests and were asked to perform TTE protocols, both of which tend to exaggerate the ergogenic benefits of experimental treatments. Clearly, the 26% improvement in TTE with carbohydrate seen in Coyle et al. (1983) is not realistic for field-based events, and resultantly, TT tests measuring time-to-complete a set distance or workload have been advocated when performance is the primary outcome of interest (Atkinson & Nevill, 2001; Laursen, Francis, Abbiss, Newton, & Nosaka, 2007).

A recent meta-analysis of placebo-controlled, randomized, crossover studies examined the performance effects of exogenous carbohydrate consumed during exercise lasting ≥1 hour (Temesi, Johnson, Raymond, Burdon, & O'Connor, 2011). Inclusion criteria were participants aged ≥16 years and studies utilizing ingestion rates between 30-80 g·hr^{-1} from beverages of ≤8% concentration. Overall, carbohydrate consumed during exercise benefited performance in comparison to placebo, but notably, the magnitude of

benefit varied substantially with the type of performance outcome assessed. Studies utilizing TT protocols showed a 2% weighted mean improvement, compared to a weighted mean improvement of 15.1% for TTE protocols. Sub-analyses of studies including only those with highly trained participants and matching for electrolyte content did not alter the estimates significantly. A clear limitation of the studies analyzed was that only eight utilized running, all of which were on a treadmill (Temesi et al., 2011).

Similar to the pre-exercise carbohydrate loading studies, the effectiveness of consuming carbohydrate during exercise varies with the intensity and duration of the exercise task being performed. Studies that have used exercise TT tests lasting between 60-90 min have frequently found no benefit (Burke, Wood, Pyne, Telford, & Saunders, 2005; Desbrow, Anderson, Barrett, Rao, & Hargreaves, 2004; Jeukendrup, Hopkins, Aragón-Vargas, & Hulston, 2008), although at least one using cycling did observe a performance improvement of 2.3% (Jeukendrup, Brouns, Wagenmakers, & Saris, 1997). Additionally, contradictory evidence exists regarding the combination of pre-exercise and during-exercise carbohydrate intake, with several studies in support (Chryssanthopoulos & Williams, 1997; Chryssanthopoulos, Williams, Nowitz, Kotsiopoulou, & Vleck, 2002; Wright, Sherman, & Dernbach, 1991) and refutation (Chryssanthopoulos, Williams, & Nowitz, 2002; Chryssanthopoulos, Williams, Wilson, Asher, Hearne, & 1994; Rollo & Williams, 2010) of this practice. Again, TTE tasks and those lasting ≥90 min were more likely to show benefits to combining pre-exercise and during-exercise carbohydrate.

Recommendations from several organizations for exogenous carbohydrate intake during exercise can be seen in **Table 2-2**. The International Olympic Committee Consensus Conference guidelines provide more specific recommendations in relation to exercise intensity and duration. As duration increases—and by necessity intensity decreases—carbohydrate recommendations increase up to 90 g·hr^{-1} for events lasting ≥2.5 hours. At these lower intensities, higher carbohydrate intakes can typically be tolerated—as long as they are MTC—whereas only smaller amounts can generally be tolerated for higher-intensity activities.

Table 2-2. Recommendations for during-exercise carbohydrate intake		
Organization	**Carbohydrate during exercise**	**Other guidelines**
ADA, ACSM, & Dietitians of Canada (Rodriguez et al., 2009)	30-60 g·hr^{-1} for events lasting longer than an hour	• CHO solutions between 6-8% • CHO should be primarily glucose • Form (liquid, solid) does not matter
IOC Consensus Conference (Burke et al., 2011)	• <45 min: none • 45-75 min: small or mouth rinse • 1-2.5 hr: up to 60 g·hr^{-1} • >2.5 hr: up to 90 g·hr^{-1}	CHO form and frequency of consumption should be individualized to each athlete
Abbreviations: ACSM, American College of Sports Medicine; ADA, American Dietetic Association; CHO, carbohydrate; IOC, International Olympic Committee.		

2.3.2 Mechanisms for improving performance.

Preventing hypoglycemia.

Exogenous carbohydrate intake may exert part of its beneficial effects by maintaining blood glucose. This mechanism, however, has been rather controversial since studies seem to both support (Coggan & Coyle, 1987; Coyle, Coggan, Hemmert, & Ivy, 1986; Nybo, Møller, Pedersen, Nielsen, & Secher, 2003) and refute (Felig, Cherif, Minagawa, & Wahren, 1982; Jentjens & Jeukendrup, 2002; Moseley, Lancaster, & Jeukendrup, 2003) the role of hypoglycemia in endurance exercise fatigue. The discrepancies may, in part, be due to the timing of hypoglycemia experienced, since a number of the studies refuting the role of hypoglycemia were designed to induce hypoglycemia early in exercise (Jentjens & Jeukendrup, 2002; Moseley et al., 2003), while those affirming its role induced hypoglycemia late in exercise (Coggan & Coyle, 1987; Coyle et al., 1986; Nybo et al., 2003). The effects of hypoglycemia may thus be more detrimental once body stores of glycogen—including the brain—become depleted. Hypoglycemia may induce fatigue during exercise by reducing the supply of glucose to the brain, thereby reducing metabolic oxygen rate, increasing perceived exertion, and exacerbating cognitive impairments (Nybo et al., 2003).

Sparing endogenous carbohydrate stores.

Exogenous carbohydrate intake during exercise may act to spare endogenous muscle glycogen, but much like the role of hypoglycemia, numerous studies support (Erickson, Schwarzkopf, & McKenzie, 1987; Tsintzas, Williams, Boobis, & Greenhaff, 1995; Tsintzas, Williams, Boobis, & Greenhaff, 1996; Yaspelkis, Patterson, Anderla, Ding, & Ivy, 1993) and refute (Flynn et al., 1987; Jeukendrup et al., 1999; Mitchell et al., 1989a) this mechanism. Interestingly, the effects of exogenous carbohydrate ingestion on muscle glycogen utilization may vary by muscle fiber type, which may help explain the equivocal findings. Specifically, exogenous carbohydrate intake during continuous moderate-intensity exercise (~70% VO_{2peak}) appears to selectively spare muscle glycogen in type I muscle fibers, while type II muscle fibers remain unaffected (Tsintzas et al., 1995; Tsintzas et al., 1996; Tsintzas et al., 2001). Thus, studies that performed muscle biopsies without considering muscle fiber type or that measured whole-body glycogen utilization may not have been sensitive enough to detect differences between carbohydrate and placebo ingestion. In addition to its putative role in sparing muscle glycogen, feeding with carbohydrate during exercise spares liver glycogen (Bosch, Weltan, Dennis, & Noakes, 1996). Theoretically, this spared liver glycogen can act as a reserve later in exercise when muscle glycogen and exogenous carbohydrate consumption can no longer meet the energy demand needed to sustain ATP generation.

Neuromuscular and psychological effects.

Exogenous carbohydrate ingestion can enhance performance in events lasting >90 min (Burke et al., 2011; Rodriguez et al., 2009). For shorter events, however, findings have been equivocal, with some studies showing no benefit to performance (Burke et al., 2005; Desbrow et al., 2004; Jeukendrup et al., 2008) while others indeed have (Anantaraman, Carmines, Gaesser, & Weltman, 1995; Below, Mora-Rodriguez, Gonzalez-Alonso, & Coyle, 1995; Jeukendrup et al., 1997; Neufer et al., 1987). Given that total body carbohydrate oxidation rates do not differ from placebo despite a continued increase in muscular glucose uptake (Carter, Jeukendrup, Mann, & Jones,

2004b; El-Sayed, Balmer, & Rattu, 1997; Millard-Stafford, Rosskopf, Snow, & Hinson, 1997), it has been suggested that other mechanisms are responsible for the performance benefits observed in events lasting <90 min. Recent studies employing carbohydrate mouth rinsing have shown performance benefits for these events, suggesting that sensory or central nervous system (CNS) mechanisms may be responsible for the improvements. Carbohydrate mouth rinsing involves swishing a carbohydrate solution in the mouth for 5-10 sec followed by expectoration. An overview of nine carbohydrate rinsing studies is presented in **Table 2-3** (Beleen et al., 2009; Carter, Jeukendrup, & Jones, 2004a; Chambers, Bridge, & Jones, 2009; Fares & Kayser, 2011; Gam, Guelfi, & Fournier, 2013; Pottier, Bouckaert, Gilis, Roels, & Derave, 2010; Rollo, Cole, Miller, & Williams, 2010; Rollo, Williams, Gant, & Nute, 2008; Whitham & McKinney, 2007). Benefits of rinsing carbohydrate have been observed in comparison to rinsing water, rinsing an artificially-sweetened placebo, and ingesting carbohydrate.

Despite the performance benefits, much is still unknown regarding the practical implementation of carbohydrate rinsing. All of the studies but one (Pottier et al., 2010) utilized glucose or maltodextrin solutions, and all of the studies used a carbohydrate concentration of ~6%. Thus, it remains unclear whether using different saccharides (e.g. fructose, sucrose) and increasing the carbohydrate concentration would elicit further improvements. In addition, only one study compared carbohydrate mouth rinsing to a non-rinsing or non-ingestion control (Gam et al., 2013). Since mouth rinsing itself may distract or slow a competitor compared to doing nothing, the effect sizes of previous studies may have been exaggerated. Indeed, Gam et al. (2013) did not find a performance benefit to carbohydrate rinsing in comparison to a non-rinse control during cycling, although there was a trend towards faster performance in the rinse condition (65.7 vs. 67.6 min, $p = .086$). In studies comparing carbohydrate mouth rinsing to ingestion, participants were required to ingest a specific volume according to a set schedule as opposed to ad libitum intake. Ad libitum fluid intake has been recommended over structured intake by various researchers, based mostly on the observation that the majority of competitors finish races with some degree of dehydration and that the degree

of dehydration is often associated with faster finishing time (Noakes, 2007). Therefore, future studies should compare ad libitum carbohydrate ingestion to carbohydrate rinsing. Finally, all of the studies were conducted in a laboratory setting, so it remains to be seen how carbohydrate mouth rinsing strategies translate to ecologically-valid field settings.

Table 2-3. Overview of carbohydrate rinsing studies

Author	Athlete/Study Characteristics	Protocol	Beverage(s)	Rinse Details	Performance Outcomes
Carter, Jeukendrup, & Jones (2004a)	• 7 cyclists (5 m, 2 f) • Randomized crossover	Cycle TT for ~1 hr	• 6.4% md • Water placebo	5-sec rinse for every 12.5% of the trial	59.57 vs. 61.37 min ($p = .011$)
Whitham & McKinney (2007)	• 10 recreationally active men • Randomized crossover	15-min of running at 65% VO_{2max} followed by 45 min TT	• 6% md • Lemon-sweetened placebo	5-sec rinse every 6-min	No differences in distance covered
Rollo et al. (2008)	• 10 recreationally active men • Randomized crossover	30-min TT run	• 6% glu • Artificially-sweetened placebo	25-ml bolus every 6-min for 5-sec	Distance run was 115 m farther during glu vs. placebo ($p < .05$)
Beelen et al. (2009)	• 14 male cyclists • Randomized crossover	Cycle TT for ~1 hr	• 6.4% md • Water placebo	5-sec rinse for every 12.5% of the trial (25-ml bolus)	No differences in TT (68.14 vs. 67.52 min) in md and placebo ($p = .57$)
Chambers, Bridge, & Jones (2009)	• 8 male cyclists • Randomized crossover	Cycle TT for ~1 hr	• 6.4% glu • 6.4 md • Artificially-sweetened placebo	10-sec rinse for every 12.5% of the trial (25-ml bolus)	TT was faster when rinsing with glu vs. placebo (60.4 and 61.6 min, $p = .007$)
Pottier et al. (2010)	• 12 triathletes • Randomized crossover	Cycle TT for ~1 hr	• 5.4% suc, 0.5% glu • Artificially-sweetened placebo • 4 trials (2 ingestion and 2 rinsing)	5-sec rinse or ingestion for every 12.5% of the trial	• In rinse conditions, TT was faster with CHO than placebo (61.7 vs. 64.1 min) • In the ingestion conditions, there was no differences

Rollo et al. (2010)	• 10 recreationally active men • Randomized crossover	Run TT for ~1 hr	• 6.4% CHO drink (saccharides not specified) • Artificially-sweetened placebo	5-sec rinse for every 15 min of the trial (25-ml bolus)	Distance run was 211 m farther during CHO vs. placebo (p = .048)
Fares & Kayser (2011)	• 13 men • Randomized crossover	TTE at 60% max power	• 6.4% md • Water placebo • 4 trials (2 fed and 2 fasted)	5-10 sec rinse every 5 min of the trial (25-ml bolus)	TTE was longer for md vs. water in both fed and fast conditions
Gam, Guelfi, & Fournier (2013)	• 10 male cyclists • Randomized crossover	Cycle TT for ~1 hr	• 6.4% md • Water placebo • No rinse	5-sec rinse for every 12.5% of the trial	• TT was faster in md (65.7 min) and no rinse (67.6) vs. water (69.4, p = .013 and p = .042) • Difference between md and no rinse showed a trend (p = .086)
Abbreviations: CHO, carbohydrate; f, female; glu, glucose; m, male; md, maltodextrin; TT, time trial; TTE, time-to-exhaustion.					

The mechanisms by which carbohydrate mouth rinsing improves performance are still being elucidated. Chambers et al. (2009) compared the effects of rinsing glucose and maltodextrin solutions to an artificially-sweetened placebo on activation of several brain regions using functional magnetic resonance imaging (fMRI). Both glucose and maltodextrin solutions activated brain regions involved in reward and motor control to a greater extent than the artificially-sweetened placebo. However, subjects were not exercising during the fMRI tests, and the solution concentrations were several-fold higher than what has been used in exercise trials. In terms of mediating factors, both sweetness and carbohydrate structure are proposed to be influential. Sweet substances cause specific cells on the tongue (G-protein-coupled receptor proteins T1R2 and T1R3) to release neurotransmitters that interact with primary afferent nerve fibers and the brainstem (Berthoud, 2003). Although data from humans is absent, experiments in rodents provide evidence that carbohydrate structure may influence receptors in the mouth separately from sweetness. Rats preferred maltodextrin over sweeter saccharrides such as sucrose, glucose, and fructose at low concentrations, and only at high concentrations did they prefer sucrose (Sclafani, 1991). In addition, experiments with knockout mice lacking either the T1R2 or T1R3 proteins demonstrated reductions in the preference for sucrose (Zukerman, Glendinning, Margolskee,& Sclafani, 2009) and artificial sweeteners (Damak et al., 2003).

Other support for CNS mechanisms comes from an investigation in which ingestion of a carbohydrate solution compared to placebo immediately increased corticomotor excitability and maximal voluntary force production from the biceps (Gant, Stinear, & Byblow, 2010). These mechanisms are compatible with other non-exercise studies showing glucose present in the mouth can trigger neural and endocrine responses prior to any significant digestion and absorption occurring (Marty, Dallaporta, & Thorens, 2007). Beyond glucose- and caloric-containing solutions, oral rehydration with water relative to intravenously may reduce thirst and perceived exertion during exercise, supporting the notion that the oral cavity is an important sensory organ that can affect neuromuscular systems (Riebe et al., 1997).

2.3.3 Evidence regarding multiple transportable carbohydrates.

Carbohydrate ingestion during prolonged exercise can enhance performance in events lasting >60-90 min. Recommendations for carbohydrate intake during exercise from the joint Position Stand of the ADA, ACSM, and Dietitians of Canada range from 30-60 g·hr,[-1] based on the observation that greater amounts increase GI distress without improving performance (Rodriguez et al., 2009). Emerging evidence, however, has demonstrated that ingesting MTC—most commonly as a mix of glucose and fructose—can simultaneously increase exogenous carbohydrate oxidation while lessoning the risk of GI distress.

The 24 studies that have examined MTC during exercise are detailed in **Table 2-4** (Adopo, Péronnet, Massicotte, Brisson, & Hillaire-Marcel, 1994; Baur et al., 2014; Clarke et al., 2012; Currell & Jeukendrup, 2008; Hulston, Wallis, & Jeukendrup, 2009; Jentjens, Achten, & Jeukendrup, 2004a; Jentjens, Moseley, Waring, Harding, & Jeukendrup, 2004b; Jentjens et al., 2005; Jentjens et al., 2006; Jentjens, Venables, & Jeukendrup, 2004c; Jeukendrup et al., 2006; Jeukendrup & Moseley, 2010; Lecoultre et al., 2010; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Pfeiffer et al., 2009; Riddell, Bar-Or, Wilk, Parolin, & Heigenhauser, 2001; Roberts, Tarpey, Kass, Tarpey, & Roberts, 2014; Rowlands et al., 2012; Rowlands et al., 2008; Tarpey et al., 2013; Triplett, Doyle, Rupp, & Benardot, 2010; Wagenmakers, Brouns, Saris, & Halliday, 1993; Wallis, Rowlands, Shaw, Jentjens, & Jeukendrup, 2005). Overall, ingesting a mix of glucose, fructose, and/or sucrose can increase exogenous carbohydrate oxidation by ~20-60% compared to an equivalent dose of a single saccharide, usually glucose. Carbohydrate dosages have ranged from 0.5-2.4 g·min,[-1] and several of those that provided carbohydrate at dosages of ≤1.0 g·min^{-1} did not demonstrate significant substrate oxidation or performance differences (Clarke et al., 2012; Hulston et al., 2009), although one study did show differences in exogenous carbohydrate oxidation at 0.8 g·min^{-1} (Adopo et al., 1994). Thus, supplying carbohydrate at >0.8-1.0 g·min^{-1} during exercise may represent the minimum amount needed to realize benefits with MTC ingestion. In addition to improving exogenous carbohydrate oxidation, MTC reduced the frequency of

GI complaints in several studies, including perceptions of stomach fullness (Jeukendrup et al., 2006; O'Brien & Rowlands, 2011; Roberts et al., 2014), nausea (O'Brien et al., 2013; Roberts et al., 2014; Tarpey et al., 2013), and abdominal cramps (O'Brien et al., 2013; Rowlands et al., 2012; Tarpey et al., 2013). All of these studies, however, were conducted using cycling, so effects on running GI symptomology remain unclear.

Several limitations to the current research are worth noting. All of the studies but two were conducted exclusively with males (Pfeiffer et al., 2009; Rowlands et al., 2012) and all but two utilized cycling (Clarke et al., 2012; Pfeiffer et al., 2009). Clarke et al. (2012) examined the effects of MTC on soccer-related performance. MTC ingestion compared to glucose-only during a 90 min soccer-specific protocol did not significantly affect performance on a subsequent 20%-grade treadmill TTE test, although there was a trend towards improved performance ($p = .06$). The amount of carbohydrate ingested (1.0 g·min^{-1}), however, was at the low end of what the literature indicates is needed to demonstrate improvements in performance. The other running study used a 16-km TT to assess performance, which may have been too short in duration to elicit significant differences (Pfeiffer et al., 2009). In addition, only two studies have measured performance in non-laboratory settings (Pfeiffer et al., 2009; Rowlands et al., 2012). Finally, all of the studies used carbohydrate formulations instead of natural or whole foods. Clearly, the use of formulated carbohydrate sources is advantageous in terms of controlling other factors such as fluid and sodium intake, but it prevents generalization to the foods many competitors choose during non-simulated events.

Table 2-4. Review of studies on multiple transportable carbohydrates.

Study	Population	Design	Blinded?	Pre-exercise Nutrition	Carbohydrate	Comments
Wagenmakers et al. (1993)	6 male cyclists	Randomized crossover trial of 120 min cycling at 65% max work-load	Not reported	*Breakfast*: 1 g·kg^{-1} bread and 5 ml·kg^{-1} of CHO drink 2 hr before	CON: water GLU: 1.85 g·kg^{-1} md MTC: 1.85 g·kg^{-1} suc	Total EXO CHO was 76 and 81 g for GLU and MTC
Adopo et al. (1994)	6 healthy men	Randomized crossover trial of 120 min cycling at 61% VO$_{2max}$	Not reported	*Dinner*: protein 70 g, CHO 110 g, fat 40 g *Breakfast*: protein 15 g, CHO 50 g, fat 15 g	CON: water GLU1: 50 g glu GLU2: 100 g glu FRU1: 50 g fru FRU2: 100 g fru MTC: 50 g glu, 50 g fru	EXO CHO for MTC was ~30% higher vs. GLU2
Riddell et al. (2001)	12 non-athlete boys (age 11-14)	Randomized crossover trial of 90 min cycling at 55% VO$_{2max}$ followed by a TTE test at 90% max power	Participant single-blind. Success not reported.	*Breakfast*: slice white bread, peanut butter and 100 ml orange juice	CON: artificially-sweetened water GLU: 1.5 glu g·kg^{-1} MTC: 0.75 glu, 0.75 fru g·kg^{-1}	• EXO CHO was less at 90 min in MTC vs. GLU • TTE in the CON was less than MTC (p = .049) but not different from GLU (p = .29)
Jentjens et al. (2004a)	8 trained male cyclists/triathletes	Randomized crossover trial of 150 min of cycling at 62% VO$_{2max}$	Not reported	10-12 hr fast	CON: plain water GLU: 2.4 glu g·min^{-1} MTC: 1.2 glu, 0.6 fru, 0.6 suc g·min^{-1}	• EXO CHO for MTC was 44% higher vs. GLU (p < .01) • More subjects had severe GI discomfort in GLU vs. MTC

Jentjens et al. (2004b)	8 trained male cyclists/triathletes	Randomized crossover trial of 120 min cycling at 63% VO_{2max}	Not reported	10-12 hr fast	CON: plain water GLU1: 1.2 glu g·min^{-1} GLU2: 1.8 glu g·min^{-1} MTC: 1.2 glu, 0.6 fru, g·min^{-1}	• EXO CHO for MTC was 55% higher vs. GLU1 or GLU2 ($p < .001$) • More subjects had severe GI discomfort in GLU2 vs. GLU1/MTC
Jentjens et al. (2004c)	9 trained male cyclists/triathletes	Randomized crossover trial of 150 min cycling at 60% VO_{2max}	Not reported	10-12 hr fast	CON: plain water GLU: 1.8 glu g·min^{-1} MTC1: 1.2 glu, 0.6 suc g·min^{-1} MTC2: 1.2 glu, 0.6 md g·min^{-1}	• EXO CHO for MTC1 was 18% higher vs. GLU or MTC2 ($p < .05$) • More subjects reported severe GI discomfort in GLU and MTC2 vs. MTC1
Jentjens et al. (2005)	8 trained male cyclists/triathletes	Randomized crossover trial of 120 min cycling at 63% VO_{2max}	Not reported	10-12 hr fast	CON: plain water GLU: 1.2 glu g·min^{-1} SUC: 1.2 suc g·min^{-1} MTC1: 0.6 glu, 0.6 suc g·min^{-1} MTC2: 1.2 glu, 1.2 suc g·min^{-1}	• EXO CHO for MTC2 was higher vs. GLU, SUC, or MTC1 ($p < .01$) • EXO CHO for SUC and MTC1 were 21% higher vs. GLU ($p < .05$)
Wallis et al. (2005)	8 trained male cyclists/triathletes	Randomized crossover trial of 150 min cycling at 64% VO_{2max}	Not reported	10-12 hr fast	CON: plain water GLU: 1.8 md g·min^{-1} MTC: 1.2 md, 0.6 fru g·min^{-1}	EXO CHO for MTC was 40% higher vs. GLU over last 30 min ($p < .01$)

Jentjens et al. (2006)	8 trained male cyclists/triathletes	Randomized crossover trial of 120 min cycling at 50% max power conducted in heat (31.9°C)	Not reported	10-12 hr fast	CON: plain water GLU: 1.5 glu g·min^{-1} MTC: 1.0 glu, 0.5 fru g·min^{-1}	• EXO CHO for MTC was 36% higher vs. GLU for last hour ($p < .05$) • RPE at the end was higher in GLU (12.8) vs. MTC (11.5) ($p < .05$)
Jeukendrup et al. (2006)	8 trained male cyclists/triathletes	Randomized crossover trial of 300 min cycling at 58% VO$_{2max}$	Participant single-blind. Success not reported.	Overnight fast	CON: water GLU: 1.5 glu g·min^{-1} MTC: 1.0 glu, 0.5 fru g·min^{-1}	• EXO CHO for MTC was higher vs. GLU ($p < .05$) • Pedal cadence was maintained only in MTC • Stomach fullness was lower in MTC during the final hour ($p < .05$)
Currell & Jeukendrup (2008)	8 trained male cyclists	Randomized crossover trial of 120 min cycling at 55% max power followed by ~1 hr TT	Not reported	Not reported.	CON: water GLU: 1.8 glu g·min^{-1} MTC: 1.2 glu, 0.6 fru g·min^{-1}	• Total CHO oxidation was not different • MTC resulted in an 8% quicker time to completion vs. GLU
Rowlands et al. (2008)	10 trained male cyclists/triathletes	Randomized crossover trial of 120 min cycling at 50% max power followed by 10 2-3 min sprints	Double-blind. Success not reported. Sweetness reported different between trials.	Overnight fast	GLU: 0.6 md g·min^{-1} MTC1: 0.6 md, 0.3 fru g·min^{-1} MTC2: 0.6 md, 0.5 fru g·min^{-1} MTC3: 0.6 md, 0.7 fru g·min^{-1}	• EXO CHO was highest for MTC2 • MTC1 and MTC2 attenuated decline in sprint power vs. GLU by 6.2% and 5.3%

Hulston et al. (2009)	7 trained male cyclists	Randomized crossover trial of 150 min cycling at 65% VO_{2max}	Participant single-blind. Success not reported.	10-12 hr fast	CON: plain water GLU: 0.8 glu g·min^{-1} MTC: 0.5 glu, 0.3 fru g·min^{-1}	EXO CHO was not significantly different between GLU and MTC
Pfeiffer et al. (2009)	48 runners (34 m, 14 f)	Randomized crossover trial of 16-km outdoor run TT	Double-blind. Success not reported.	Consumed their "usual" pre-race meal	GLU: 1.4 glu g·min^{-1} MTC: 0.9 glu, 0.5 fru g·min^{-1}	No differences between GLU and MTC for performance or GI distress
Jeukendrup & Moseley (2010)	8 male subjects	Randomized crossover trial of 120 min cycling at 61% VO_{2max}	Participant single-blind. Success not reported.	10-11 hr fast	CON: water GLU: 1.5 glu g·min^{-1} MTC: 1.0 glu, 0.5 fru g·min^{-1}	MTC resulted in faster gastric emptying and lower RPE_{legs} vs. GLU
Lecoultre et al. (2010)	7 trained male cyclists	Randomized crossover trial of 120 min cycling at 60% VO_{2max}	Participant single-blind. Success not reported.	Overnight fast	GLU: 2.0 glu g·min^{-1} MTC: 1.2 glu, 0.8 fru g·min^{-1}	MTC resulted in higher rates of total carbohydrate (7%) and lactate oxidation (30%) vs. GLU
Triplett et al. (2010)	9 male cyclists	100-km TT on a cycle ergometer	Double-blind. Success not reported.	10-12 hr fast	GLU: 2.4 glu g·min^{-1} MTC: 1.2 glu, 1.2 fru g·min^{-1}	• Finishing time was faster in MTC (204 vs. 221 min) • 7 participants reported feeling very full during GLU

Study	Participants	Protocol	Blinding	Diet	Treatments	Results
O'Brien & Rowlands (2011)	10 trained male cyclists/triathletes	Randomized crossover trial of 150 min cycling at 50% max power followed by an incremental test to exhaustion	Double-blind. Success non-formally reported.	Overnight fast	CON: artificially-sweetened water MTC1: 1.2 md, 0.6 fru $g \cdot min^{-1}$ MTC2: 1.0 md, 0.8 fru $g \cdot min^{-1}$ MTC3: 0.8 md, 1.0 fru $g \cdot min^{-1}$	• MTC2 and MTC3 resulted in higher peak power vs. MTC1 and CON • Stomach fullness, abdominal cramping, and nausea were lowest with the MTC2
Clarke et al. (2012)	11 male university soccer players	Randomized crossover trial of 90 min soccer-specific protocol followed by a run at a 20% gradient at 12.8 km·hr^{-1}	Double-blind. Success not reported.	Average daily intake of 375 g CHO, but no report of meal before protocol	CON: CHO placebo GLU: 1.0 glu $g \cdot min^{-1}$ MTC: 0.66 glu, 0.33 fru $g \cdot min^{-1}$	• Performed at 30°C and 45% humidity • CHO oxidation rates were not different • Trend for greater performance in the graded run for MTC ($p = .06$)
Rowlands et al. (2012)	*Field*: 10 trained cyclists (7 m, 3 f) *Lab*: 16 trained male cyclists	Randomized crossover trials *Field*: ~150 min mountain bike race *Lab*: 94-min set-workload followed by a set-distance performance trial	Double-blind. Success not reported.	*Field*: CHO of 6.5 g·kg^{-1} for day before *Lab*: 250 mL water + 14 g cereal bar 10-min before	*Field*: MTC1: 0.9 md, 0.4 glu $g \cdot min^{-1}$ MTC2: 0.9 md, 0.4 fru $g \cdot min^{-1}$ *Lab*: MTC1: 1.0 md, 0.5 glu $g \cdot min^{-1}$ MTC2: 1.0 md, 0.5 fru $g \cdot min^{-1}$	• TT and lab performance improved with MTC2 • MTC2 reduced abdominal cramps in TT and nausea in the lab test

O'Brien et al. (2013)	12 trained male cyclists	Randomized crossover trial of 120 min cycling at 57% peak power followed 10 sprints	Double-blind. There were differences in sweetness reported between experimental beverages.	Overnight fast	CON: artificially-sweetened water MTC1: 0.67 md, 0.33 glu, 0.5 fru g·min^{-1} MTC2: 0.67 md, 0.16 glu, 0.67 fru g·min^{-1} MTC3: 0.67 md, 0 glu, 0.83 fru g·min^{-1}	• With MTC2, EXO CHO was 18% and 5% higher vs. MTC1/MTC3 • Mean sprint power was highest with MTC2
Tarpey et al. (2013)	7 trained male cyclists	Randomized crossover trial of 150 min cycling at 50% peak power followed 60-km TT	Double-blind. Success not reported.	Overnight fast	MTC1: 0.84 md, 0.52 fru, 0.34 protein g·min^{-1} MTC2: 1.1 md, 0.6 fru g·min^{-1} GLU: 1.7 md g·min^{-1}	• Peak EXO CHO was 40-45% higher in MTC2 • TT was 2% and 5% faster with MTC2 vs. MTC1 and GLU • Most GI symptoms recorded were most prevalent in GLU
Baur et al. (2014)	8 trained male cyclists	Randomized crossover trial of 120 min cycling at 50% peak power followed 30-km TT	Double-blind. Success not reported.	~500 calorie meal 2 hr before	CON: artificially-sweetened water GLU1: 1.03 glu g·min^{-1} GLU2: 1.55 glu, g·min^{-1} MTC: 1.03 glu, 0.52 fru g·min^{-1}	• MTC resulted in improved TT by 3% compared to GLU2 • MTC resulted in 1.2% improvement compared to GLU1, although statistically unclear

Roberts et al. (2014)	14 male club cyclists	Randomized crossover trial of 150 min cycling at 50% peak power followed 60-km TT	Double-blind. Success not reported.	12 hr fast	CON: artificially-sweetened water GLU: 1.7 md g·min^{-1} MTC: 1.1 md, 0.6 fru g·min^{-1}	• With MTC, EXO CHO was ~40% higher at end of exercise vs. GLU • Most GI symptoms were more prevalent in GLU • MTC resulted in greater fluid delivery vs. GLU

Abbreviations: BM, body mass; CHO, carbohydrate; CON, control; EXO, exogenous oxidation; f, female; fru, fructose; glu, glucose; hr, hour; m, male; md, maltodextrin; MTC, multiple transportable carbohydrates; RPE, rating of perceived exertion; suc, sucrose; TT, time trial; TTE, time-to-exhaustion.

Multiple transportable carbohydrate mechanisms.

Glucose and fructose rely on distinct intestinal transporters for absorption from the intestinal lumen into enterocytes, and therefore, supplying a mix of glucose and fructose should theoretically increase carbohydrate absorption and reduce GI distress when carbohydrate intake is high. The major transporters for glucose and fructose in the intestine are the sodium-dependent glucose cotransporter 1 (SGLT1) and glucose transporter-5 (GLUT5) (Wood & Trayhurn, 2003). When ingested alone, fructose appears to have a lower capacity for absorption during exercise (Fujisawa et al., 1993), resulting in 20-30% lower exogenous oxidation rates when compared to an equivalent amount of glucose (Jandrain et al., 1993; Massicotte, Péronnet, Adopo, Brisson, & Hillaire-Marcel, 1994).

Ingestion of fructose alone or with other carbohydrates at rest and during exercise leads to an increase in blood lactate concentrations (Jentjens et al., 2004a; Jentjens et al., 2004b; Macdonald, Keyser, & Pacy, 1978). Upon ingestion, fructose is phosphorylated to fructose-1-phosphate (F1P) in the liver by hepatic fructokinase, and increased concentrations of F1P upregulate pyruvate kinase, ultimately resulting in an increased conversion of pyruvate to lactate (Mayes, 1993). Lactate produced during exercise is hypothesized to serve as substrate for oxidative energy production, via both cell-to-cell and intracellular pathways (Brooks, 2002; Hashimoto & Brooks, 2008). Lecoultre et al. (2010) provided an estimation of exogenous fructose oxidation through the lactate pathway during 120 min of cycling exercise. Seven participants ingested 2.0 g glucose·min^{-1} or 1.2 g glucose·min^{-1} plus 0.8 g fructose·min.$^{-1}$ The glucose plus fructose feeding led to a 30% increase in plasma lactate appearance in comparison to glucose, and lactate oxidation accounted for approximately half of all exogenous fructose oxidation. A review of tracer studies—under both resting and exercise conditions— estimated that approximately 25-30% of ingested fructose is converted into lactate within a few hours of ingestion (Sun & Empie, 2012).

Gluconeogenesis from fructose also increases in response to fructose feeding during exercise, which provides an additional pathway by which fructose may increase carbohydrate oxidation. The same aforementioned study from Lecoultre et al. (2010)

used isotope labeling of exogenous fructose to estimate fructose oxidation via gluconeogenesis, and approximately half of the fructose oxidized was estimated to be from fructose-derived gluconeogenesis. The same review of tracer studies estimated that anywhere between 29-54% of ingested fructose is converted into glucose within 2-6 hours of ingestion, depending on the dose and metabolic health of the individual (Sun & Empie, 2012).

Effects of MTC on gastric emptying may explain some of the observed benefits in terms of performance, exogenous carbohydrate oxidation, and GI distress. Under resting conditions, a highly-concentrated fructose solution (10-15%) empties faster from the stomach than an isocaloric glucose solution (Guss, Kissileff, & Pi-Sunyer, 1994; Sole & Noakes, 1989). These gastric emptying differences may be explained by the inhibitory-feedback effects glucose has on afferent nerves in the small intestine (Zittel, Rothenhofer, Meyer, & Raybould, 1994) and on SGLT1 transporters (Raybould & Zittel, 1995). Subsequent studies support the notion that gastric fluid emptying is more rapid with MTC compared to an equivalent concentration of glucose (Jeukendrup & Moseley, 2010). Jeukendrup and Moseley (2010) used several methods to compare ingested fluid dynamics during exercise while ingesting a 100% glucose solution or a 2:1 glucose-to-fructose solution (1.5 g·min^{-1}) during 120 min of cycling at 61% VO_{2peak}. Sampling of stomach contents with a nasogastric tube was used to estimate gastric emptying and an ingested deuterium tracer was used to estimate fluid delivery. After 45 min of exercise, a greater amount of the glucose-fructose solution had emptied from the stomach, and 5 min after the tracer ingestion, plasma deuterium enrichment was significantly greater with the glucose-fructose solution, suggesting a more rapid delivery of fluid (Jeukendrup & Moseley, 2010). Theoretically, improvements in gastric emptying and fluid delivery could help maintain plasma volume and reduce cardiac demand, especially in hot and humid environmental conditions. However, these potential benefits of MTC are currently speculative in nature.

The performance benefits of MTC may be partially mediated by these GI system effects. Rowlands et al. (2012) used statistical modeling (polynomial with linear and

quadratic components) to assess the magnitude of performance benefit attributable to reductions in GI symptoms. Overall, reduced abdominal cramps and lower nausea with MTC appeared to positively mediate performance outcomes. O'Brien et al. (2013) used a similar approach and found that a reduction in abdominal cramps was likely a mediator of end-exercise sprint power improvement when comparing beverages with varying ratios of glucose and fructose. Moreover, one of the only studies to utilize a pure TT to assess performance clearly showed that GI distress can substantially impair performance. Participants cycled a 100-km TT 8% faster when consuming a glucose-fructose beverage compared to a glucose-only beverage, and out of nine participants, two experienced diarrhea and one experienced vomiting with the glucose-only beverage while no severe symptoms were reported with the glucose-fructose beverage (Triplett et al., 2010).

2.3.4 Natural food versus commercial sport nutrition products.

The sport nutrition industry now represents a multi-billion dollar global entity capable of exerting tremendous marketing and financial influence (Cohen, 2012; Noakes & Speedy, 2007). Countless carbohydrate supplements intended for sport are on the market, including drinks, gels, semi-solids, sport beans, and others. Several studies have compared the effectiveness of different forms of carbohydrate, and overall, liquid, semi-solid, and solid forms of carbohydrate appear to be equally effective in terms of performance (Campbell, Prince, Braun, Applegate, & Casazza, 2008; Murdoch, Bazzarre, Snider, & Goldfarb, 1993; Pfeiffer, Stellingwerff, Zaltas, & Jeukendrup, 2010). Despite the increased prevalence of sport nutrition products in the marketplace, an increasing number of consumers prefer natural food alternatives that are minimally processed and contain no artificial ingredients (Food Marketing Institute, 2003).

The purported benefits of commercial carbohydrate products are many, but intriguingly, only a handful of studies have directly compared the efficacy of these commercial products to natural foods containing high-levels of carbohydrate. Although the term natural is not specifically defined by the Food and Drug Administration, it generally refers to foods with no added colors, artificial flavors, or synthetic ingredients

(Food and Drug Administration, 2012). Two randomized crossover studies have compared the effectiveness of raisins to sport gels on cycling and running performance (Kern, Heslin, & Rezende, 2007; Too et al., 2012). For the cycling trial, eight male and female cyclists on two occasions consumed 1 g·kg^{-1} of body weight of raisins and a sport gel 45 min before exercise and subsequently completed 45-min cycling trials at 70% VO$_{2peak}$ (Kern et al., 2007). Although pre-exercise insulin levels were significantly greater for the sport gel condition, no differences in power output were apparent between the conditions. For the running trial, eleven males completed two sessions consisting of 80 min of running at 75% VO$_{2peak}$ followed by a 5-km TT. Carbohydrate was consumed at 0.5 g·kg^{-1} of body weight pre-exercise and 0.2 g·kg^{-1} of body weight every 20-min during exercise. The 5-km TT results were 20.6 and 20.7 min for the raisin and sport gel conditions, which were both significantly faster than water (Too et al., 2012). Notably, GI symptoms were not significantly different between the raisin and sport gel conditions.

Other studies have compared natural foods to other commercial carbohydrate formulations. Rietschier et al. (2011) compared the efficacy of raisins to commercial sport jelly beans during 120 min of sub-maximal cycling followed by a 10-km TT. Trial times were 17.3 min for both the raisin and sport jelly bean conditions. The participants, however, rated the raisins as more pleasant than the jelly beans in terms of sensory characteristics. Another study compared bananas to a 6% carbohydrate drink on metabolic and performance parameters during a 75-km cycling TT (Nieman et al., 2012), and performance in the TT tests were similar, with times of 2.41 and 2.36 hours for the banana and carbohydrate drink conditions, respectively ($p = .26$).

Despite the lack of research comparing foods not originally intended for sport to commercially-developed sport nutrition products, endurance athletes frequently choose non-sport nutrition foods during competition. Fresh fruit, dried fruit (raisins), fruit juices, sweet/fruit cakes, cookies, sandwiches, and cereal represent some of the foods commonly consumed by endurance athletes (Black, Skidmore, & Brown, 2012; Havemann & Goedecke, 2008). In terms of MTC, athletes have limited ability to assess the saccharide

profiles of these and other foods because manufacturers are not required to divulge specific saccharide amounts in foods or beverages.

2.4   Ultra-endurance Marathon and Triathlon Nutrition Research

2.4.1 Research quantifying carbohydrate intake.

Despite the abundance of studies on pre-exercise and during-exercise carbohydrate intake, the vast majority have been conducted under laboratory-based conditions, which can distort the relationship between any given variable and its relevance to field performance (Atkinson & Nevill, 2001). The logistical and practical difficulties of conducting a randomized trial before a non-simulated endurance event such as a marathon or triathlon are numerous. Both recreational and professional runners invest substantial physical, mental, and emotional resources into training and are likely reluctant to be randomized to a potentially inferior treatment (e.g. placebo ingestion). Furthermore, feeding the number of athletes required for adequate statistical power poses an additional barrier.

In light of these difficulties, several investigations have utilized observational approaches to explore whether pre-race and in-race carbohydrate intakes are associated with performance in non-simulated running events. **Table 2-5** provides an overview of studies that have examined dietary factors in relation to running performance in non-simulated events lasting at least two hours (Atkinson, Taylor, Morgan, Ormond, & Wallis, 2011; Downey & Hopkins, 2001; Fallon, Broad, Thompson, & Reull, 1998; Frentsos & Baer, 1997; Glace, Murphy, & McHugh, 2002b ; Kimber, Ross, Mason, & Speedy, 2002; Kruseman, Bucher, Bovard, Kayser, & Bovier, 2005; Pfeiffer et al., 2012 Stuempfle, Hoffman, Weschler, Rogers, & Hew-Butler, 2011). **Table 2-6** covers studies that quantified dietary intakes without examining associations with performance (Colombani, Mannhart, Wenk, & Frey, 2002; Cox, Snow, & Burke, 2010; Glace, Murphy, & McHugh, 2002a; Stuempfle, Hoffman, & Hew-Butler, 2013). Overall, significant heterogeneity exists with respect to the methods employed and populations

studied. Only two studies were done in the setting of a traditional road-race marathon (Atkinson et al., 2011; Pfeiffer et al., 2012). By far the largest study came from an investigation of 257 runners participating in the London Marathon (Atkinson et al., 2011), and average carbohydrate intake over the day prior to the marathon was 5.0 g·kg^{-1} of body weight. Notably, carbohydrate intake the day before the race significantly predicted marathon speed, independent of gender, body mass index, and training measures. Specifically, for every 1 g·kg^{-1} of body weight increase in carbohydrate intake for the day before the race, running speed would be predicted to increase by 0.17 km·hr^{-1} (Atkinson et al., 2011). Pfeiffer et al. (2012) used post-race recalls to gather information on in-race carbohydrate intake (35 g·hr^{-1} carbohydrate) and bivariately examined the association with marathon time. In the 28 runners sampled, carbohydrate intake during the race was negatively associated with marathon time ($r = -.49$).

Overall, five of the remaining studies listed in **Table 2-5** had sample sizes n <30, precluding the ability to detect small-to-moderate associations with performance, although in two of these studies some significant associations or differences emerged (Frentos & Baer 1997; Kimber et al., 2002). Frentos and Baer (1997) identified six triathletes with potentially inadequate nutrient intakes and subsequently provided them with dietary counseling and supplements to increase nutritional intakes. After four weeks, carbohydrate intake increased (from 4 to 8 g·kg^{-1} of body weight) in parallel with time improvements for a triathlon (from 5.42 to 5.00 hours). Despite the impressive performance improvement, the non-randomized nature of the study and concomitant increases in fat and protein make ascribing the improvements to carbohydrate impossible. Kimber et al. (2002) studied the nutritional intake of 18 triathletes during an Ironman race, and the associations between carbohydrate intake and performance varied by leg of the race and sex. Specifically, carbohydrate intakes expressed as g·kg^{-1} of body weight per hour during the cycle and running legs were positively correlated with finishing time for women ($r = .59$ and $.30$). Conversely, finishing time for men was negatively correlated with carbohydrate intake during the run ($r = -.75$) but positively correlated for the cycle ($r = .32$). These results seemed to indicate that women did not benefit from in-

race carbohydrate intake, while men seemed to benefit primarily from consuming larger amounts of carbohydrate during the run. However, the cross-sectional nature of these studies and lack of control for potential confounders limit causal inferences.

Largely, the available literature regarding the effects of carbohydrate on non-simulated endurance running is inconclusive. While several studies provide evidence that consuming carbohydrate before and during non-simulated running events is associated with performance, the body of research is limited by small sample sizes, poor dietary collection methodology, and failure to adjust for potential confounders. In addition, the amounts of carbohydrate consumed have often been <50-60 g·hr^{-1} and no effort has been made to evaluate the effects of MTC on performance or GI distress. Thus, it is unknown whether the benefits observed in laboratory studies are transferable to non-simulated settings where numerous other factors converge to influence performance.

Table 2-5. Studies examining diet and performance in non-simulated events

Author	Athlete/Study Characteristics	Event	Carbohydrate Intake	Performance Outcomes	Comments
Frentos & Baer (1997)	• 6 elite triathletes (4 m, 2 f) • Non-randomized intervention	Two 1.3-km swim, 40-km bike, 10-km run triathlons	*Daily intake* • Pre-intervention: 4 $g \cdot kg^{-1}$ • Post-intervention: 8 $g \cdot kg^{-1}$	Event times decreased from 5:25 to 5:00 ($p < .05$)	Daily intakes of energy, fat, and protein also increased
Fallon et al. (1998)	• 10 male runners • In-race intake recorded by observers	100-km ultra-marathon	42.8 $g \cdot hr^{-1}$	No significant correlations were found between CHO and speed or time	Correlations would need to be very strong to detect a significant association
Downey & Hopkins (2001)	• 59 triathletes (52 m, 7 f) • Post-race diet recall	Ironman	0.96 $g \cdot kg^{-1} \cdot hr^{-1}$ during race	CHO intake negatively correlated with time ($r = -.59$)	Water intake was also negatively correlated with finish time ($r = -.45$)
Glace et al. (2002b)	• 26 runners (21 m, 5 f) • Twelve hours pre-race diet record • In-race intake recorded by observers and recall	160-km trail race	• Pre-race: 318 g • In-race: 0.13 $g \cdot kg^{-1} \cdot km^{-1}$	CHO intakes were slightly higher for finishers vs. non-finishers, but no associations with performance were found	Only 13 runners finished the race

Kimber et al. (2002)	• 18 triathletes (10 m, 8 f) • Interviews in-race and post-race recall	Ironman	• Cycle: 1.5 & 1.2 g·kg^{-1}·hr^{-1} for men and women • Run: 0.6 & 0.8 g·kg^{-1}·hr^{-1} for men and women	• Total CHO on bike was correlated with time for women (r = .77, p < .05) • CHO (g·kg^{-1}·hr^{-1}) on run was correlated with time for men (r = -.75, p < .05) • CHO (g·kg^{-1}·hr^{-1}) on bike was correlated with time for men (r = .32, p > .05)	Small sample size and no adjustment for confounders
Kruseman et al. (2005)	• 42 runners • In-race intake recorded by observers	44-km mountain race	In-race: 31 g·hr^{-1}	Individuals in the highest tertile of CHO intake finished faster than those in lowest (26 g·hr^{-1} vs. 37.6 g·hr^{-1})	Association was no longer significant after adjusting for fat mass and race experience
Atkinson et al. (2011)	• 257 runners • Pre-race diet record (1-day)	Marathon	5.0 g·kg^{-1} day before race	Day-before race CHO significantly predicted marathon speed, independent of gender, BMI, and training	In-race CHO not assessed
Stuempfle et al. (2011)	• 16 runners (12 m, 4 f) • In-race intake recorded by post-race recall	161-km trail race	In-race: 0.98 and 0.56 g·kg^{-1}·hr^{-1} for finishers vs. non-finishers	• Kcal, fluid, and Na intakes were greater during first segment of the race for finishers vs. non-finishers(p < .05)	Only 6 runners finished the race (4 m, 2 f)
Pfeiffer et al. (2012)	• 150 triathletes (115 m, 35 f) • 28 marathoners (22 m, 6 f) • Post-race diet recall	2 Ironmans, 1 1/2-Ironman, and 1 marathon	• IMs: 62, 71, 65 g·hr^{-1} • Marathon: 35 g·hr^{-1}	CHO was associated with finishing time for both IMs and marathon (r = -.55, r = -.45, r = -.49)	CHO was also positively associated with GI symptoms
Abbreviations: CHO, carbohydrate; f, female; GI, gastrointestinal; hr, hour; m, male.					

Author	Athlete/Study Characteristics	Event	Carbohydrate Intake	Comments
Glace et al. (2002a)	• 19 ultra-runners (18 m, 1 f) • Twelve hours pre-race diet record • In-race intake recorded by observers and recall	160-km trial race	• Pre-race: 450 g • In-race: 6.8 $g \cdot km^{-1}$	• 14 of the men and 1 woman finished • GI distress was unrelated to intake
Colombani et al. (2002)	• 26 competitors (sex not specified) • Recall completed after each stage	244-km race of road cycling, mountain biking, roller blading, swimming, and running	• Mt biking: 0.9 $g \cdot min^{-1}$ • Cycling: 1.1 $g \cdot min^{-1}$ • Roller blading: 0.1 $g \cdot min^{-1}$ • Swimming: 1.2 $g \cdot min^{-1}$ • Running: 0.9 $g \cdot min^{-1}$	12 men completed the race
Cox, Snow, & Burke (2010)	• 51 triathletes (36 m, 15 f) • Total 62 pre-race and 67 in-race assessments	Olympic-distance triathlons	• 25 and 23 $g \cdot hr^{-1}$ for males and females	Approximately 56% of CHO consumed during races was from gels
Stuempfle, Hoffman, & Hew-Butler (2012)	• 15 runners (10 m, 5 f) • Recall after each of several "laps" completed	161-km trail race	• Carbohydrate consumption was 0.65 and 0.45 $g \cdot kg^{-1} \cdot hr^{-1}$ for those without and with GI distress	• Fat and fluid intakes were higher in runners without GI distress vs. runners with GI distress • 9 had GI distress [nausea (89%), abdominal cramps (44%), diarrhea (44%), and vomiting (22%)]

Table 2-6. Studies quantifying diet during endurance running events

Abbreviations: CHO, carbohydrate; f, female; GI, gastrointestinal; m, male.

2.4.2 Gastrointestinal distress during endurance events.

Substantial laboratory and field research has revealed that both endurance exercise and food consumption during exercise are associated with an increased occurrence of GI distress (de Oliveira & Burini, 2009; de Oliveira & Burini, 2011; Ho, 2009). The incidence of GI symptoms during endurance exercise depends on a number of factors, including the intensity/duration of exercise, exercise modality, environmental conditions, personal history of GI symptoms, and quantity/composition of food/fluid ingested. Splanchnic blood flow generally decreases proportionally as exercise intensity increases, although chronic endurance training attenuates these effects (McAllister, 1998). Fecal blood loss can often be detected after endurance events, and the prevalence appears to be positively related to race distance. For instance, 87% of runners competing in a 100-mile ultra-marathon had microscopic evidence of blood in the stool (Baska, Moses, & Deuster, 1990) compared to 23% after a standard marathon (McCabe, Peura, Kadakia, Bocek, & Johnson, 1986). Likewise, a study exploring the prevalence of GI distress during various endurance competitions found that 30% of Ironman, 14% of Half-Ironman, and 4% of 26.2-mile marathon participants reported severe GI distress (>4 on a 0-9 scale; Pfeiffer et al., 2012). Running—as compared to cycling—seems to elicit more GI distress, at least when carbohydrate is consumed during exercise (Peters et al., 1993). A mechanical theory postulates that running causes GI distress via jostling, although little direct evidence exists to support this theory (Gil, Yazaki, & Evans, 1998). Indirect evidence comes from a study that showed abdominal acceleration/deceleration, as measured by an actometer, was more than doubled during running compared to cycling (Rehrer & Meijer, 1991).

One of the most important risk factors for GI distress during endurance exercise is a history of symptoms during training or previous competition. Pfeiffer et al. (2012) found that a history of GI symptoms was positively correlated with scores for upper and lower GI symptoms ($r = .37$ and $.51$) experienced during marathon and Ironman races. This field data confirmed observations from a series of randomized crossover studies comparing GI symptoms during 16-km runs (Pfeiffer et al., 2009). Participants consumed

various carbohydrate supplements during each trial, and scores on a 10-point GI symptom history questionnaire were moderately-to-highly correlated ($r = .46-.90$) with scores reported during the 16-km runs.

The quantity and composition of foods and fluids consumed during exercise can also have an impact on GI distress. Increasing fluid volume appears to increase gastric emptying up to a certain point, after which minimal gastric emptying increases are observed (Coyle & Montain, 1992; Costill & Saltin, 1974). Thus, large fluid volumes ($>1-1.5$ l·hr^{-1}) contribute to GI distress in some individuals. Conversely, too little fluid consumption resulting in severe dehydration may exacerbate GI symptoms; in one study, 80% of those who lost at least 4% of their body weight during a marathon experienced GI symptoms, whereas ~50% of those who lost less than 4% experienced GI symptoms (Rehrer, Janssen, Brouns, & Saris 1989). Reverse causality, however, may have contributed to these findings (e.g. those with GI symptoms may have been unable to consume adequate fluid). Carbohydrate concentration has an effect on gastric emptying and GI symptoms. Beverages above 12% concentration slow emptying of fluid from the stomach (Mitchell et al., 1989b) and cause symptoms of fullness and nausea, especially when consumed in hot/humid conditions (Davis, Burgess, Slentz, Bartoli, & Pate, 1988). While evidence during endurance events is limited, both fat and fiber consumption during exercise is often discouraged since they are inhibitors of gastric emptying under resting conditions (Hunt & Knox, 1968; Welch, Cunningham, & Read, 1988). The most supportive data for this comes from a retrospective study that interviewed 55 male triathletes regarding food and fluid consumption from their most recent half-iron triathlon (Rehrer, Van Kemenade, Meester, Brouns, & Saris, 1992a). A variety of in-race GI symptoms were associated with nutritional factors; pre-race fat intake was associated with nausea and pre-race fiber was associated with intestinal cramping. It must be noted, however, that the typical time gap between triathlon completion and the interviews was six to seven months, which could have severely affected accuracy. The use of post-race questionnaires is typical of most studies assessing GI distress, and given potential biases with recall, future studies should attempt to ascertain GI distress ratings during events.

2.5   Conclusion

Carbohydrate ingestion prior to and during endurance exercise appears to improve performance, although the magnitude of benefit varies substantially with several factors. Exercise lasting 60-90 min is less likely to benefit from carbohydrate ingestion, although small worthwhile differences may be difficult to detect given the typical sample sizes of most studies. Carbohydrate rinsing may be a worthwhile alternative to carbohydrate ingestion for events lasting between 45-75 min. The use of MTC to increase exogenous carbohydrate oxidation and improve performance has been an exciting advancement in sport nutrition research, but no observational studies to date have described MTC use during non-simulated events. Furthermore, running and women have largely been ignored in previous studies of MTC. Given the popularity of endurance running and the increasing participation by women, it is important to address these shortcomings in the literature.

3

Intake of Multiple Transportable Carbohydrates
during an Ultra-endurance Triathlon

Introduction

Carbohydrate ingestion during endurance exercise is purported to enhance performance in events lasting >60-90 min (Burke et al., 2011; Rodriguez et al., 2009). Recommendations for carbohydrate intake during exercise from the joint Position Stand of the ADA, ACSM, and Dietitians of Canada range from 30-60 g·hr,[-1] based on the observation that greater amounts increase the likelihood of GI distress without improving performance (Rodriguez et al., 2009). Emerging evidence, however, has demonstrated that supplying a mix of saccharides—referred to as MTC—can increase exogenous carbohydrate oxidation while lessoning the risk of GI distress when carbohydrate intakes exceed 50-60 g·hr^{-1} (Jeukendrup, 2010). Several pathways may be responsible for these observed benefits, including that glucose and fructose rely on separate, saturable intestinal transporters (SGLT1 and GLUT5; Wood & Trayhurn, 2003). Furthermore, highly-concentrated fructose or mixed saccharide solutions (10-15%) empty faster from the stomach than isocaloric glucose solutions (Guss et al., 1994; Sole & Noakes, 1989), which may be explained by the inhibitory-feedback effects glucose has on afferent nerves (Zittel et al., 1994) and SGLT1 transporters (Raybould & Zittel, 1995) in the small intestine. Beyond the GI effects, fructose ingestion at rest and during exercise leads to an increase in blood lactate through its up-regulation of pyruvate kinase (Jentjens et al., 2004a; Jentjens et al., 2004b; Macdonald et al., 1978), and this lactate can serve as substrate for oxidative metabolism during exercise (Miller et al., 2002).

At least 24 randomized experimental studies have examined the effects of MTC during exercise (Adopo et al., 1994; Baur et al., 2014; Clarke et al., 2012; Currell & Jeukendrup, 2008; Hulston et al., 2009; Jentjens et al., 2004a; Jentjens et al., 2004b; Jentjens et al., 2005; Jentjens et al., 2006; Jentjens et al., 2004c; Jeukendrup et al., 2006; Jeukendrup & Moseley, 2010; Lecoultre et al., 2010; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Pfeiffer et al., 2009; Riddell et al., 2001; Roberts et al., 2014; Rowlands et al., 2012; Rowlands et al., 2008; Tarpey et al., 2013; Triplett et al., 2010; Wagenmakers et al., 1993; Wallis et al., 2005), demonstrating that ingesting a mix of

glucose, fructose, and/or sucrose can increase exogenous carbohydrate oxidation and reduce the severity of stomach fullness (O'Brien & Rowlands, 2011), nausea (O'Brien et al., 2013; Tarpey et al., 2013), and abdominal cramps (Rowlands et al., 2012; Tarpey et al., 2013). While firm guidelines are not yet in place, it appears that a glucose-to-fructose ratio of 1.2:1 to 1:1 may be optimal for improving exogenous carbohydrate oxidation and reducing GI distress (Jentjens et al., 2005; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Rowlands et al., 2008). Despite these findings, several limitations in the research are apparent. All but two studies utilized cycling (Clarke et al., 2012; Pfeiffer et al., 2009), which is unfortunate given that GI distress tends to be more common during running (Peters et al., 1993). Pfeiffer et al. (2009) found no reduction in GI distress for runners ingesting a 2:1 glucose-to-fructose gel versus a 100% glucose gel during 16-km runs. A distance of 16-km, however, may not have been long enough for significant differences to emerge. Furthermore, only two studies were conducted in the field (Pfeiffer et al., 2009; Rowlands et al., 2012) and only one involved exercise lasting >4 hours (Jeukendrup et al. 2006), both of which are factors that may induce more frequent GI distress (Pfeiffer et al., 2012).

Presently, no studies have descriptively quantified the saccharide sources used by athletes competing in non-simulated endurance events. Likewise, no study has examined whether consuming a mix of saccharides is associated with reduced GI distress during an endurance event. Consequently, the purpose of this observational investigation was to quantify the saccharide sources used during a half-iron triathlon and to compare them to the recommendations from the MTC literature. A secondary purpose was to conduct an exploratory analysis to examine the associations between saccharide intake and GI distress. Specifically, we hypothesized that glucose intake would be positively associated with GI distress while fructose ingestion would be negatively associated with GI distress during the run among participants consuming ≥ 50 g·hr^{-1} of carbohydrate during the swim and bicycle.

Methods

Participants.

A convenience sample of individuals competing in the Chisago Lakes Half-Iron Triathlon (1.2-mile swim, 56-mile bike, 13.1-mile run; Chisago Lakes, Minnesota) was used. Participants that had competed in previous years' races and triathlon clubs were sent an email detailing the study requirements. Eligibility criteria were participation in at least one triathlon over the past year (≥Olympic distance), age 18-64 years, and agreement to bring only foods and fluids with a nutrition label for use during the triathlon (excluding water). Participants received a 50% discount on the registration fee as incentive to participate. The race was sanctioned by USA Triathlon, and informed consent was obtained from all participants using protocols approved by the University of Minnesota Institutional Review Board.

In-race nutrition assessment.

A variety of methods were employed to estimate the in-race intake of energy, carbohydrate, saccharides, fiber, fat, protein, sodium, fluid, and caffeine. Approximately three to four weeks prior to the triathlon, participants were sent several forms requiring them to document foods and fluids they planned consume during the race. Participants recorded brands, flavors, and amounts. For solid and semi-solid products, participants were restricted to bringing products that had packaging with a nutrition label and ingredient list, and foods that were homemade with multiple ingredients were prohibited. Participants submitted sample wrappers for each solid and semi-solid food they brought for consumption. For fluids, participants were allowed to transfer contents from original packaging to bottles but were required to record the brand, flavor, and amount. If the fluid was mixed (e.g. powder and water), participants provided the relative amounts of solid and fluid. Participants submitted these forms at a main research station one to four hours before the race start.

To quantify foods and fluids consumed from race aid stations, a combination of post-race recall and in-race measurement were utilized. For the bicycle leg, two aid

stations were available with bottled fluids, carbohydrate gels, and electrolyte tablets. Participants were instructed to mentally track the number of products taken and consumed from these stations. In addition, participants were asked to bring any bottles in their possession to the main research station for measurement post-race. To assess solid and semi-solid foods consumed from run stations, participants were provided with a list of available products and were instructed to mentally track the number of products taken and consumed. To assess fluid consumed from run stations, designated research stations were set-up to provide bottled fluids (water and carbohydrate-electrolyte beverage). Bottles with sport caps were pre-filled with 5.5 ounces (163 ml) of tap water or carbohydrate-electrolyte beverage and weighed on a digital scale to ± 2 g (iBalance 500; My Weigh, Vancouver, BC, Canada). Participants submitted bottles to study staff 25-50 m past aid stations, and bottles were labeled with stickers so that participants' race numbers could be recorded at drop-off. Bottles were reweighed post-race to estimate fluid consumed. Lastly, participants went through a checklist immediately post-race, during which they reported foods consumed from aid stations and those listed on pre-race forms. Participants were emailed within three days if clarification was required.

Saccharide quantification.

Several methods were utilized to estimate the amounts of glucose, fructose, and sucrose in foods and the amounts of each saccharide consumed by participants. First, ingredient lists—when available—were inspected to determine whether foods contained fructose or sucrose as a source of carbohydrate. Race-provided foods not coming in packages (e.g. fruit) were assumed to potentially contain fructose or sucrose. If packaged foods potentially contained fructose or sucrose, manufacturers were contacted to provide saccharide quantities. Manufacturers were not made aware of the purpose of the request. When manufacturers refused, samples were sent to an ISO/IEC 17025 accredited laboratory for analysis by high-performance liquid chromatography using the Association of Analytical Communities 977.20 method (Medallion Laboratories, MN; De Vries, Heroff, & Egberg 1979). Saccharides were reported as $g \cdot 100 \ g^{-1}$ of sample, with a detection level of 0.1%. To check validity, a sample containing 15 g each of glucose

(Cerelose, Ingredion, IL), fructose (Krystar 300, Tate & Lyle, IL), and sucrose (Domino Foods, NJ) was submitted. This analysis identified 32.2%, 32.6%, and 32.9% of the sample as glucose, fructose, and sucrose.

While many foods had only refined carbohydrate sources (maltodextrin, sucrose, crystalline fructose) on ingredient lists, some foods such as bars contained unrefined ingredients (whole grains, nuts). To estimate glucose from higher-chained carbohydrates in products with unrefined ingredients, total sugars and fiber were subtracted from total carbohydrate (TC). An additional 10% of TC was subtracted since an examination of similar foods from the United States Department of Agriculture (USDA) Database revealed that approximately 10% of TC was not identifiable (U.S. Department of Agriculture, 2012). Thus, the formula to determine glucose from starch and higher-chained sources in these foods was:

$$TC - fiber - total\ sugars - (0.1 \times TC)$$

This formula was applied to 28.8% of foods. Finally, the USDA Database provided an estimate of saccharides from fruits (U.S. Department of Agriculture, 2012). Lactose was not quantified since no food contained a significant amount. A glucose-to-fructose ratio was calculated for each food and beverage, with sucrose considered as an equal source of glucose and fructose. Products with multiple flavors without differing carbohydrate sources on ingredient lists were considered as one food (e.g. lemon and grape flavors of a beverage brand).

Gastrointestinal distress assessment.

GI distress was assessed in-race and post-race. For in-race assessments, participants rated overall GI distress on a 0-10 scale, where 0 meant "no discomfort," 5 meant "moderate discomfort," and 10 meant "unbearable discomfort." This methodology was chosen primarily for ease of implementation and logistical reasons, as recruitment

for the study would have been hampered by requiring extensive in-race interviews. Participants were verbally prompted to report GI distress at run miles 1 and 12.

More specific GI symptoms were solicited immediately after completion of the triathlon. Participants rated nausea, regurgitation/reflux, bloating/stomach fullness, gas/flatulence, lower abdominal cramps, and urge to defecate on the same 0-10 scale. Ratings were solicited for the bicycle and run legs separately, and participants were instructed to rate distress over the entire leg (not peak). Symptoms of nausea, regurgitation/reflux, and bloating/fullness were also combined into an upper GI distress category, while the symptoms abdominal cramps, gas/flatulence, and urge to defecate were combined into a lower category with scores ranging from 0-30.

Additional variables.

Pre-race questionnaires inquired about age, training practices, competition history, and GI distress history during training. Briefly, participants reported average weekly distances for swimming, cycling, and running over the past three months. Participants reported the number of previous half-irons completed, triathlon experience (years), and goal time. Frequency of GI distress over the last three months of training was solicited, with participants reporting each of the aforementioned six symptoms on a 0-4 scale from "never" to "almost always." Participants reported use of over-the-counter and prescription pain medications during the 48 hours prior to and during the triathlon, given the high prevalence of use in ultra-endurance athletes (Wharam et al., 2006) and their potential for GI damage (Warden, 2010).

Pre-race weight (within 15-45 min before race start) was measured to the nearest 0.1 kg using a digital scale (Model #7411; Taylor Precision Products, Oak Brook, IL) with participants wearing light clothing, no shoes, and no wetsuit. Upon race completion, participants immediately reported to the main research station to have their weight recorded. Height was self-reported. Finishing times were retrieved online, and overall and split times were documented. Finally, participants were asked about their awareness of MTC during the post-race interview. Specifically, they were asked, "Have you ever heard of the recommendation to consume products with multiple sugar types during races (mix

of glucose, fructose)?" If the participant answered yes, they were subsequently asked, "Did you attempt to meet that recommendation today?"

Statistical analysis.

Analyses were performed with SPSS version 21 (IBM, Armonk, NY). Data were assessed for normality using the Shapiro-Wilk test. The Pearson chi-square test was used for any comparisons between dichotomous variables. Descriptive statistics for non-normal data are presented as medians and interquartile ranges (IQR), while normal data are presented as means and standard deviations (SD). Foods and fluids consumed within 30 min of the triathlon start were included in the swim leg. Foods and fluids consumed during the first transition were included in the bicycle leg, while those consumed during the second transition were included in the run leg. GI distress scores were non-normally distributed with many zero values, making logarithmic transformation unfeasible. Thus, the data was converted into dichotomous categories. Participants reporting 0 for a symptom were considered as not experiencing that symptom while participants reporting >0 were considered as experiencing GI distress.

Descriptive information on the saccharide content of foods and beverages used during the race was summarized in several ways. The mean proportion of TC represented by glucose, fructose, and sucrose was quantified for each. Additionally, the proportion of products containing a glucose-to-fructose ratio of 1.2:1 to 1:1 was determined because this has been the optimal ratio in previous laboratory investigations (Jentjens et al., 2005; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Rowlands et al., 2008). Product flavors without significant differences in carbohydrate source were considered as one food product (e.g. lemon and grape flavors of a beverage brand).

Finally, an exploratory analysis between saccharides ingested and GI distress at run mile 1 was conducted. Since a minimum of 50 g·hr^{-1} is likely needed to show benefits of MTC (Adopo et al., 1994), a sub-analysis was conducted on participants consuming ≥50 g·hr^{-1} over the swim and bicycle. Using data from the swim and bicycle combined (while excluding run intake) ensured that the saccharide data preceded GI distress at run mile 1 in terms of temporality. Associations with GI distress at run mile 12 were not

examined because only a small proportion of participants maintained a carbohydrate intake $\geq$50 g·hr^{-1} for the entire race (27%) and run (22%). Square root transformations were done for glucose, fructose, sucrose, and combined-glucose (estimates including glucose from sucrose) to correct non-normal distributions. Point-biserial Pearson correlations were used to examine the associations between saccharide intake and incident GI distress at run mile 1. Associations between saccharides and GI symptoms reported post-race were not examined to minimize the inflation of type I error. Associations between saccharides and performance were not examined due to the large variation in finishing time and because nutritional factors explain only a small amount of performance variation (Atkinson et al., 2011), making detecting small-to-modest significant associations unlikely. A two-sided $p < .05$ was used for all statistical tests.

Results

Environmental and participant characteristics.

Temperature ranged from 51˚F at race start to 65˚F by the time the last participant finished. Mean relative humidity was 77%. Seventy-six participants were initially consented and enrolled in the study, and of those, 61 presented to the main research station during pre-race check-in. Fifty-four participants finished the triathlon and returned to the main research station post-race. Participant characteristics, including goal and actual finishing times, of these 54 individuals are presented in **Table 3-1**. The majority of men (83.7%) and women (63.6%) had previously completed a half-iron triathlon. Fifteen participants (27.8%) reported using pain medications 48 hours before or during the triathlon. Median finishing times for the entire race field were 5:34 and 5:59 for men and women, respectively, which were similar to our participants' finishing times.

	Men (*n* = 43)	Women (*n* =11)
Table 3-1. Demographic, anthropometric, training, and performance characteristics		
Age (years)	38.5 (9.4)	34.7 (9.1)
Height (cm)	180.1 (5.5)	168.8 (7.5)
Weight (kg)	79.0 (9.2)	61.3 (7.0)
BMI (kg·m^{-2})	22.3 (2.0)	19.7 (1.4)
Competition experience (years)	4 (3-7)*	3 (3-5)*
Previous half-irons (#)	2 (1-4)*	1 (0-2)*
Running volume (km·week^{-1})	38 (16)	39 (11)
Cycling volume (km·week^{-1})	146 (64)	163 (72)
Swimming volume (m·week^{-1})	4186 (2745)	5718 (2682)
Goal time (hr:min)	5:30 (5:00-6:10)*	6:00 (5:38-6:11)*
Finish time (hr:min)	5:27 (5:03-5:56)*	5:52 (5:29-6:12)*
Relative goal (actual ÷ goal)	1.01 (0.1)	0.98 (0.1)
Weight lost pre-to-post race (kg)	-1.7 (0.9)	-0.9 (0.7)
Mean (SD) or Median* (IQR).		

Food composition and saccharide intake.

Overall, 127 carbohydrate-containing foods and beverages were used during the triathlon. After considering multiple flavors, 80 foods and beverages were determined to have a unique saccharide profile. Seven (8.8%) contained a single saccharide based on ingredient lists. Saccharide profiles for the remaining were determined by HPLC, manufacturer data, and the USDA Database in 38 (47.5%), 31 (38.8%), and 4 (5.0%) cases. The median proportions of TC as glucose, fructose, and sucrose in these foods can be seen in **Table 3-2**. **Figure 3-1** shows the distribution of the foods and beverages by glucose-to-fructose ratio. Seven foods (8.8%) fell within a glucose-to-fructose ratio of 1.2:1 to 1:1, while over half (55.0%) had greater than a 3:1 ratio. The individual foods and beverages and categorization by glucose-to-fructose ratio are shown in **Table 3-3**.

Quantities of saccharides ingested during the triathlon—along with several other nutrients—are presented in **Table 3-4**. Glucose was consumed in the highest quantities

for each leg, with peak amounts during the bicycle (median: 29 g·hr^{-1}). The median glucose-to-fructose ratio ingestion over the entire race was 2.9:1 (2.2:1-5.3:1).

Table 3-2. Saccharide profile of the 80 foods and beverages used during the triathlon	
	Median (IQR)
Proportion of total carbohydrate as glucose	0.64 (0.38-0.75)
Proportion of total carbohydrate as fructose	0.05 (0.01-0.23)
Proportion of total carbohydrate as sucrose	0.10 (0.00-0.32)
Glucose-to-fructose ratio	3.4:1 (1.5:1-7.6:1)
Glucose-to-fructose ratio includes sucrose as an equal source of glucose and fructose	
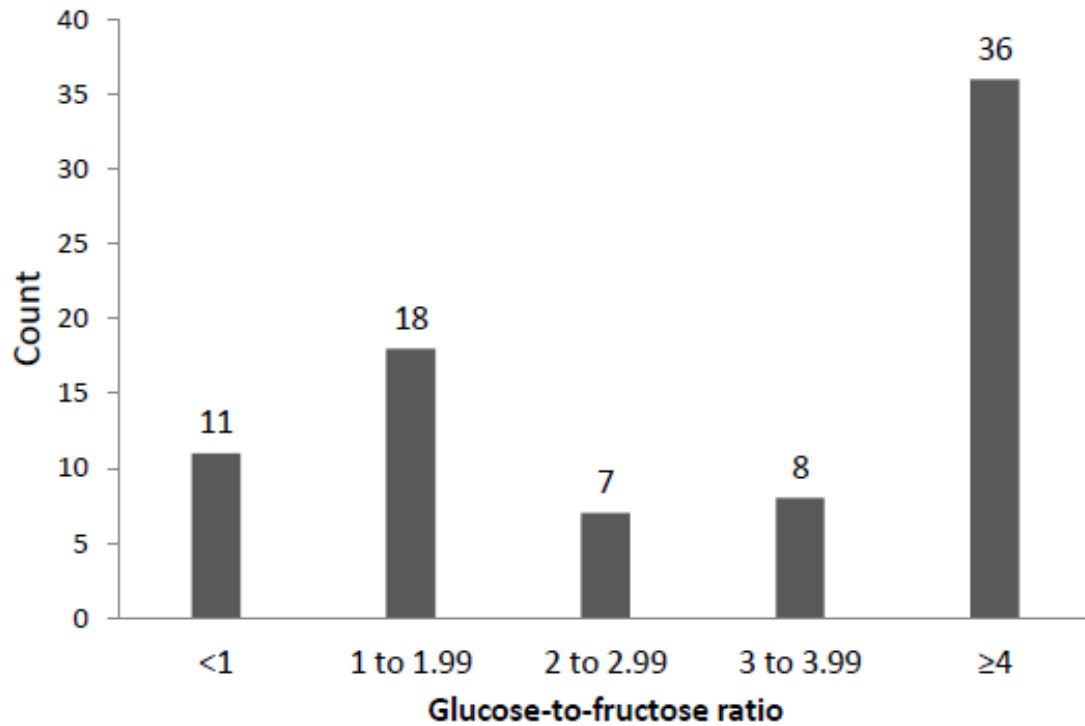
Figure 3-1. Glucose-to-fructose ratio distribution of the foods

Table 3-3. Glucose-to-fructose ratio categorization of the foods and beverages

Glucose-to-fructose ratio	Individual Foods and Beverages
< 1:1	Accelerade™ Orange; Accel Gel® Chocolate; Coca-Cola; GoGo squeeZ Apple Banana; Grapes; Hammer Bar™ Chocolate Chip; Honey Stinger™ Gel Ginsting; Powerade® (melon, mountain berry); Raw Revolution® Bar Chocolate Coconut Bliss; V-8® Juice; Vita CoCo® with Peach & Mango.
1:1 to 1.99:1	Banana; Cytomax® (cool citrus, tropical fruit); G2® Low Calorie Thirst Quencher (grape, raspberry melon); G2® Low Calorie Powder Grape; Gatorade Prime® Fruit Punch; Gatorade® Series Pro Orange; Gatorade® Thirst Quencher (cool blue, grape, lemon lime, orange, riptide rush); Gatorade® Thirst Quencher Powder Lemon Lime; Honey Stinger™ Energy Chews Fruit Smoothie; Nectarine; Pearson's® Salted Nut Roll; PowerBar® Perform Drink Lemon Lime; PowerGel® (berry blast, green apple, strawberry banana, vanilla); Skratch Labs™ Everyday Hydration Lemon Lime; Skratch Labs™ Exercise Hydration (lemon lime, pineapple); Kellogg's™ Special K Protein™ Bar Strawberry; Vita CoCo® Coconut Water; Zija xm³ ™.
2:1 to 2.99:1	Extreme Sports Beans® (assorted, pomegranate); GU Electrolyte Brew™ Lemon Lime; GU® Energy Gel (espresso love, mandarin orange, plain, strawberry banana, vanilla bean); GU® Energy Gel Chocolate Outrage; GU® Roctane Gel Chocolate Raspberry; PowerBar® Performance Energy Blasts Strawberry Banana; PowerBar® Performance Energy Bar (banana, chocolate).
3:1 to 3.99:1	Clif Shot® Gel (chocolate, double espresso); Fig Newtons; Gatorade® Prime Energy Chews (fruit punch, orange); GU® Energy Gel (cherry blaze, lemon sublime, tri-berry); GU® Roctane Drink; GU® Roctane Gel (blueberry pomegranate, cherry lime, vanilla orange); LARABAR uber® Roasted Nut Roll; Quaker® Chewy® Granola Bar Peanut Butter Chocolate Chip.
≥ 4:1	3Fu3l; Bonk Breaker (peanut butter and jelly, peanut butter and banana); CARBO-PRO; Clif Bar Blueberry Crisp; Clif Bar Chocolate Brownie; Clif Bar Chocolate Chip; Clif Bar Chocolate Chip Peanut Crunch; Clif Bar Coconut Chocolate Chip; Clif Bar Crunchy Peanut Butter; Clif Bar Oatmeal Raisin Walnut; Clif Bar Peanut Toffee Buzz®; Clif Bar White Chocolate Macadamia; Clif Shot Bloks® (black cherry, chocolate cherry, cran-razz®, margarita, mountain berry, orange, strawberry, tropical punch); e-Gel® Tropical Blast; EFS™ Sports Drink (fruit punch, lemon lime, grape); EFS™ Liquid Shot (kona mocha, vanilla); Fiber One® Bar Chocolate Peanut Butter; Fit & Active® Cheese Crackers; Generation UCAN™ Plain; Generation UCAN™ Cranberry-Raspberry; GU® Energy Gel Jet Blackberry; Hammer Gel® (apple-cinnamon, banana, orange, raspberry, tropical, unflavored, vanilla); Hammer Gel® (chocolate, espresso, huckleberry); Hammer HEED® (lemon lime, melon, orange); Hammer Perpetuem® Mix (orange-vanilla, strawberry-vanilla); Hammer Perpetuem® Solids (caffe latte, strawberry-vanilla); Hammer Recoverite® Citrus; Honey Stinger™ Waffle Chocolate; Infinit Custom Blend 1; Infinit Custom Blend 2; Infinit Go Far; Infinit Speed; LG1 Gel (concord grape/apple, goji/blueberry); Nature Valley™ Trail Mix Fruit and Nut; Peanut Butter Crackers; Smucker's® Uncrustable® Grape.
Product flavors without significant differences in saccharide profile are shown in parentheses.	

Table 3-4. Median intakes of selected nutrients during the triathlon				
	Total	**Swim**	**Bike**	**Run**
Energy (kcal·hr^{-1})	185 (124-233)	0 (0-146)	223 (168-302)	140 (70-202)
Carbohydrate (g·hr^{-1})	41 (28-55)	0 (0-28)	49 (35-69)	32 (17-47)
Glucose (g·hr^{-1})	23 (15-36)	0 (0-14)	29 (20-47)	15 (4-27)
Fructose (g·hr^{-1})	3 (2-6)	0 (0-1)	4 (1-10)	1 (0-6)
Sucrose (g·hr^{-1})	9 (5-13)	0 (0-1)	9 (2-15)	12 (7-19)
Combined glucose (g·hr^{-1})	30 (19-41)	0 (0-22)	35 (23-56)	22 (11-35)
Combined fructose (g·hr^{-1})	9 (6-13)	0 (0-6)	9 (5-16)	10 (4-15)
Fiber (g·hr^{-1})	0 (0-1)	0 (0-0)	0 (0-1)	0 (0-0)
Fat (g·hr^{-1})	1 (0-2)	0 (0-0)	2 (0-3)	0 (0-0)
Protein (g·hr^{-1})	2 (0-3)	0 (0-0)	3 (1-6)	0 (0-0)
Sodium (mg·hr^{-1})	235 (154-319)	0 (0-81)	276 (171-427)	170 (95-303)
Fluid (ml·hr^{-1})	446 (354-600)	0 (0-0)	502 (402-616)	493 (359-615)
Caffeine (mg·hr^{-1})	8 (0-20)	0 (0-0)	0 (0-20)	0 (0-21)
Values are presented as medians (IQR). Combined values include sucrose as a source of 50% fructose and 50% glucose.				

Gastrointestinal distress.

The occurrence of GI distress over the past three months of training is detailed in **Table 3-5**. The majority of participants reported never or rarely experiencing most symptoms; however, flatulence and urge to defecate were relatively common, although most participants still only experienced them rarely or occasionally. Frequency and medians of GI distress symptoms experienced during the triathlon are presented in **Table 3-6**. Two participants at run mile 1 and one at run mile 12 failed to report GI distress; thus, data from 52 and 53 participants are available for these ratings. Approximately 56% of participants reported GI distress at run mile 1, and the frequency increased to 89% by run mile 12. Median severity of GI distress increased from 1 (0-2) at mile 1 to 3 (1-5) by mile 12, with 26% of participants rating GI distress ≥5 by mile 12. Overall, GI distress severity reported post-race tended to be lower than in-race. However, the majority of participants reported at least some GI distress (>0) during the run for both upper and lower symptoms.

Table 3-5. Gastrointestinal distress over the past three months					
	Never	**Rarely**	**Occasionally**	**Frequently**	**Almost always**
Symptom					
Nausea	59.3%	33.3%	5.6%	1.9%	0%
Regurgitation/reflux	64.8%	22.2%	11.1%	1.9%	0%
Bloating/fullness	48.1%	38.9%	11.1%	1.9%	0%
Lower abdominal cramps	46.3%	38.9%	13.0%	1.9%	0%
Gas/flatulence	18.5%	27.8%	35.2%	14.8%	3.7%
Urge to defecate	35.2%	37.0%	24.1%	3.7%	0%

	% reporting any (>0)	Median (IQR)
Table 3-6. Gastrointestinal distress occurrence during the triathlon		
During the bicycle		
Nausea (0-10)	21%	0 (0-0)
Regurgitation/reflux (0-10)	24%	0 (0-0.3)
Bloating/fullness (0-10)	33%	0 (0-1)
Total upper (0-30)	53%	1 (0-3.3)
Lower abdominal cramps (0-10)	15%	0 (0-0)
Gas/flatulence (0-10)	21%	0 (0-0)
Urge to defecate (0-10)	7%	0 (0-0)
Total lower (0-30)	30%	0 (0-1)
During the run		
Run mile 1 overall (0-10)†	56%	1 (0-2)
Run mile 12 overall (0-10)†	89%	3 (1-5)
Nausea (0-10)	30%	0 (0-2)
Regurgitation/reflux (0-10)	24%	0 (0-0.5)
Bloating/fullness (0-10)	53%	1 (0-2)
Total upper (0-30)	72%	2 (0-4)
Lower abdominal cramps (0-10)	35%	0 (0-2)
Gas/flatulence (0-10)	41%	0 (0-2)
Urge to defecate (0-10)	23%	0 (0-0)
Total lower (0-30)	56%	2 (0-5)

GI symptoms during the triathlon were rated from "no discomfort" = 0 to "unbearable discomfort" = 10. Symptoms of nausea, regurgitation/reflux, and bloating/fullness were combined into upper category. Symptoms of abdominal cramps, gas/flatulence, and urge to defecate were combined into lower category.
†Two participants at mile 1 and one at mile 12 failed to report.

Associations between saccharide intake and gastrointestinal distress.

Of the 54 participants, 20 consumed ≥ 50 g·hr^{-1} of carbohydrate over the swim and bicycle (16 men and 4 women). The median glucose-fructose ratio of carbohydrate consumed over the bike and swim for these participants was 3.9:1 (2.4:1-7.4:1), and median intakes of glucose, fructose, and sucrose were 45 (38-54), 5 (2-11), and 11 (5-17) g·hr.$^{-1}$ Nine of these 20 participants reported GI distress at run mile 1, and the Point-biserial Pearson correlations between saccharide intakes and GI distress are shown in **Table 3-7**. There was a significant positive correlation between glucose intake and GI distress ($r = .480$, $p = .032$) and a significant negative correlation between fructose intake and GI distress ($r = -.454$, $p = .044$). With the inclusion of sucrose into glucose and fructose totals, only the association with glucose remained significant ($r = .469$, $p = .037$). GI distress was not significantly correlated with sodium, fluid, calorie, protein, or total carbohydrate (data not shown), which demonstrates that confounding by these factors was not obvious. Because of many zero values, correlations with fiber, fat, and caffeine were not examined. GI distress was not more common among participants using pain medications (n = 7) compared to those not using (n = 13) ($\chi(1) = 0.02$, $p = 0.888$). Median scores for upper and lower GI symptoms during training were 4 (3-4.5) and 6 (4-7) for participants not reporting GI distress at run mile 1, compared to scores of 5 (4-6) and 6 (5-7) for those that did report GI distress at run mile 1.

Table 3-7. Correlations between gastrointestinal distress incidence at run mile 1 and saccharide intakes during the swim and bicycle

	r coefficient	p-value
Glucose (g·hr-1)†	0.480*	0.032
Fructose (g·hr-1)†	-0.454*	0.044
Sucrose (g·hr-1)†	-0.115	0.631
Combined glucose (g·hr-1)†	0.469*	0.037
Combined fructose (g·hr-1)	-0.419	0.066
n = 20. Combined values include sucrose as a source of 50% fructose and 50% glucose. Significant correlations marked with (*). Values marked with (†) were square root transformed.		

Multiple transportable carbohydrate knowledge.

Thirty participants (55.6%) reported being aware of the recommendation to consume foods with multiple sugar types during races. Of these 30 participants, 16 (29.6% of the analytical sample) reported attempting to meet the recommendation. The median glucose-to-fructose ratio consumed over the entire race was 2.8:1 (2:1-5.3:1) and 3.4:1 (2.2:1-6.5:1) for participants that were aware and unaware of the MTC recommendations. The median glucose-to-fructose ratio of 16 participants that reported attempting to follow the recommendations was 3.3:1 (2:1-5.5:1).

Discussion

This is the first report to provide saccharide profiles of foods and beverages consumed during a sporting event and the first report to estimate the quantity of saccharides consumed by individual athletes. Research on MTC began nearly two decades ago (Adopo et al., 1994; Wagenmakers et al., 1993), and as outlined by Jeukendrup (2010), exogenous carbohydrate ingestion of up to 90 g·hr^{-1} may be well tolerated if a mix of saccharides is ingested. While firm guidelines are not yet in place, it appears that a glucose-to-fructose ratio of 1.2:1 to 1:1 may be optimal for improving exogenous carbohydrate oxidation and reducing GI distress (Jentjens et al., 2005; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Rowlands et al., 2008). In this convenience sample, the median glucose-to-fructose ratio of foods and fluids used was 3.4:1, and the vast majority of foods (91.3%) fell outside of the 1.2:1 to 1:1 range. Furthermore, over half of the foods and fluids had a glucose-to-fructose ratio greater than 3:1. As a result, the median glucose-to-fructose ratio of saccharides ingested by participants was 2.9:1. Interestingly, 55.6% of participants reported they had heard of MTC recommendations, and 29.6% said they actively attempted to use products with MTC. The median glucose-to-fructose intake for these individuals, however, was 3.3:1, which was similar to the entire sample median of 2.9:1. Given the complexity of asking about MTC knowledge, it is plausible that a number of participants misreported being

aware of MTC recommendations, and therefore, these estimates should be taken with caution.

This investigation also provides a detailed description of GI symptoms experienced during an endurance event. While not completely original, the use of in-race assessments has rarely been achieved in the past and represents a significant advancement, especially considering our relatively large sample size of 54. The validity of recall for many psychologically-based reports needs to be questioned, as they are susceptible to misreporting (Miranda, Gold, Gore, & Punnett, 2006). Since post-race GI distress ratings were mild in magnitude, it would be tempting to conclude that GI distress had little-to-no effect on race performance. In-race assessments, however, showed larger effects, as 26% of participants rated overall GI distress ≥ 5 by mile 12. Furthermore, mechanism analyses from previous studies provide evidence that mild GI distress may meaningfully impair performance (O'Brien & Rowlands, 2011; O'Brien et al., 2013).

Two previous studies have collected GI distress information during half-iron triathlons (Rehrer et al., 1992a; Pfeiffer et al., 2012). Rehrer et al. (1992a) conducted retrospective interviews on 55 men regarding their most recent half-iron, and mean carbohydrate intake during the race was 54 g·hr.$^{-1}$ A variety of nutritional factors were related to GI symptoms; pre-race fat intake was related to nausea, beverage osmolality during the bicycle was related to nausea/vomiting, and pre-race fiber was related to intestinal cramping. It must be noted, however, that the typical time gap between triathlon completion and the interviews was six to seven months, which could have severely affected the accuracy of diet and GI reports. A more recent study from Pfeiffer et al. (2012) used post-race email questionnaires to assess in-race nutrition for 43 participants (36 males, 7 females) of a half-iron triathlon in Germany, with the questionnaires being completed from several hours to two days post-race. Mean carbohydrate intake was 65 g·hr^{-1} for the entire race, 70-75 g·hr^{-1} for the bicycle leg, and 55-60 g·hr^{-1} for the run leg. Overall, 14% of the participants reported >4 on a 0-9 scale for at least one of 12 GI symptoms, and carbohydrate intake was modestly correlated with in-race flatulence ($r = .35$). Unlike the previous investigations, our study used on-site interviews and food

packaging samples to confirm products, both of which increase the likelihood of accurate reports.

A secondary aim of this study was to conduct an exploratory analysis of the associations between saccharide intakes and GI distress. This exploratory analysis was limited to individuals consuming ≥ 50 g·hr^{-1} during the swim and bicycle, which is likely the minimum threshold needed to observe differences (Adopo et al., 1994). Glucose intake—alone and after adding glucose from sucrose—was moderately positively correlated with GI distress at run mile 1. As hypothesized, fructose intake was negatively correlated with GI distress incidence; however, the association became borderline insignificant after including fructose from sucrose ($r = -.419$, p = .066). These observations could be explained by several mechanisms. Gastric emptying is slowed by concentrated beverages (>10% carbohydrate) containing glucose as the sole source of carbohydrate (Guss et al., 1994; Sole & Noakes, 1989), and glucose has an inhibitory-feedback effect on afferent nerves in the small intestine (Zittel et al., 1994). Furthermore, since glucose and fructose rely on separate intestinal transporters, consuming foods with a mix of each may speed absorption and reduce fluid secretion into the intestine, which may lesson symptoms of cramping and urge to defecate. This is supported by the observation that concentrated glucose solutions cause net fluid secretion into the intestine during exercise (Rehrer et al., 1992b).

There are several strengths to this study. The sample size was relatively large compared to other field-based studies that have examined in-race nutrition during ultra-endurance events (Fallon et al., 1998; Glace et al., 2002a), especially considering the thorough methodology used to assess in-race nutrition. The methodology used to assess fluid intake (especially during the run) is superior to methods used previously, particularly compared to reports that exclusively used recall (Downey & Hopkins, 2001; Pfeiffer et al., 2012; Rehrer et al., 1992a). The in-race GI assessments were also novel, given that most previous investigations have relied exclusively on post-race assessments (Pfeiffer et al., 2012; Rehrer et al., 1992a). Finally, the use of validated laboratory testing to quantify saccharide sources is a completely novel strategy in this setting.

As with any study, limitations should be mentioned. A convenience sample was used, and it is impossible to know how the nutrition intake of our 54 participants represented the entire race field. Finishing times for our sample, however, were similar to men and women in the entire field. The accuracy of the methodologies used to quantify the food saccharide compositions is not completely known. To some extent, the data is reliant on information provided by manufacturers, and while there is no specific reason to suspect misreporting, this possibility cannot be ruled out entirely. Information provided by manufacturers, however, was checked against ingredient lists (since ingredients are listed by weight). Furthermore, previous studies have noted that foods sold nationally are less likely to have label inaccuracies (Allison, Heshka, Sepulveda, & Heymsfield, 1993) and are usually accurate within 10% of listed calories and macronutrients (Jumpert et al., 2013). Notably, all of the packaged foods in this study were marketed and sold nationally. Moreover, the majority of the foods and beverages fell outside of a glucose-to-fructose ratio of 1.2:1 to 1:1, and small-to-modest inaccuracies in our methodology would not substantially change this fact, given that over half were estimated to contain a glucose-to-fructose ratio greater than 3:1. Finally, a causal relationship between saccharides ingested and GI distress cannot be absolutely inferred from these data because of the observational nature of the study. However, care was taken in the analysis to ensure that the temporal relationship between saccharide intake (during the swim and bicycle) and GI distress (run mile 1) was such that reverse causality is unlikely. Confounding by other factors, however, remains a possibility.

Conclusion

This is the first investigation to provide saccharide profiles for foods and beverages consumed during a sporting event. Practitioners and athletes can use the saccharide profiles herein to guide food and beverage selection for competition. In our convenience sample of half iron triathlon finishers, the majority of foods and fluids did not meet the recommendations for saccharide composition. As a result, the median

glucose-to-fructose ratio ingested by participants was 2.9:1. Likewise, a majority of participants reported they did not actively attempt to consume foods and beverages with a mix of saccharides. What's more, glucose intake was associated with GI distress incidence during the run among participants consuming a high rate of carbohydrate. While it is clear that MTC can increase performance and reduce GI distress during laboratory-based cycling, much is still unknown regarding their effects during non-simulated field events and events involving running. More field-based experimental and observational studies are needed to elucidate the practical efficacy of MTC during a variety of endurance events.

4

The Effects of Glucose-Fructose versus Glucose-Only on Metabolism, Gastrointestinal Comfort, and Performance during Prolonged Running

Introduction

Supplying a mix of saccharides—referred to as MTC—during prolonged exercise can increase exogenous carbohydrate oxidation while lessoning GI distress (Jeukendrup, 2010). Glucose and fructose utilize separate, saturable intestinal transporters (SGLT1 and GLUT5; Wood & Trayhurn, 2003), providing a biologically plausible mechanism for the improvements in exogenous carbohydrate oxidation and reductions in GI distress. Likewise, fructose ingestion leads to an increase in blood lactate concentrations through an up-regulation of pyruvate kinase (Jentjens et al., 2004a; Jentjens et al., 2004b; Macdonald et al., 1978), and this lactate can be oxidized by the muscle during exercise (Miller et al., 2002). Beyond its effect on lactate production, fructose can be converted to glucose or incorporated into glycogen in the liver (Sun & Empie, 2012). In addition, concentrated fructose solutions (10-15%) empty faster from the stomach than glucose solutions (Guss et al., 1994; Sole & Noakes, 1989) and may result in more rapid fluid delivery during exercise (Jeukendrup & Moseley, 2010; Roberts et al., 2014).

These separate mechanisms provide solid rationale for the use of MTC, and to date, at least 24 studies have examined the efficacy of MTC during exercise (Adopo et al., 1994; Baur et al., 2014; Clarke et al., 2012; Currell & Jeukendrup, 2008; Hulston et al., 2009; Jentjens et al., 2004a; Jentjens et al., 2004b; Jentjens et al., 2005; Jentjens et al., 2006; Jentjens et al., 2004c; Jeukendrup et al., 2006; Jeukendrup & Moseley, 2010; Lecoultre et al., 2010; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Pfeiffer et al., 2009; Riddell et al., 2001; Roberts et al., 2014; Rowlands et al., 2012; Rowlands et al., 2008; Tarpey et al., 2013; Triplett et al., 2010; Wagenmakers et al., 1993; Wallis et al., 2005). Despite the heterogeneity between studies, it appears that MTC increase exogenous carbohydrate oxidation by 20-60% and can reduce perceptions of stomach fullness (O'Brien & Rowlands, 2011), nausea (O'Brien et al., 2013; Tarpey et al., 2013), and abdominal cramps (Rowlands et al., 2012; Tarpey et al., 2013). In spite of these exciting findings, several limitations to the research need to be addressed. All of the studies but two (Pfeiffer et al., 2009; Rowlands et al., 2012) were conducted with men,

66

limiting generalizations that can be made to women. Furthermore, cycling was used in all but two studies (Clarke et al., 2012; Pfeiffer et al., 2009), which is unfortunate since GI distress tends to be more common during running (Peters et al., 1993). Neither of the studies that utilized running demonstrated significant benefits with MTC, but one was likely too short in duration (Pfeiffer et al., 2009) and the other did not feed a high rate of carbohydrate (>1.0 g·min^{-1}; Clarke et al., 2012). All but six studies (Adopo et al., 1994; Baur et al., 2014; Pfeiffer et al., 2009; Riddell et al., 2001; Rowlands et al., 2012; Wagenmakers et al., 1993) had participants fast for at least 10 hours or did not report pre-exercise nutrition. Finally, only two studies provided detailed information on beverage flavor characteristics, both of which reported differences in sweetness between conditions (Rowlands et al., 2008; O'Brien et al., 2013).

Based on these outlined shortcomings, this crossover study aimed to determine whether ingestion of MTC would alter performance, metabolism, GI symptoms, and psychological affect during prolonged running. The effects of a beverage containing glucose-fructose (GF; 55% maltodextrin/45% fructose) were compared to a glucose-only beverage (G; 55% maltodextrin/45% glucose) during 120 min of steady-state running. Both beverages supplied 1.3 g·min^{-1} of carbohydrate in a double-blind fashion, with the goal of matching sweetness. Following the 120-min steady-state period, participants completed a 4-mile TT to assess performance. The following hypotheses were examined:

1. GF will result in a faster 4-mile TT compared to G.
2. GF will result in less GI distress compared to G.
3. GF will result in improved psychological affect compared to G.
4. GF will result in greater blood lactate compared to G.
5. GF will result in greater total carbohydrate oxidation at the end of steady-state running compared to G.

Methods

Participants.

Participants were recruited from the Minneapolis-St. Paul area via flyers and emails to running groups. Eligibility criteria included the completion of at least one marathon within the past year (men, <210 min; women, <225 min), running ≥30 miles per week for the previous three months, and completion of at least two 20-mile runs over the past two months. Participants were required to complete a physical activity health screener and a University of Minnesota Institutional Review Board approved consent form. Participants were provided with $100 remuneration upon completion of the study.

General experimental design.

Each participant underwent two prolonged running tests, during which they consumed G and GF. The initial 120 min of each test consisted of sub-maximal running during which the carbohydrate beverages were consumed and outcome data were collected. Participants ran at a constant velocity during this 120-min protocol so that the effects of the beverages could be directly compared. After the completion of the 120-min protocol, participants completed a 4-mile TT to assess performance. Data collection began October 2013 and was completed by March 2014. A general overview of the study design is presented in **Figure 4-1**.

Baseline Visit
- Informed Consent
- Background questionnaire
- Hydrostatic weighing
- VO_{2peak} test

Pre-Visit 1
- Training log (5-days)
- Diet log (2 days)
- Taper training
- Consume provided meals night before and morning of

Visit 1
- 120-minute sub-max run
- 4-mile TT

Pre-Visit 2
- Training log (5-days)
- Diet log (2 days)
- Match training/diet
- Taper training
- Consume provided meals night before and morning of

Visit 2
- 120-minute sub-max run
- 4-mile TT

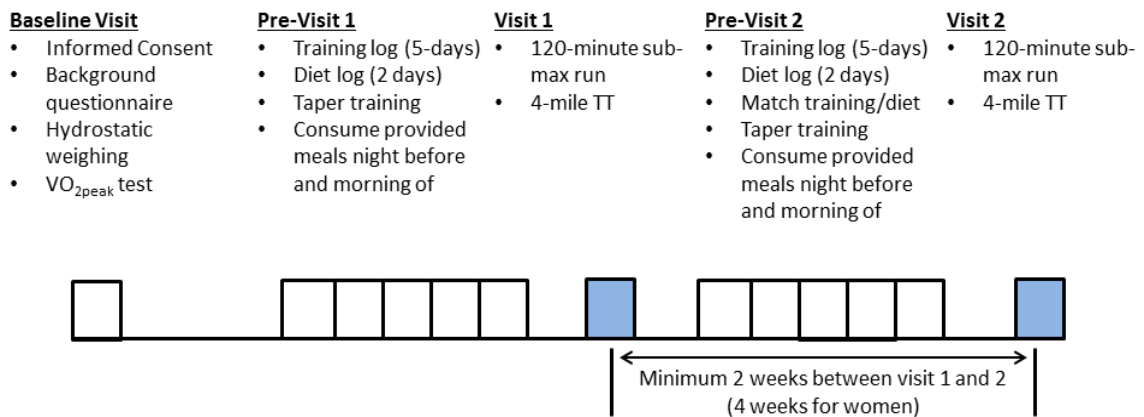Minimum 2 weeks between visit 1 and 2 (4 weeks for women)

Figure 4-1. Overview of the study schedule

Test beverages.

Participants were assigned to the beverages in a randomized, counter-balanced, crossover fashion. Beverages supplied carbohydrate at 1.3 g·min^{-1} during the sub-maximal period, since a rate <0.8-1.0 g·min^{-1} is unlikely to elicit physiologic or performance differences (Jeukendrup, 2010). GF was a 10.3% carbohydrate mixture (103 g per 1 kg tap water) containing maltodextrin (Star-Dri® 10, Tate & Lyle, Decatur, IL) and crystalline fructose (Krystar® 300, Tate & Lyle, Decatur, IL). The glucose and fructose were supplied in a 1.2:1 ratio (5.61% maltodextrin and 4.66% fructose) because four studies have indicated it is optimal for improving exogenous carbohydrate oxidation and GI distress (Jentjens et al., 2005; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Rowlands et al., 2008). G was a 10.3% concentration supplying carbohydrate solely as glucose. A 5.61% maltodextrin (Star-Dri® 10, Tate & Lyle, Decatur, IL) and 4.66% dextrose anhydrous (Cerelose®, Ingredion, Westchester, IL) mixture was used to achieve a comparable osmolality to GF. A concentration of 10.3% was chosen because previous investigations have demonstrated that gastric emptying is substantially reduced with higher concentrations (Mitchell et al., 1989b; Sole & Noakes, 1989). Moreover, fluid intakes for runners competing in events lasting 1-3 hours rarely exceed 600 ml·hr^{-1} (Rehrer et al., 1989; Pfeiffer et al., 2012; Rollo, James, Croft, & Williams, 2012), and 1000 ml·hr^{-1} of a traditional 6% carbohydrate beverage would be necessary to supply carbohydrate at ≥1.0 g·min.$^{-1}$ Both beverages contained sodium chloride (540 mg·kg^{-1} water) and lemon juice (9 g·kg^{-1} water). Since fructose is sweeter than glucose (Moskowitz, 1970), G was treated with aspartame (90 mg·kg^{-1} water).

Beverage ingredients were weighed to the nearest 0.1 g on a digital scale (iBalance 500; My Weigh, Vancouver, BC, Canada). The scale was calibrated with a 100 g weight before each use. To ensure researcher blinding, one investigator mixed both beverages at the same time in two identical containers, labeled them, and left the room. An individual not involved with the data collection subsequently chose one of the beverages by drawing assignments from sex-specific envelopes. Envelopes contained blocks of six for men and four for women. The process was repeated for the next visit, except that the opposite beverage was used.

Baseline visit.

Participants reported to the Human and Sport Performance Laboratory (HSPL) approximately one to four weeks before their first prolonged run and filled out a background questionnaire inquiring about demographics, training history, competition history, exercise-related GI symptom history, and menstrual status (for females). Height was taken without shoes to the nearest 0.1 cm with a stadiometer (Accustat Genentech, San Francisco, CA) and weight was recorded to the nearest 0.05 kg using a digital scale (ProDoc, Detecto Scale, Webb City, MO) with participants wearing light clothing. Hydrostatic weighing was used to estimate body density. Residual lung volume was estimated (Quanjer, 1983) and percent body fat was determined using the equation from Brozek, Grande, Anderson, and Keys (1963).

Participants completed a cardiorespiratory fitness test on a motorized treadmill (Pro XL, Woodway USA, Waukesha, WI) to determine VO_{2peak}. The protocol began with a 3-min walk at 3.1 mph and 0% grade. Subsequently, 1-min stages at 1% grade with 0.4 mph speed increases were used to achieve a speed equal to the participant's 5-km pace by the eleventh minute. The grade was increased by 1.5% every minute thereafter until volitional exhaustion.

Pre-test training and diet.

Participants recorded training-related activities for five days prior to each prolonged run. Diet was recorded with prospective records for two days before and the morning of each run. Pre-visit intakes of energy, carbohydrate, fiber, fat, and protein were calculated based on manufacturer information (if available) or the USDA Food Database (U.S. Department of Agriculture, 2012). Participants were asked to avoid strenuous physical activity and alcohol for 48 hours and caffeine 12 hours before visits. For the second prolonged run, participants were instructed to match their training and diet from the first prolonged run. To further standardize nutrition, participants were supplied two meals that were consumed the night before (between 5-7 p.m.) and morning of the test (2 hours before arrival). The meals were standardized against body mass as follows:

Table 4-1. Diet composition for two meals prior to the protocol				
Body weight (kg)	Energy (kcals)	Carbohydrate (g)	Fat (g)	Protein (g)
		Night Before		
<60	690	142	9	14
60-75	850	177	9	18
>75	1010	212	9	22
		Morning		
<60	380	77	5	10
60-75	480	96	7	14
>75	580	115	9	18

Respiratory gases.

A metabolic cart (Ultima Series, Medical Graphics Corporation, St. Paul, MN) measured breath-by-breath respiratory exchange of oxygen and carbon dioxide during the sub-maximal protocol. The gas sensor was calibrated using two gas mixes (21% O_2, 79% N_2; 5% CO_2, 12% O_2, 83% N_2), and a pneumotachograph was calibrated with a 3-liter syringe. During periods of respiratory gas collection, participants were fitted with a rubber mouthpiece (SDI Diagnostics, Easton, MA) attached to the pneumotachograph, and a nose clip was utilized to ensure breathing via the mouth. Oxygen consumption volume (VO_2), carbon dioxide expiration volume (VCO_2), and respiratory exchange ratio (RER) were calculated automatically by the software Breeze (Medical Graphics Corporation, St. Paul, MN). Rates of carbohydrate and fat oxidation were estimated using the exercise-specific stoichiometric equations from Jeukendrup and Wallis (2005):

Carbohydrate: $(4.210 \cdot VCO_2) - (2.962 \cdot VO_2) - 2.37 \cdot n$.
Fat: $(1.695 \cdot VO_2) - (1.701 \cdot VCO_2) - 1.77 \cdot n$.

VCO_2 and VO_2 were in $l \cdot min^{-1}$ and n (nitrogen excretion) was considered to be negligible.

Blood lactate and heart rate.

Capillary blood lactate was assessed using a handheld analyzer (Lactate Plus, Nova Biomedical, Waltham, MA). The Lactate Plus requires 0.7 mcl of blood and is reasonably valid and reliable compared to bench-top laboratory analyzers (Hart, Drevets, Alford, Salacinski, & Hunt, 2013; Tanner, Fuller, & Ross, 2010). The meter was tested monthly with control solutions to ensure calibration. Since lactate readings can vary between test strip batches, strips from one lot were used for each subject. The same meter and skin cleaning protocol were used for all tests. Briefly, the finger was cleaned with an alcohol pad and a damp cotton pad was used to remove excess alcohol. The finger dried for 1 min, after which the treadmill was stopped and the participant's finger was immediately pricked with a lancet device.

HR was recorded with a chest-strap monitor for the duration of the protocols (Polar, Kempele, Finland). The validity of HR monitors using chest-based electrodes is exceptionally high (Achten & Jeukendrup, 2003).

Psychometric scales.

The Feeling Scale (FS) is an 11-point bipolar scale that assesses pleasure and displeasure with descriptors of "very bad" at -5, "neutral" at 0, and "very good" at +5 (Hardy & Rejeski, 1989). Although the FS is related to the frequently used Borg Rating of Perceived Exertion (RPE; Borg, 1970; Borg, 1982), it is believed to capture a slightly different affect construct (Hardy & Rejeski, 1989). In support of this, Backhouse, Bishop, Biddle, and Williams (2005) evaluated RPE and FS during two hours of cycling while participants consumed a carbohydrate beverage or placebo on two occasions. Carbohydrate ingestion maintained FS ratings in comparison to placebo, while RPE did not differ between conditions over most of the exercise. Consequently, we believed that differences between conditions would be more likely with the FS than RPE during constant-velocity exercise.

A number of common GI symptoms during running have been reported in previous investigations (Peters et al., 1993; Peters et al., 1999; Too et al., 2012). The following symptoms were used based on an analysis of relevant studies: (1) nausea, (2)

belching/regurgitation/reflux, (3) bloating/fullness, (4) gas/flatulence, (5) lower abdominal cramps, and (6) urge to defecate. A 7-point scale with anchors ranging from "no discomfort" at 1 to "very severe discomfort" at 7 was used. The 7-point scale and accompanying descriptors approximated those from the Gastrointestinal Symptom Rating Scale, which has been validated previously (Revicki, Wood, Wiklund, & Crawley, 1998).

To assess participant blinding, participants were asked to rate beverage sweetness, saltiness, and overall likability on a labeled hedonic scale (LHS; Lim, Wood, & Green, 2009; Lim & Fujimaru, 2010). Sweetness and saltiness scores ranged from 0 to +100 ["neutral" to "most (sweet or salty) sensation imaginable"] while overall likability ranged from -100 to +100 ("most disliked sensation imaginable" to "most liked sensation imaginable"). The LHS has several advantages over traditional hedonic scales, including that it more frequently satisfies parametric assumptions and is resistant to end effects (Lim & Fujimaru, 2010). LHS ratings were completed at rest as well as during the sub-maximal protocols.

Familiarization.

Participants were familiarized to the FS during VO_{2peak} testing, and were provided with verbal descriptions of GI symptoms and were visually shown the 7-point scale prior to the protocols. Participants were accustomed to the rubber mouthpiece used for gas collection prior to the runs. A full familiarization of the prolonged runs, however, was not completed for several reasons. Based on feedback, recruitment would have been hampered had participants been required to complete three full trials instead of two. In addition, all participants had significant experience running on treadmills since they resided in a cold climate. Finally, the counter-balanced design mitigated order effects, since any participant learning was balanced equally between treatments (Hopkins, 2003).

Sub-maximal running protocol.

Participants completed two sub-maximal, constant-velocity, 120-min runs separated by at least 14 days. For women, the objective was to schedule the runs 25-31 days apart since menstrual phase can influence substrate oxidation (Hackney, Curley, &

Nicklas, 1991; Lebrun, McKenzie, Prior, & Taunton, 1995; Zderic, Coggan, & Ruby, 2001). Participants reported to the HSPL between 6:00-9:00 a.m. for their first prolonged run and subsequently reported within one hour of the same time for their second prolonged run. Temperature and relative humidity were within a relatively narrow range for all tests (22.5-25.3 ºC; 6-19%). Upon arrival, participants voided, if necessary, and were weighed while wearing dry light clothing. Participants then changed into exercise attire, so that the clothing worn for weighing remained dry for post-exercise weighing.

Participants' resting GI symptoms, FS ratings, and HR were recorded 25 min before starting the sub-maximal protocol. Next, participants consumed the first beverage dose supplying 55.4 g of carbohydrate (~600 ml) over a period of 5 min while they simultaneously rated the beverage on the LHS. Ten minutes before the start of the sub-maximal protocol, participants completed a 5-min warm-up, after which they rested for 5 min and were asked if any clarifications regarding the protocol were needed. Treadmill velocity was set at 85-90% of the average pace from participants' most recent marathon. Previous marathon time was used to set intensity because the percentage of VO_{2peak} that can be sustained during prolonged running varies between 60-75% (Maughan & Leiper, 1983), and therefore, choosing an arbitrary value (e.g. 70% VO_{2peak}) may have led to some participants being either over- or under-challenged. Participants subsequently consumed beverage doses after 20, 40, 60, 80, and 100 min of running, and immediately after the sub-maximal protocol. The feedings at 20, 40, 60, and 80 min provided 18.4 g of carbohydrate while the feedings at 100 min and the finish provided 14.7 and 11 g, respectively. The feeding volumes decreased over time because it was the most tolerable strategy during pilot testing. Treadmill velocity was slowed to 75% of marathon pace for up to 2 min while participants consumed the beverages. Beverages were kept at 2.8-4.0 °C until 15 min before the first dose was consumed. Beverages were administered in 480-ml plastic bottles with sport caps to minimize spillage. The weight of any remaining beverage was recorded immediately after the last dose was administered, with a consumption goal of 1682 g.

At specified intervals, respiratory gases (5, 91, 117 min), HR/FS/GI symptoms (-25, 10, 30, 50, 70, 90, 110 min), and LHS ratings (-20, 20, 60, 100 min) were collected. Respiratory gases were collected and averaged over 2 min, while HR was recorded every 20 sec over 1 min. Blood lactate was taken at 55 and 115 min. A fan for cooling was placed adjacent to the treadmill and set at medium velocity. Treadmill belt velocity was verified every two weeks with a tachometer (RPM33, Extech Instruments, Nashua, NH) to ensure there were no significant deviations over the study.

4-mile time trial.

Participants completed a 4-mile TT after the 120-min sub-maximal protocol to evaluate performance. TT tests are the preferred method to assess performance, since they have a lower coefficient of variation compared to TTE tasks (Laursen et al., 2007). After the sub-maximal protocol, the treadmill was stopped for 2 min to allow participants to consume the last beverage dose, allow participants to void, repeat instructions, and reset the treadmill distance display. Participants were instructed to complete 4 miles as fast as possible and were told they could change the treadmill velocity as frequently as desired. They were told they could use the restroom, if necessary, but that it would count against their time. The restroom was located in close proximity to the treadmill (~15 ft). Participants were unable to view time elapsed but were able to see distance covered. Interaction between the investigators and participants was limited to soliciting FS ratings and GI symptoms, and no encouragement was provided. FS ratings and HR were recorded at miles 0.5, 1.5, 2.5, 3.5, and 4. GI symptoms were solicited at miles 0.5 and 3.5. After the TT, participants dried off with a towel and changed into dry clothing for weighing. Finally, participants were asked to indicate (yes or no) whether they would consider using the beverage during training or competition.

Statistical analysis.

An approach that reports uncertainty of outcomes as 90% confidence limits (CL) was utilized to evaluate treatment effects. This approach, referred to as inferential statistics, calculates effects with 90% CL and interprets them in relation to the smallest

worthwhile effect (Batterham & Hopkins, 2006). Interpretation is done using probabilities (chances) that the true (population) effect is greater, trivial, or lower in relation to the smallest worthwhile effect. The use of inferential statistics is advantageous because within-person variability for athletic performance is small and conventional statistics are insensitive to small effects in this setting. Moreover, this approach helps interpret the practical meaningfulness of the results (Batterham & Hopkins, 2006). Effects, 90% CL, and chances that effects were positive, trivial, or negative were calculated using a specifically-designed spreadsheet for post-only crossover trials (Hopkins, 2006b). The smallest worthwhile effect for performance was set at 0.8%, using the recommendation of 0.3 times the co-efficient of variation (~2.5%) for endurance running performance (Hopkins, 2004; Hopkins & Hewson, 2001). For physiological measures, GI distress, and FS ratings, differences were interpreted using a Cohen effect (Cohen, 1988), calculated with the between-subject standard deviations. Chances that the true value of the effects were at least small (Cohen = 0.2) were quantified. Chance thresholds for all variables were accompanied by qualitative descriptors: <1%, almost certainly not; 1-4%, very unlikely; 5-24%, unlikely; 25-74%, possibly; 75-94%, likely; 95-98%, very likely; ≥99%, almost certain. If the chances of positive and negative effects were both >5%, the effect was considered unclear.

Performance times and physiological measures were natural log-transformed based on recommendations from Hopkins (2003), and performance times were back-transformed to obtain percentage differences between conditions. Peak GI ratings and LHS ratings were percentile rank-transformed because of resistance to log-transformation. Nadir and change (rest – 110 min) FS ratings were used for the sub-maximal protocol (instead of every time point) to limit the number of inferences. Average FS ratings were used for the TT since they were normally-distributed and nadir values for the TT were not. Effects for all outcomes were calculated using the entire sample, while TT performance was also examined sex-specifically. Sex-specific effects were not done for other outcomes because the number of inferences would have increased drastically, and TT performance was the main study outcome. To account for any order (learning)

76

effect on TT performance, differences in finishing time (G minus GF) were also analyzed separately for groups based on randomization sequence (G/GF and GF/G). The independent effects were then combined using a spreadsheet that accounts for order effects (Hopkins, 2006a).

TT data for two participants was excluded. One participant experienced hip pain that prevented running during the latter half of his second TT, whereas a treadmill malfunction occurred during another participant's second TT, such that the treadmill stopped on three occasions without the participant's action. Notably, this malfunction was fixed and did not occur again. Additionally, one participant's first TT was winsorized (replaced with a value equal to two standard deviations from the mean) because it was an outlier, even after log-transformation. She used the restroom because of a severe urge to defecate. Gas exchange for one participant was not available due to a computer problem. Finally, blood lactate was not available for two participants at 55 min and five participants at 115 min due to inadequate sample volume, which occurs for up to 10% of Lactate Plus readings (Hart et al., 2013).

To maximize ease of interpretation, means (± standard errors) for normal-data and medians (inter-quartile ranges) for non-normal data are presented for outcome variables (including variables transformed for inferential statistics). Normality was assessed via the Shapiro-Wilk test. Descriptive statistics were generated using SPSS version 22 (IBM, Armonk, NY).

Results

Sample characteristics.

A total of 26 participants (17 men, 9 women) were enrolled in the study (**Figure 4-2**). Five participants completed only the baseline visit, and reasons for not presenting to further visits included a personal medical issue (n = 1), personal reasons (n = 1), loss to follow-up (n = 2), and because the fluid volume would not have been tolerable for their size (n = 1). One woman failed to complete the second prolonged run due to self-reported over-training (occupation as a fitness instructor). Characteristics of the 20 completers (14

men, 6 women) are presented in **Table 4-2**. Randomization was successfully counter-balanced among study completers, with 10 participants randomized to G first and 10 participants randomized to GF first. Randomization was also counter-balanced for each sex.
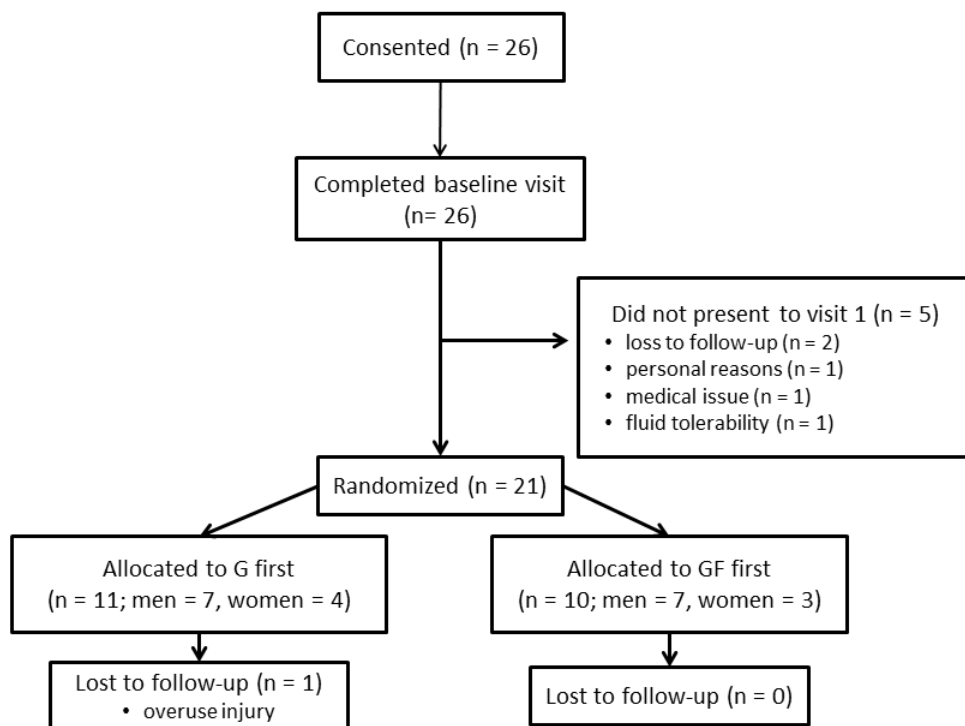
Figure 4-2. Flow of participants through the study

Table 4-2. Participant physical and performance characteristics		
	Men (n = 14)	**Women (n = 6)**
Age (years)	35.8 (2.2)	31.3 (2.9)
Height (cm)	179.6 (1.7)	165.9 (1.6)
Weight (kg)	73.8 (1.9)	59.9 (1.5)
BMI (kg·m^{-2})	22.9 (0.5)	21.8 (0.5)
Body composition (% fat)	13.0 (1.4)	19.1 (1.7)
Personal best marathon (min)	182 (2)	201 (6)
Most recent marathon (min)	191 (4)	213 (4)
Marathon experience (#)	13 (2)	12 (4)
Running volume (miles·week^{-1})	45 (4)	44 (5)
VO$_2$peak (ml·kg^{-1}·min^{-1})	58.7 (1.9)	55.0 (2.4)
Values expressed as mean (SE).		

Environmental, time, and dietary control.

Mean temperatures during the G and GF visits were 23.4 ± 0.1 and 23.6 ± 0.2 ºC, while median relative humidity was 7% (7-9) for both visits. A median of 23 (15-33) days elapsed between visits for men, while all women completed visits within 26-29 days. Intakes of energy, carbohydrate, fiber, fat, and protein over the two days prior to the trials are shown in **Table 4-3**.

Table 4-3. Pre-visit energy and macronutrient intake by condition		
	G	**GF**
Energy (kcals)	5318 (256)	5300 (204)
Carbohydrate (g)	779 (39)	770 (28)
Carbohydrate (g · kg body mass^{-1})	11.0 (0.5)	10.9 (0.4)
Fiber (g)	77 (5)	74 (4)
Protein (g)	208 (14)	223 (17)
Fat (g)	159 (11)	155 (12)
Values expressed as mean (SE) and summed for two days before and morning of visit.		

Time trial performance.

Finishing times for the 4-mile TT ranged from 23:50 to 35:37, and mean finishing times for G and GF were 28:46 ± 0:44 and 28:11 ± 0:44. Men completed the TT faster than women (27:34 vs. 31:08 for G and 27:08 vs. 30:17 for GF), while finishing times for visits 1 and 2 were 28:54 ± 0:46 and 28:02 ± 38, respectively.

Respiratory gases and substrate metabolism.

Respiratory gases and calculated rates of carbohydrate and fat oxidation are shown in **Table 4.4** and **Figure 4-3**. VCO_2 and RER tended to decline from 5 min to 117 min, resulting in increased fat oxidation rates over time. VO_2 remained relatively stable over the duration of the sub-maximal protocol. Participants exercised, on average, at 64-65% of VO_{2peak} during G and GF, providing support that the use of marathon time to set intensity was appropriate and comparable to other MTC studies.

Table 4-4. Gas exchange data during the sub-maximal protocol						
	5 min		**91 min**		**117 min**	
	G	**GF**	**G**	**GF**	**G**	**GF**
VO_2 (l·min^{-1})	2.64 (0.10)	2.68 (0.10)	2.64 (0.10)	2.67 (0.10)	2.64 (0.09)	2.68 (0.10)
VCO_2 (l·min^{-1})	2.43 (0.09)	2.43 (0.09)	2.35 (0.09)	2.37 (0.09)	2.31 (0.09)	2.32 (0.08)
RER	0.92 (0.01)	0.91 (0.01)	0.89 (0.01)	0.89 (0.01)	0.88 (0.01)	0.87 (0.01)
% VO_{2peak}	64.1 (0.01)	65.1 (0.01)	64.3 (0.01)	64.9 (0.01)	64.1 (0.01)	65.1 (0.01)
Values are expressed as mean (SE). Data not available for one participant. Abbreviations: RER, respiratory exchange ratio.						
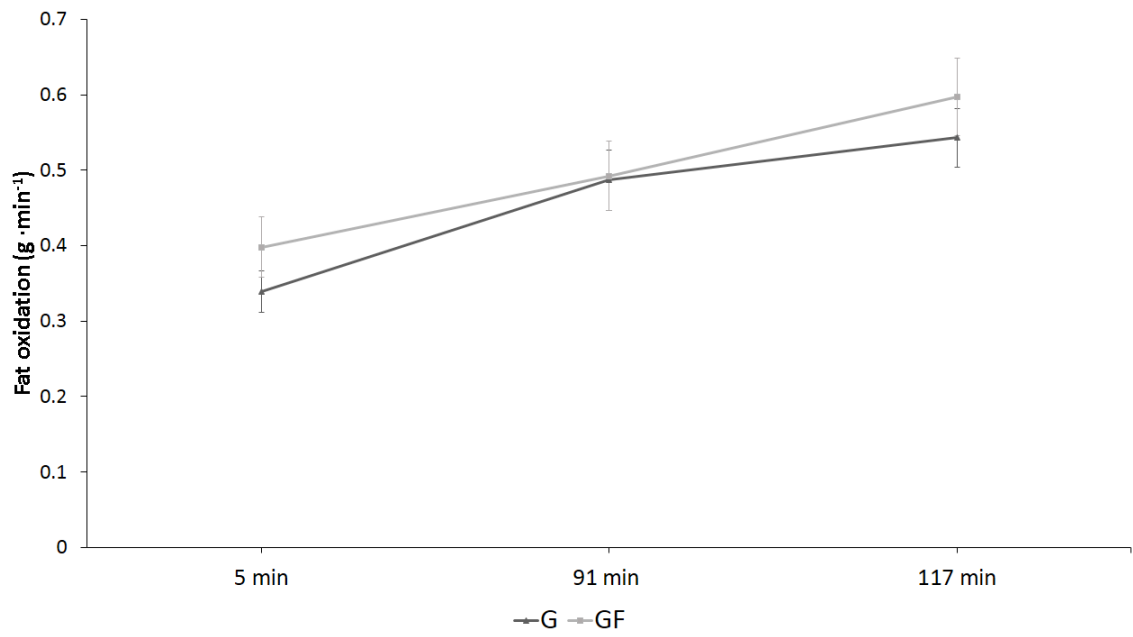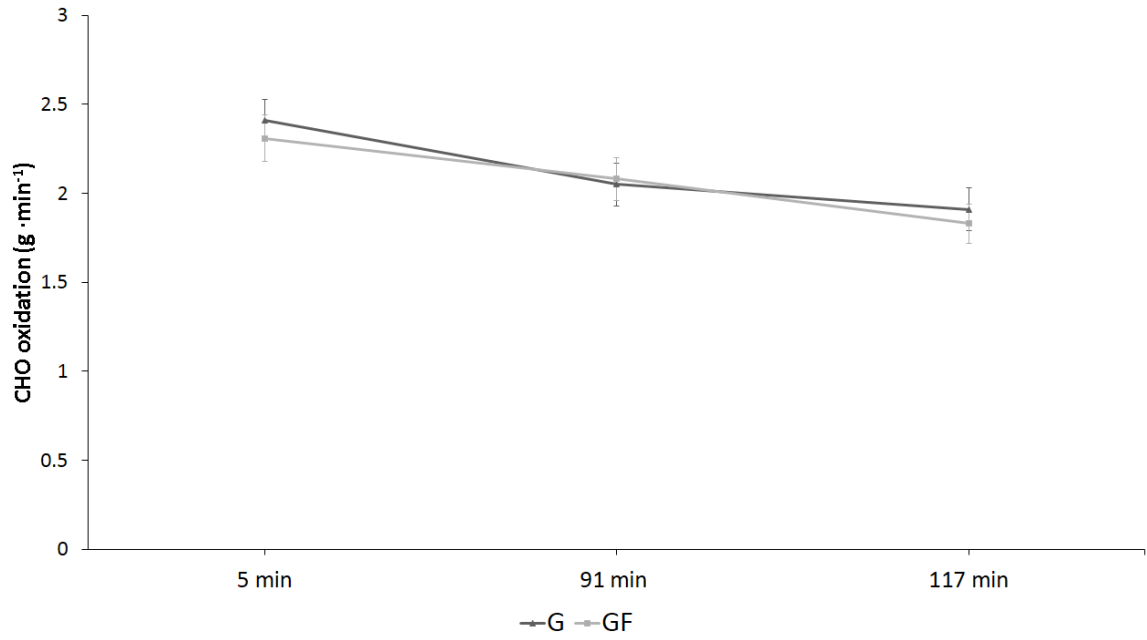
Figure 4-3. Carbohydrate and fat oxidation during the sub-maximal protocol

Blood lactate and heart rate.

Median (IQR) blood lactate concentrations at 55 min were 2.3 (1.6-3.4) and 1.9 (1.4-3.3) mmol·l^{-1} for G and GF, respectively. Lactate concentrations dropped to 1.9 (1.3-2.7) and 1.7 (1.4-3.0) mmol·l^{-1} for G and GF at 115 min. Mean HR over the sub-maximal protocol was 145.4 ± 2.3 and 144.8 ± 2.1 b·min^{-1} for G and GF, respectively. During the 4-mile TT, mean HR was 167.9 ± 2.6 and 168.3 ± 2.5 b·min^{-1} for G and GF.

Psychometric scales.

Incidence of GI distress is shown in **Table 4-5**. Values are reported as frequencies of experiencing any symptoms (>1) and at least mild symptoms (≥3) for the sub-maximal protocol and TT. FS ratings during the sub-maximal protocol and TT are shown in **Figure 4-4**. Median LHS ratings for beverage sweetness, saltiness, and overall likability are presented in **Figure 4-5.**

Additional data.

Mean amounts of beverage consumed for G and GF were 1660 ± 2 g and 1659 ± 2 g, respectively. Again, the consumption goal was 1682 g. The apparent 20 g difference between actual and goal consumption was likely due to small amounts of beverage remaining in bottles after each administration. Fifteen of 20 (75%) participants reported they would consider using G during training or competition, while 16 of 20 (80%) reported they would consider using GF. Body weight decreased by 1.8 ± 0.1 kg for both trials.

Table 4-5. Incidence of gastrointestinal distress	# reporting >1 (%)		# reporting ≥3 (%)	
	G	GF	G	GF
Sub-maximal (n = 20)				
Nausea	3 (15%)	1 (5%)	1 (5%)	1 (5%)
Belching/regurgitation/reflux	13 (65%)	9 (45%)	2 (10%)	1 (5%)
Fullness/bloating	14 (70%)	10 (50%)	6 (30%)	3 (15%)
Lower abdominal cramps	9 (45%)	8 (40%)	3 (15%)	1 (5%)
Gas/flatulence	7 (35%)	4 (20%)	3 (15%)	0 (0%)
Urge to defecate	4 (20%)	3 (15%)	3 (15%)	0 (0%)
Time Trial (n = 18)				
Nausea	4 (22%)	1 (6%)	1 (6%)	1 (6%)
Belching/regurgitation/reflux	4 (22%)	4 (22%)	0 (0%)	0 (0%)
Fullness/bloating	5 (28%)	4 (22%)	3 (17%)	1 (6%)
Lower abdominal cramps	7 (39%)	5 (28%)	3 (17%)	3 (17%)
Gas/flatulence	5 (28%)	4 (22%)	2 (11%)	1 (5%)
Urge to defecate	4 (22%)	2 (11%)	3 (17%)	1 (5%)
GI symptoms rated from "no discomfort" = 1 to "very severe discomfort" = 7. Based on peak values reported.				
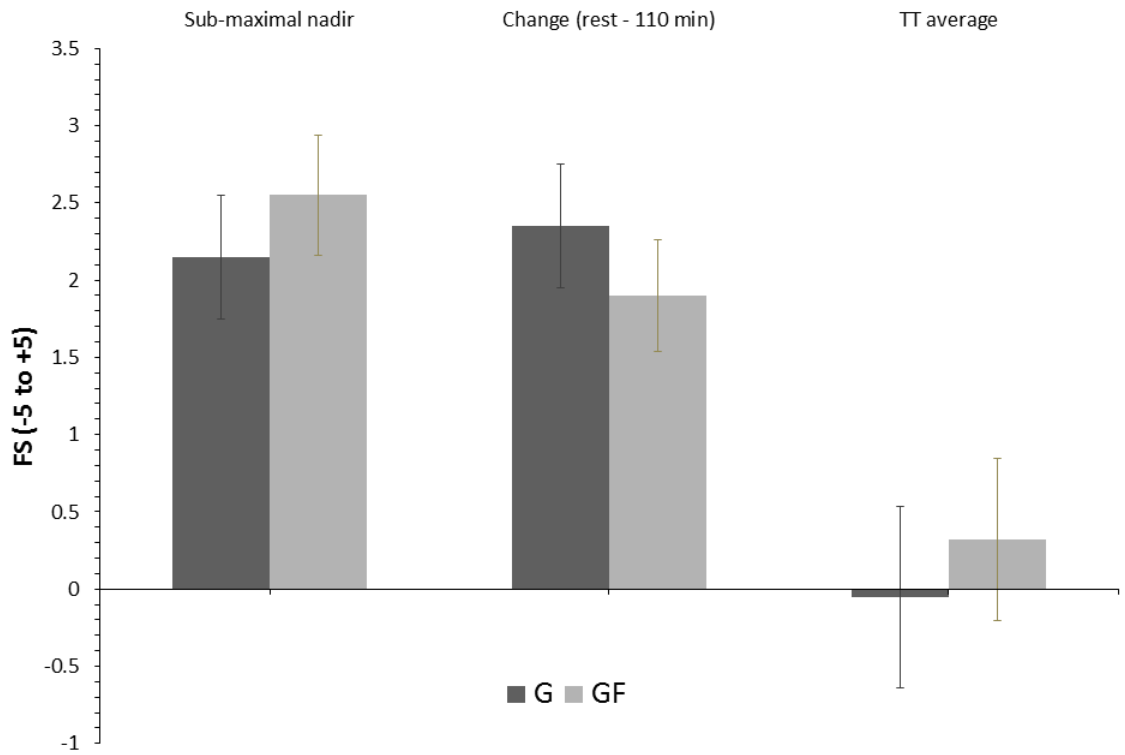
Figure 4-4. Feeling Scale ratings during the sub-maximal protocol and time trial
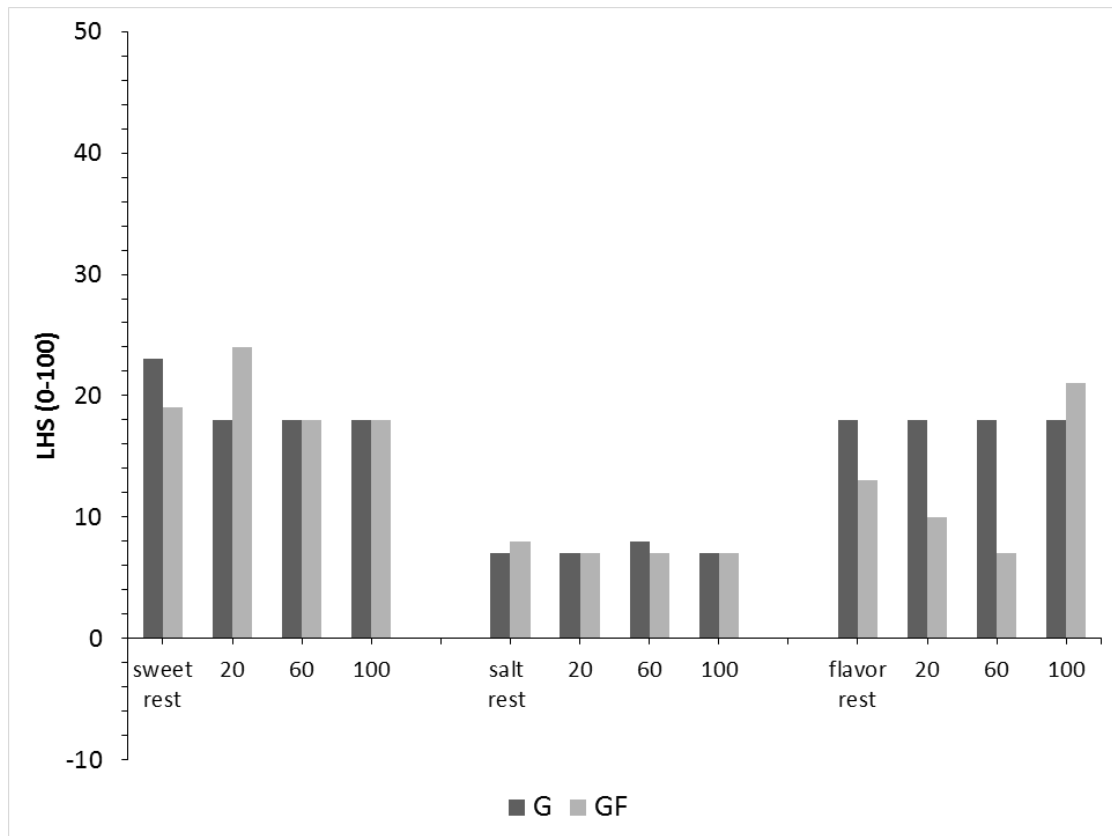
Figure 4-5. Median LHS ratings of beverages at rest and during the sub-maximal protocol

Inferential statistics.

Effect sizes and qualitative inferences for 4-mile TT performance are presented in **Table 4-6** for the entire sample and by sex. Participants completed the 4-mile TT 1.9% (-1.9; -4.2, 0.4) faster with GF compared to G, and there was 79% chance that the true population effect was at least 0.8%. The effect was similar after accounting for order effects (-2.2; -4.3, -0.1). While the effects were in the same direction for men and women, the effect size for women was slightly larger (-2.6; -8.1, 3.1) than for men (-1.6; -4.2, 1.2).

Table 4-6. Inferential statistics for 4-mile time trial performance					
	G¥	**GF¥**	**% Difference (90% CL)†**	**Chances of GF being higher, trivial, and lower relative to G‡**	**Interpretation**
Combined data (n = 18)§	28:46	28:11	-1.9 (-4.2, 0.4)	3%, 18%, 79%	Likely lower
Men (n = 12)	27:34	27:08	-1.6 (-4.2, 1.2)	8%, 24%, 68%	Unclear
Women (n= 6)	31:08	30:17	-2.6 (-8.1, 3.1)	14%, 13%, 73%	Unclear
¥Means (min:sec) prior to transformation. †Based on natural log-transformation. ‡Based on a smallest worthwhile difference of 0.8%. §Excludes two participants due to a treadmill malfunction and hip pain.					

Table 4-7 presents inferential statistics for physiological variables hypothesized to be different between the beverage conditions. Contrary to our hypothesis, carbohydrate oxidation was not higher with GF at the end of exercise, and in fact, there was a 32% chance that carbohydrate oxidation was lower with GF by at least a Cohen effect of 0.2. At both 5 and 120 min, GF resulted in possibly higher fat oxidation rates relative to G. Lactate effects were unclear at both time points due to a substantial amount of variability.

Table 4-7. Inferential statistics for substrate use and physiological markers					
	G¥	GF¥	Difference expressed as Cohen (90% CL)†	Chances of GF being higher, trivial, and lower relative to G‡	Interpretation
CHO oxidation (g·min⁻¹)					
5 min	2.41	2.32	-0.19 (-0.44, 0.07)	1%, 52%, 47%	Possibly lower
91 min	2.05	2.08	0.06 (-0.16, 0.28)	13%, 84%, 3%	Likely trivial
117 min	1.91	1.83	-0.14 (-0.36, 0.08)	1%, 68%, 32%	Possibly lower
Fat oxidation (g·min⁻¹)					
5 min	0.34	0.40	0.33 (-0.15, 0.80)	67%, 29%, 4%	Possibly higher
91 min	0.49	0.49	-0.04 (-0.36, 0.28)	10%, 70%, 20%	Unclear
117 min	0.54	0.60	0.18 (-0.05, 0.41)	45%, 55%, 0%	Possibly higher
Lactate (mmol·l⁻¹)					
55 min	2.68	2.39	-0.19 (-0.63, 0.25)	7%, 44%, 49%	Unclear
115 min	2.07	2.12	-0.02 (-0.50, 0.45)	21%, 53%, 26%	Unclear
¥Means prior to transformation. †Based on natural log-transformation. ‡Based on a Cohen effect size of 0.2. CHO and fat oxidation unavailable for one participant. Lactate unavailable for two participants at 55 min and five participants at 115 min. Abbreviations: CHO, carbohydrate.					

Lastly, **Table 4-8** shows the inferential statistics for psychometric variables, with all chances expressed relative to a Cohen of 0.2. Nadir FS ratings during the sub-maximal protocol were possibly higher with GF (indicating a benefit), and FS ratings possibly showed a smaller reduction with GF from rest to 110 min. FS ratings averaged over the TT were possibly higher with GF. While not true for every GI symptom, most were possibly-to-likely lower with GF, and none of the symptoms showed any evidence of being worse with GF. The LHS ratings showed no consistent differences for sweetness or overall likability, although sweetness and likability were possibly higher for GF at 20 and 100 min, respectively.

Table 4-8. Inferential statistics for psychometric scales

	G¥	GF¥	Difference expressed as Cohen (90% CL)†	Chances of GF being higher, trivial, and lower relative to G‡	Interpretation
FS (-5 to +5)					
sub-max nadir	2.15	2.55	0.22 (-0.05, 0.49)	55%, 44%, 1%	Possibly higher
change (rest – 110 min)	2.35	1.90	-0.25 (-0.49, -0.01)	0%, 35%, 65%	Possibly lower
TT average	-0.06	0.32	0.15 (-0.17, 0.48)	40%, 56%, 4%	Possibly higher
Sub-maximal GI symptoms§ (1 to 7)					
belching/regurgitation/reflux	1.75	1.50	-0.38 (-0.81, 0.04)	1%, 22%, 77%	Likely lower
bloating/fullness	2.20	1.70	-0.45 (-0.79, -0.10)	0%, 11%, 89%	Likely lower
abdominal cramps	1.60	1.50	-0.16 (-0.55, 0.23)	6%, 50%, 43%	Unclear
gas/flatulence	1.50	1.20	-0.37 (-0.78, 0.04)	1%, 22%, 76%	Likely lower
urge to defecate	1.35	1.15	-0.16 (-0.54, 0.21)	6%, 51%, 43%	Unclear
Time trial GI symptoms (1 to 7)					
nausea	1.28	1.11	-0.44 (-1.01, 0.14)	4%, 21%, 76%	Likely lower
belching/regurgitation/reflux	1.22	1.22	0.00 (-0.55, 0.55)	27%, 46%, 27%	Unclear
bloating/fullness	1.67	1.33	-0.16 (-0.52, 0.20)	5%, 52%, 43%	Possibly lower
abdominal cramps	1.72	1.56	-0.20 (-0.56, 0.16)	4%, 47%, 50%	Possibly lower
gas/flatulence	1.50	1.33	-0.14 (-0.60, 0.33)	11%, 48%, 41%	Unclear
urge to defecate	1.67	1.22	-0.29 (-0.78, 0.19)	5%, 32%, 63%	Possibly lower
LHS ratings (0 to 100)					
sweet rest	25.1	24.0	-0.08 (-0.48, 0.31)	12%, 58%, 30%	Unclear
sweet 20 min	22.8	27.1	0.23 (-0.16, 0.63)	56%, 41%, 4%	Possibly higher
sweet 60 min	26.4	24.3	-0.12 (-0.44, 0.21)	6%, 62%, 33%	Unclear
sweet 100 min	21.8	22.4	0.07 (-0.39, 0.53)	32%, 52%, 16%	Unclear
likability rest	12.0	10.8	-0.11 (-0.46, 0.24)	7%, 59%, 33%	Unclear
likability 20 min	16.0	15.1	-0.04 (-0.33, 0.25)	8%, 74%, 18%	Unclear
likability 60 min	16.3	18.6	0.04 (-0.32, 0.39)	22%, 65%, 13%	Unclear
likability 100 min	13.7	21.3	0.30 (-0.02, 0.61)	69%, 30%, 1%	Possibly higher

¥Means prior to transformation. †LHS ratings and peak GI symptoms were based on percentile rank-transformation. ‡Based on smallest worthwhile Cohen effect size of 0.2. §Sub-maximal nausea was not examined due to low overall incidence (10%). Sub-maximal, n = 20; TT, n = 18.

Discussion

The primary finding of this investigation was that ingestion of a glucose-fructose beverage likely improved endurance running performance compared to ingestion of a glucose-only beverage. This finding should be interpreted within the framework of the study design, with contextual factors including a carbohydrate feeding rate of 1.3 g·min,$^{-1}$ a carbohydrate concentration of 10%, and exercise duration of ~2.5 hours. Notably, this is the first study to find a performance benefit with MTC during running (Clarke et al., 2012; Pfeiffer et al., 2009). Previously, Pfeiffer et al. (2009) examined the effects of glucose-only or glucose-fructose gels on performance during 16-km outdoor runs. Both conditions provided carbohydrate at 1.4 g·min,$^{-1}$ and overall, run times were not significantly different between conditions (1:14:25 for glucose vs. 1:14:41 for glucose-fructose). The fact that our study used a protocol approximately double in duration may partly explain the discrepant findings. The other running-based study had 11 men complete a 90-min soccer protocol while ingesting carbohydrate at 1 g·min^{-1} from exclusively glucose or a 2:1 glucose-to-fructose mix (Clarke et al., 2012). After the 90-min protocol, participants ran to exhaustion on a treadmill at 12.8 km·hr^{-1} and 20% grade. TTE and post-exercise muscle glycogen levels were not significantly different between trials, but both outcomes were statistically underpowered and there was a trend for longer TTE in the glucose-fructose trial ($p = .06$). Moreover, average TTE was only ~80 seconds, suggesting that the performance task likely made it challenging to detect differences between conditions. Given the inconsistencies between the previous research and our study, more research on MTC is needed for a range of running distances and intensities.

The effects of MTC on the GI system may explain a portion of the performance benefit in our study, as previous investigations indicate that GI distress can substantially impact performance. Rowlands et al. (2012) used polynomial modeling with linear and quadratic components to assess the magnitude of performance benefit attributable to reductions in GI symptoms during endurance cycling and found that abdominal cramps

significantly mediated performance outcomes. O'Brien et al. (2013) used a similar approach and found that a reduction in abdominal cramps was likely a mediator of end-exercise sprint power when comparing beverages with varying ratios of glucose and fructose. Moreover, one of the only studies to utilize a pure TT to assess performance (with no sub-maximal steady-state period) clearly showed that GI distress can substantially impair performance. Specifically, participants finished a 100-km cycle TT 8% faster when consuming a glucose-fructose beverage compared to a glucose-only beverage, and out of nine participants, two experienced diarrhea and one experienced vomiting with the glucose-only beverage (Triplett et al., 2010). Additionally, seven of nine participants reported feeling as if their stomachs were not emptying during the glucose-only trial, while none of the participants reported significant GI distress during the glucose-fructose trial. These observations seem to be supported by our data, as GI distress during the TT for G was possibly higher for several symptoms. In addition, one participant stopped to use the restroom during the TT for G due to severe urge to defecate.

Several mechanisms may be responsible for the observed GI effects, including altered gastric emptying and carbohydrate absorption. Under resting conditions, highly-concentrated fructose solutions (10-15%) empty faster from the stomach than isocaloric glucose solutions (Guss et al., 1994; Sole & Noakes, 1989). These gastric emptying differences are best explained by the inhibitory-feedback effects of glucose on intestinal afferent nerves (Zittel et al., 1994) and SGLT1 transporters (Raybould & Zittel, 1995). Subsequent studies with exercise support the notion that gastric fluid emptying is more rapid with glucose-fructose compared to an equivalent concentration of glucose (Jeukendrup & Moseley, 2010; Roberts et al., 2014). Additionally, SGLT1 transporters may become saturated with large, rapid glucose feedings, and could cause carbohydrate malabsorption and osmotic fluid shifts into the intestines, although this is somewhat speculative (Jeukendrup, 2010). These differences could explain the increased frequency of abdominal cramps and gas observed in this and previous studies. Not all investigations, however, have found reduced GI distress with glucose-fructose mixtures.

Pfeiffer et al. (2009) found that a glucose-fructose gel was actually associated with higher scores for reflux, intestinal cramps, and loose stools during 16-km outdoor runs (Pfeiffer et al., 2009).

In terms of psychological effects, it is possible the GF resulted in higher FS ratings compared to G. This positive effect for GF was apparent when expressing FS ratings as nadir and change values, as well as average values during the TT. In light of the multiple physiological effects of fructose, we are not able to delineate precisely which mechanisms were responsible for the possible differences in FS ratings. A few possible explanations, however, are worth noting. Interestingly, a recent blinded study found that glucose and fructose activate different brain regions and may have differential effects on reward and motivational processing (Page et al. 2013), although it is unknown whether sweetness differences or other carbohydrate-specific oral receptors explain these findings. Others have argued that sweetness partially mediates the performance benefit of glucose-fructose ingestion (O'Brien et al., 2013), but sweetness differences were not generally apparent in this study (with the exception of a small possible difference at 20 min). In addition, the participants did not consume any beverage during the 4-mile TT, which should have minimized any acute effect of sweetness on performance. Beverage likability was similar between beverages throughout the sub-maximal protocol, but ratings for GF were likely higher at 120 min despite no clear differences in sweetness. It is therefore possible, but speculative, that the maintenance of FS observed with GF could have been partly the result of changes in brain activity. At least two other studies have found fructose feeding relative to glucose improves rating of exertion or psychological affect during or after exercise lasting 30-60 min (Da Silva-Grigoletto et al., 2010; Folarin et al., 2014), which would support a CNS effect. Alternatively, increased GI distress with G could have contributed to differences in FS ratings.

Despite the apparent confirmation of performance, GI, and psychological benefits, our hypotheses that glucose-fructose ingestion would result in higher blood lactate and end-exercise carbohydrate oxidation were not confirmed. Previous studies have found higher concentrations of lactate with fructose compared to glucose feeding, but the timing

of ingestion in relation to exercise may mediate this effect. Specifically, fructose ingestion prior to exercise elevates blood lactate during the post-prandial period, but lactate falls with the onset of exercise, at least in comparison to glucose ingestion (Hargreaves, Costill, Katz, & Fink, 1985; Sun, Wong, Huang, Chen, & Tsang, 2012; Wu, Nicholas, Williams, Took, & Hardy, 2003). Thus, feeding a substantial amount of fructose (~25 g) 25 min prior to the onset of exercise possibly minimized elevations in lactate measured 80 min later. In regards to carbohydrate oxidation, some (Currell & Jeukendrup, 2008; Lecoultre et al., 2010; Roberts et al., 2014) but not all studies (Adopo et al., 1994; Jentjens et al., 2004b; Jentjens et al. 2006; Jeukendrup & Moseley, 2010; Riddell et al., 2001) found differences in total carbohydrate oxidation with MTC. Of note, many of the previous studies required participants to be fasted, making it more likely for differences to emerge with exogenous feedings (Massicotte, Péronnet, Brisson, Boivin, & Hillaire-Marcel, 1990). Additionally, the duration of running used in the present study may not have been long enough to deplete muscle glycogen, especially since running does not elicit as high of carbohydrate oxidation as cycling (Knechtle et al., 2004). Interestingly, fat oxidation was possibly higher for GF at 5 min and 117 min. Lower fat oxidation with G, especially at 5 min, could have been due to a higher insulinemic response, leading to insulin-associated fat oxidation suppression (Koivisto, Karonen, & Nikkila, 1981). It should be mentioned that rates of exogenous and endogenous carbohydrate oxidation could have differed between beverage trials, but we did collect data to examine this possibility.

There are several novel approaches and strengths to this study. Unlike much of the previous literature, this investigation was double-blinded with data on the effectiveness of participant blinding. While several studies reported single- (Hulston et al., 2009; Jeukendrup et al., 2006; Jeukendrup & Moseley, 2010; Lecoultre et al., 2010; Riddell et al., 2001) or double-blinding (Baur et al., 2014; Clarke et al., 2012; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Pfeiffer et al., 2009; Roberts et al., 2014; Rowlands et al., 2012; Rowlands et al., 2008; Triplett et al., 2010), only two formally evaluated beverage flavor characteristics (Rowlands et al., 2008; O'Brien et al., 2013).

Importantly, our goal of matching beverage sweetness was relatively well-achieved. The participants also received two standardized meals to ensure nutrition was similar between participants and trials. Only six of the previous studies reported acute pre-protocol diet or provided foods for participants (Adopo et al., 1994; Baur et al., 2014; Pfeiffer et al., 2009; Riddell et al., 2001; Rowlands et al., 2012; Wagenmakers et al., 1993), and the majority were conducted with participants fasted. Furthermore, the beverage volume was similar to intakes observed during field running studies (Rehrer et al., 1989; Pfeiffer et al., 2012; Rollo et al., 2012), and since many of the previous investigations used volumes (~1,000 ml·hr^{-1}) exceeding ad libitum intake even for cycling (Pfeiffer et al., 2012; Rose & Peters-Futre, 2010; Speedy et al., 2001), the generalizability and practicality of the previous data may be limited. Finally, the inclusion of women was a clear strength given their lack of representation in past research

Despite this study's strengths, several limitations need to be acknowledged. We did not use a non-carbohydrate control, mainly because participant burden would have been increased to three prolonged runs and previous MTC studies have consistently shown carbohydrate ingestion to be superior to non-caloric placebo ingestion. Recruitment was likely enhanced by requiring only two prolonged runs, which was evident by the relatively large sample size of 20. Moreover, most previous investigations used cycling, which does not cause as much muscular damage (Koller et al., 1998), and we wished to minimize injury risk to participants. Another limitation is the lack of data specific to exogenous carbohydrate oxidation. Estimation of exogenous carbohydrate oxidation requires the use of tracers, and since the main outcome was performance, the use of invasive and time-consuming testing was avoided to maximize recruitment. Finally, the amount of fluid ingested was not standardized to body size or to participant preference. Competitors that experience GI distress in real events often adjust their intake to mitigate symptoms, but our participants were required to drink a prescribed rate regardless of symptoms experienced.

Conclusions

To summarize, this study showed that ingestion of glucose-fructose—compared to glucose-only—likely improved performance, possibly reduced GI distress, and possibly improved psychological affect during prolonged running. Performance benefits were apparent for both men and women, with magnitudes ranging from 1.6-2.6%. The magnitude of benefit for GI distress and psychological affect were relatively small (Cohen = 0.2-0.4). These results apply to athletes consuming fluid and carbohydrate at relatively aggressive rates (500-600 ml·hr^{-1} and 1.0-1.3 g·min^{-1}) during prolonged running at 60-70% VO_{2peak}. More studies are needed to determine if MTC are beneficial for a variety of running-specific physiological markers and performance tasks.

5

The Effects of Glucose-Fructose versus

Glucose-Only on Stride Parameters during

Prolonged Running

Introduction

Traditional guidelines limit carbohydrate intake during exercise to 60 g·hr,[-1] mainly because greater amounts increase GI distress without improving performance (Rodriguez et al., 2009). Over the last two decades, however, numerous studies have shown that feeding multiple saccharides—compared to a single saccharide—increases exogenous carbohydrate oxidation, reduces GI distress, and improves performance when carbohydrate intake exceeds 50-60 g·hr^{-1} (Jeukendrup, 2010). Glucose and fructose utilize separate, saturable intestinal transporters (SGLT1 and GLUT5; Wood & Trayhurn, 2003), and hence, they have been referred to in the literature as MTC (Jeukendrup, 2010). Additional studies have found that MTC improve fluid absorption (Jeukendrup & Moseley, 2010) and increase gastric emptying (Jeukendrup & Moseley, 2010). Of note, the greatest benefits have occurred when glucose and fructose were ingested in a 1.2:1 to 1:1 ratio (Jentjens et al., 2005; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Rowlands et al., 2008).

Despite the relatively sizeable literature on the metabolic and GI effects of MTC, several limitations are apparent. Cycling has been used in all but two studies (Clarke et al., 2012; Pfeiffer et al., 2009), limiting inferences for endurance running. What's more, no research has examined how MTC affect running stride parameters, including stride frequency (SF), stride time (ST), contact time (CT) and stride length (SL). Stride changes have been studied during treadmill and field running, and in general, SF decreases (Chan-Roper, Hunter, Myrer, Eggett, & Seeley, 2012) and ground CT increases (Chan-Roper et al., 2012; Elliott & Roberts, 1980) over time. A portion of these changes is attributable to decreases in running velocity, but even when standardizing velocity, SF generally decreases with exhaustive running tasks (Avogadro, Dolenec, & Belli, 2003; Borrani et al., 2003; Dutto & Smith, 2002; Hanley & Mohan, 2014; Hunter & Smith, 2007). These stride changes are accompanied by increased oxygen uptake and decreased metabolic economy (Hunter & Smith, 2007), and may arise partially from a shift to fat metabolism with muscle glycogen depletion (Suriano et al., 2010). Previous studies have noted

running economy decreases in parallel as RER drops closer to 0.85, indicating greater relative reliance on fat metabolism (Bosch, Goslin, Noakes, & Dennis, 1990; Brueckner et al., 1991). Relevantly, the performance benefits of MTC have been hypothesized to result, in part, from the maintenance of carbohydrate oxidation (Jeukendrup, 2010), and therefore, it is plausible that MTC could alter the stride changes associated with fatigue. Alternatively, psychological and CNS effects of carbohydrate ingestion could impact stride parameters, particularly SF. Previous research, albeit limited, demonstrates that SF and perceived exertion are inter-related (Messier, Franke, & Rejeski, 1986), and given that previous studies have found MTC maintain psychological affect to a greater extent than glucose-alone (Jentjens et al., 2006; Jeukendrup et al., 2006; Roberts et al., 2014), it is conceivable that stride parameters could be influenced by MTC independently of substrate use.

We are aware of only two experimental studies that have examined the effects of carbohydrate intake on stride parameters (Rollo & Williams, 2009; Williams et al., 1992). Williams et al. (1992) found that seven days of a high-carbohydrate diet prior to a 30-km treadmill run better maintained running velocity and SL than a control diet. In contrast, Rollo and Williams (2009) found no differences in SF or SL when carbohydrate and placebo beverages were ingested before and during 1-hour of self-paced running. In terms of research specific to MTC, neither of the two previous studies that utilized running measured stride parameters (Clarke et al., 2012; Pfeiffer et al., 2009). In light of these shortcomings, the aim of this study was to determine whether MTC alter stride parameters during prolonged running. Explicitly, the effects of ingesting a glucose-fructose beverage (GF; 55% maltodextrin/45% fructose) were compared to a glucose-only beverage (G; 55% maltodextrin/45% glucose) during 120 min of constant-velocity running and a subsequent 4-mile TT. Beverages supplied carbohydrate at 1.3 g·min^{-1} during the constant-velocity period in a double-blind fashion. The following hypotheses were tested:

1. GF will result in higher SF over 120 min of steady-state running compared to G.

2. GF will result in lower CT over 120 min of steady-state running compared to G.

We did not have any hypotheses regarding the effects of GF on stride parameters during the self-paced TT but wished to compare stride parameters during the TT to elucidate which, if any, explained performance differences between G and GF.

Methods

Participants.

Participants were recruited from Minneapolis-St. Paul area. Eligibility criteria included the completion of at least one marathon within the past year (men, <210 min; women, <225 min), running ≥30 miles per week for the previous three months, and completion of two 20-mile runs over the previous two months. Participants completed a physical activity health screener and a University of Minnesota Institutional Review Board approved consent form. Participants were provided with $100 remuneration upon completion of the study.

General experimental design.

Participants underwent two prolonged running tests during which they consumed G and GF. The first 120 min was a constant-velocity, sub-maximal protocol during which the beverages were consumed and stride parameter data was collected. Immediately after the completion of the sub-maximal protocol, participants completed a self-paced 4-mile TT. Data collection began October 2013 and was completed by March 2014.

Test beverages.

Participants were assigned to the beverages in a randomized, counter-balanced, crossover fashion. Each beverage supplied approximately 1.3 $g \cdot min^{-1}$ of carbohydrate during the sub-maximal protocol. GF was a 10.3% carbohydrate mixture (103 g for 1 kg tap water) containing maltodextrin (Star-Dri® 10, Tate & Lyle, Decatur, IL) and

crystalline fructose (Krystar® 300, Tate & Lyle, Decatur, IL). Glucose and fructose were supplied in a 1.2:1 ratio (5.61% maltodextrin and 4.66% fructose) because four studies have indicated it is optimal for a variety of outcomes (Jentjens et al., 2005; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Rowlands et al., 2008). G was a 10.3% concentration supplying carbohydrate as 5.61% maltodextrin (Star-Dri® 10, Tate & Lyle, Decatur, IL) and 4.66% dextrose anhydrous (Cerelose®, Ingredion, Westchester, IL). Sodium chloride (540 mg·kg^{-1} water) and lemon juice (9 g·kg^{-1} water) were added to both beverages. Given the sweetness difference between fructose and glucose, aspartame (90 mg·kg^{-1} water) was added to G to match sweetness.

Beverages were mixed before each visit, and ingredients were weighed to ± 0.1 g on a scale (iBalance 500; My Weigh, Vancouver, BC, Canada) calibrated with 100 g before each use. To ensure blinding of the researchers, one study investigator mixed both beverages simultaneously in two indistinguishable containers, labeled them, and left the room. An individual not involved with the data collection subsequently chose one of the beverages by drawing treatment assignments from sex-specific envelopes. The chosen beverage was used for each participant's first condition. The process was repeated for the next visit, except that the opposite beverage was chosen.

Baseline visit.

Participants reported to the HSPL one to four weeks before their first prolonged run. Participants completed a background questionnaire inquiring about demographics, training history, competition history, exercise-related GI symptom history, and menstrual cycle status (for females). Height was taken without shoes to the nearest 0.1 cm with a stadiometer (Accustat Genentech, San Francisco, CA) and weight, with light clothing, was recorded to the nearest 0.05 kg on a digital scale (ProDoc, Detecto Scale, Webb City, MO). Hydrostatic weighing was used to estimate body density. Residual lung volume was estimated (Quanjer, 1983) and percent body fat was determined using the equation from Brozek et al. (1963).

To establish VO$_{2peak}$, participants completed a maximal cardiorespiratory running test on a motorized treadmill (Pro XL, Woodway USA, Inc., Waukesha, WI). The

protocol began with a 3-min walk at 3.1 mph and 0% grade. Subsequently, 1-min stages at 1% grade with 0.4 mph speed increases were used to achieve a speed equal to the participant's 5-km pace by the eleventh minute. The grade was increased by 1.5% every minute thereafter until volitional exhaustion.

Pre-test training and diet.

Participants recorded all training activities for five days prior to each prolonged run, while diet was recorded with prospective records for two days. Participants were asked to avoid vigorous physical activity and alcohol for 48 hours and caffeine 12 hours before each run. Participants were instructed to repeat training and diet between visits. Pre-protocol nutrition is listed in **Tables 4-1** and **4-3** (refer to Chapter 4).

Stride parameter data.

Sagittal plane movies recorded with a high frame rate camera (Nikon 1™ J3; shutter speed = 1/400, 400 frames·sec^{-1}) were used to assess stride parameters. The camera was fixed on a tripod at a height of 41.5 cm and was placed 60 cm perpendicular to the treadmill. Video was analyzed with QuickTime (version 7, Apple Corp, Cupertino, CA) using the frame counting feature, where each frame represented 0.0025 sec. Since the camera's features limited each recording to 3 sec, three recordings were taken for every collection period to ensure nine strides were captured. The three recordings were taken at 15 sec intervals for each collection time point. Recordings were taken at 3, 53, and 113 min during the sub-maximal protocol. During the 4-mile TT, video recordings were taken at miles 1.7 and 3.7. A stride cycle was defined as foot contact to foot contact on the right leg. Treadmill speed was converted to m·sec^{-1} using the following formula: miles·hr^{-1} x (1609 ÷ 3600). SL was calculated by dividing treadmill velocity (m·sec^{-1}) by SF (strides· sec^{-1}). Average SF, SL, ST, and CT were quantified from the first nine strides. Participants chose their shoes but were required to wear the same shoes for both trials. No music or visual stimuli were allowed during the protocols.

Respiratory gases.

Indirect calorimetry was used to assess energy expenditure and substrate oxidation, since they can vary with differences in SF (Saunders, Pyne, Telford, & Hawley, 2004). A metabolic cart (Ultima Series, Medical Graphics Corporation, St. Paul, MN) measured breath-by-breath respiratory exchange of O_2 and CO_2 during the sub-maximal protocol. The gas sensor was calibrated using two gas mixes (21% O_2, 79% N_2; 5% CO_2, 12% O_2, 83% N_2), and a pneumotachograph was calibrated with a 3-liter syringe. Participants were fitted with a rubber mouthpiece (SDI Diagnostics, Easton, MA) attached to the pneumotachograph, and a nose clip ensured breathing via the mouth. Oxygen consumption and carbon dioxide expiration were calculated automatically by the software Breeze (Medical Graphics Corporation, St. Paul, MN). Estimates of carbohydrate oxidation, fat oxidation, and energy expenditure were derived from the exercise-specific stoichiometric equations from Jeukendrup and Wallis (2005):

Carbohydrate: $(4.210 \cdot VCO_2) - (2.962 \cdot VO_2) - 2.37 \cdot n.$

Fat: $(1.695 \cdot VO_2) - (1.701 \cdot VCO_2) - 1.77 \cdot n.$

Energy expenditure: $(0.55 \cdot VCO_2) + (4.471 \cdot VO_2)$

VCO_2 and VO_2 were in $l \cdot min^{-1}$ and n (nitrogen excretion) was considered to be negligible.

Psychometric scales.

The 11-point bipolar FS was used to assess pleasure and displeasure, with anchors of "very bad" at -5, "neutral" at 0, and "very good" at +5 (Hardy & Rejeski, 1989). To evaluate beverage blinding, participants rated beverages on sweetness, saltiness, and overall flavor likability on the LHS (Lim et al., 2009; Lim & Fujimaru, 2010). Sweetness and saltiness scores ranged from 0 to +100 ["neutral" to "most (sweet or salty) sensation imaginable"] while flavor likability ranged from -100 to +100 ("most disliked sensation imaginable" to "most liked sensation imaginable"). LHS ratings were collected every 40 min (-20, 20, 60, 100 min).

Sub-maximal running protocol.

The two sub-maximal, constant-velocity, 120-min runs were separated by at least 14 days. Women completed visits 26-29 days apart to control for menstrual cycle. Participants reported to the HSPL between 6:00-9:00 a.m. for their first trial and within one hour of the same time for their second trial. After voiding and recording pre-exercise weight, participants consumed the first beverage dose 25 min prior to the start of the sub-maximal protocol. The initial dose supplied 55.4 g of carbohydrate and was consumed over 5 min. Participants then completed a 5-min warm-up 10 min before the start of the sub-maximal protocol. The pace for the sub-maximal protocol was set at 85-90% of the average velocity from their most recent marathon. Marathon time was used to set intensity because the percentage of VO_{2peak} that can be sustained during prolonged running varies from 60-75% (Maughan & Leiper, 1983). Participants subsequently consumed the beverages after 20, 40, 60, 80, and 100 min, and immediately after the 120 min protocol. Feedings at 20, 40, 60, and 80 min provided 18.4 g of carbohydrate whereas those at 100 min and upon completion provided 14.7 and 11 g, respectively. Feeding volumes were decreased over time based on reported tolerability during pilot testing. Treadmill velocity was slowed to 75% of marathon velocity for up to 2 min during beverage administration. Beverages were kept at 2.8-4.0 °C until 15 min before the first dose was consumed and were subsequently administered in 480-ml plastic squeeze bottles to minimize spillage. Weight of any remaining beverage was recorded after the last dose was administered, with a consumption goal of 1682 g.

Respiratory gases were collected at two time points (5 and 117 min) in proximity to stride parameter data (3 and 113 min), allowing for reasonable comparisons relative to one another. Respiratory gases were collected and averaged over 2 min. FS ratings were also measured in proximity to stride parameters at 10, 50 and 110 min. Treadmill belt velocity was verified every two weeks with a tachometer (RPM33, Extech Instruments, Nashua, NH) to ensure no significant deviations over the study. A fan set at medium velocity was used for cooling during all tests.

4-mile time trial.

Participants completed a self-paced 4-mile TT after the sub-maximal protocol. A TT is the preferred performance task because of a lower coefficient of variation compared to TTE tasks (Laursen et al., 2007). The treadmill was stopped for 2 min after the sub-maximal protocol to administer the last beverage dose, reset the distance display, repeat instructions, and allow participants to use the restroom. Participants were told to finish the TT as fast possible, and they were allowed to adjust the speed as much as desired but were not allowed to view time elapsed. No encouragement was given during the TT and interaction with the researchers was minimized as much as possible. Participants were not allowed to change the treadmill speed when video was recorded at 1.7 and 3.7 miles. Treadmill velocity was recorded during the video recordings.

Statistical analysis.

A statistical approach reporting uncertainty of outcomes as 90% CL was employed to make inferences about treatment effects. This approach calculates effects with CL and interprets them in relation to the smallest worthwhile effect (Batterham & Hopkins, 2006). Interpretation is facilitated using probabilities (chances) that the true (population) effect is positive, trivial, or negative. In comparison to null-hypothesis testing, the use of inferential statistics helps interpret the practical meaningfulness of results, especially with the smaller sample sizes often employed in sport performance research (Batterham & Hopkins, 2006). Effects, 90% CL, and probabilities that the effects were positive, trivial, or negative were calculated using a specifically-designed spreadsheet for post-only crossover trials (Hopkins, 2006b). Differences between G and GF for stride parameters, FS ratings, and substrate use were interpreted using a Cohen effect statistic (Cohen, 1988), calculated using between-subject standard deviations. The chances the true value of the differences were at least small (Cohen = 0.2) were calculated. The smallest worthwhile difference in treadmill velocity was set at 0.8%, using the recommendation of 0.3 times the co-efficient of variation (~2.5%) for endurance running performance (Hopkins, 2004; Hopkins & Hewson, 2001). Based on recommendations from Hopkins (2003), stride parameters, substrate use, and treadmill

velocity were natural log-transformed when calculating inferential statistics. Treadmill velocity was back-transformed to obtain percentage differences between conditions. Chances of effects were accompanied by qualitative descriptors: <1%, almost certainly not; 1-4%, very unlikely; 5-24%, unlikely; 25-74%, possibly; 75-94%, likely; 95-98%, very likely; ≥99%, almost certain. If the chances of positive and negative effects were both >5%, the effect was deemed unclear.

CT effects were calculated for the right foot, but not the left foot, because it is unlikely any treatment effect would differ by leg and we wished to minimize the number of inferences. Additionally, sub-maximal protocol inferences were calculated for SF, but not ST and SL, since they are directly proportional to SF when velocity is constant and would show the same effects. SL inferences were calculated for the TT, however, since treadmill speed was different between trials for many participants, and therefore SL could differ between TT even if SF did not. FS ratings at 10 and 50 min were percentile rank-transformed because of resistance to log transformation (grossly non-normal with some zero values), while ratings at 110 min were normally distributed and were analyzed using untransformed values.

TT data for two participants was excluded due to hip pain and a treadmill malfunction. In the latter case, the treadmill belt slowed to a stop on three occasions without the participant's action. This malfunction was fixed and did not occur again. Gas exchange for one participant was not available due to a computer problem. Means (± standard errors) for normal-data and medians (inter-quartile ranges) for non-normal data are presented for descriptive statistics to simply interpretation (including variables transformed for inferential statistics). Normality was assessed via the Shapiro-Wilk test. Descriptive statistics were generated using SPSS version 22 (IBM, Armonk, NY).

Results

Sample characteristics.

A total of 26 participants (17 men, 9 women) were enrolled in the study (**Figure 4-2**, refer to Chapter 4). The characteristics of the analytical sample (14 men, 6 women)

are presented in **Table 5-1**. Randomization was successfully counter-balanced, with 10 participants randomized to G first and 10 participants randomized to GF first. Additionally, randomization was counter-balanced for each sex.

Table 5-1. Participant anthropometric, training, and performance characteristics		
	Men (n = 14)	**Women (n = 6)**
Age (years)	35.8 (2.2)	31.3 (2.9)
Height (cm)	179.6 (1.7)	165.9 (1.6)
Weight (kg)	73.8 (1.9)	59.9 (1.5)
BMI (kg·m^2)	22.9 (0.5)	21.8 (0.5)
Body composition (% fat)	13.0 (1.4)	19.1 (1.7)
Personal best marathon (min)	182 (2)	201 (6)
Most recent marathon (min)	191 (4)	213 (4)
Marathon experience (#)	13 (2)	12 (4)
Running volume (miles·week^{-1})	45 (4)	44 (5)
VO$_2$peak (ml·kg^{-1}·min^{-1})	58.7 (1.9)	55.0 (2.4)
Values expressed as mean (SE).		

Environmental, time, and dietary control.

Mean temperatures during the G and GF trials were 23.4 ± 0.1 and 23.6 ± 0.2 ºC, while median relative humidity was 7% (7-9) for both trials. A median of 23 (15-33) days elapsed between visits for men, while all women fell within a range of 26-29 days. Refer to Chapter 4 (**Table 4-3)** for intakes of energy, carbohydrate, fiber, fat, and protein over the two days prior to the experimental trials.

Treadmill speed.

Treadmill velocity was 3.24 ± 0.4 m·sec^{-1} for both conditions during the sub-maximal protocol. Average TT velocities for G were 3.81 ± 0.08 m·sec^{-1} at mile 1.7 and 3.95 ± 0.10 m·sec^{-1} at mile 3.7. Average velocities for GF were 3.87 ± 0.10 m·sec^{-1} at mile 1.7 and 3.96 ± 0.09 m·sec^{-1} at mile 3.7.

Stride parameters.

CT for both feet is presented in **Table 5-2**. CT increased by approximately 0.010 sec over the sub-maximal protocol for both G and GF. CT was generally lower during the 4-mile TT relative to the sub-maximal protocol. Means for ST, SF, and SL are presented in **Figures 5-1**, **5-2**, and **5-3**.

| Table 5-2. Foot contact time during the sub-maximal period and time trial										
	3 min		53 min		113 min		mile 1.7		mile 3.7	
	G	GF	G	GF	G	GF	G	GF	G	GF
CT right (sec)	0.279 (0.006)	0.279 (0.005)	0.288 (0.005)	0.288 (0.005)	0.289 (0.006)	0.290 (0.006)	0.262 (0.005)	0.261 (0.005)	0.259 (0.006)	0.258 (0.007)
CT left (sec)	0.279 (0.006)	0.281 (0.005)	0.287 (0.005)	0.288 (0.005)	0.287 (0.005)	0.289 (0.005)	0.261 (0.005)	0.260 (0.005)	0.258 (0.006)	0.256 (0.006)
Values presented as means (SE). Sub-maximal, n = 20; time trial, n = 18.										
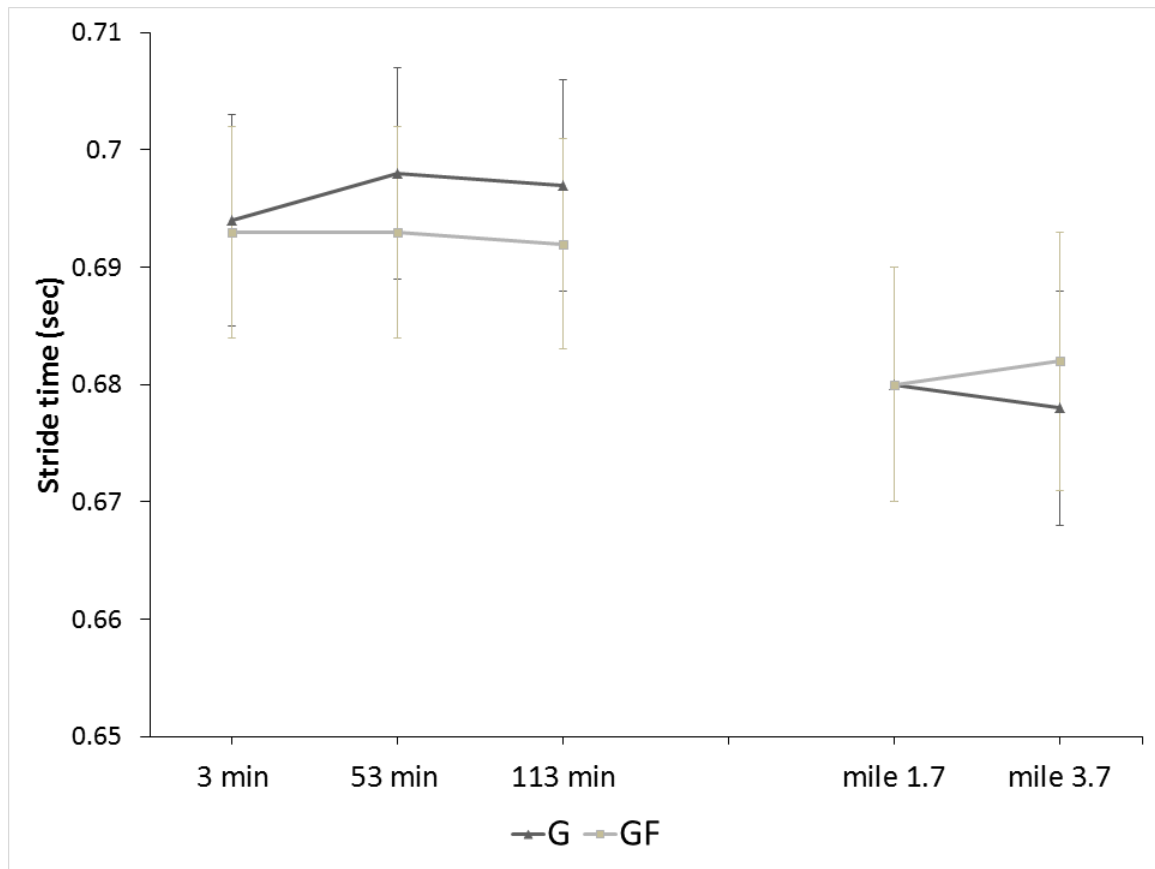
Figure 5-1. Stride time during the sub-maximal protocol and time trial
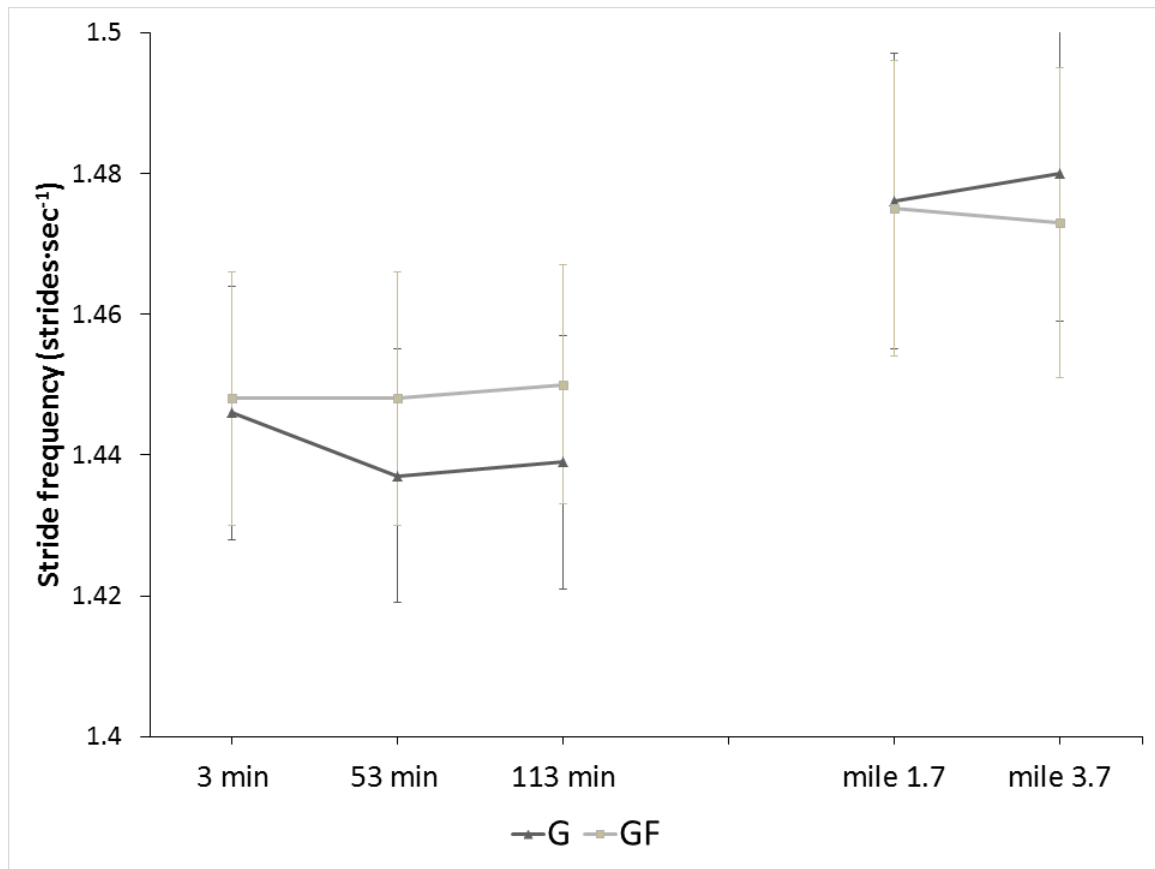
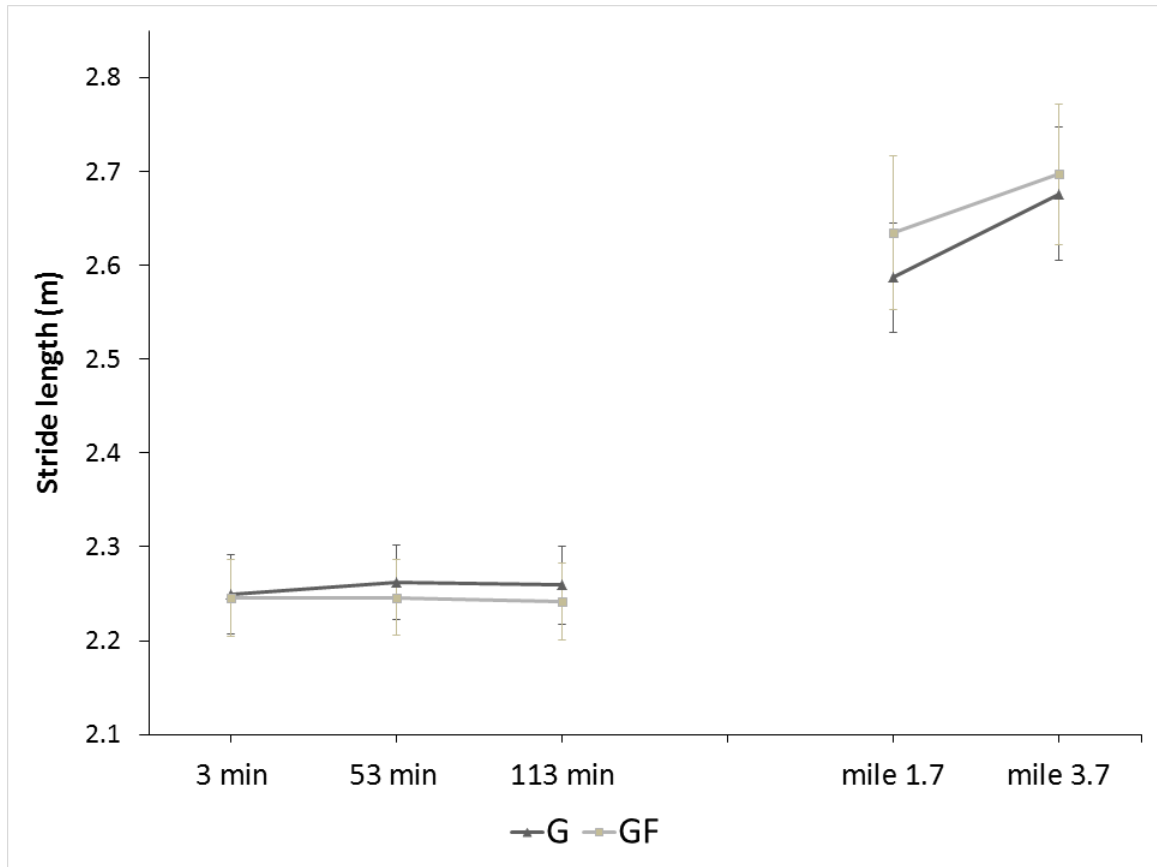**Figure 5-2.** Stride frequency during the sub-maximal protocol and time trial

Figure 5-3. Stride length during the sub-maximal protocol and time trial

Additional data.

Mean amounts of beverage consumed during the G and GF trials were 1660 ± 2 g
and 1659 ± 2 g, respectively (goal of 1682 g). The ~20 g difference between actual and
goal consumption was likely due to small amounts of beverage remaining in bottles after
each dose administration. Body weight decreased 1.8 ± 0.1 kg for both conditions.
Medians for beverage sweetness, saltiness, and overall likability are presented in **Figure
4-5** (see Chapter 4).

Inferential statistics.

Differences between G and GF for CT and SF during the sub-maximal protocol
are presented in **Table 5-3**. Relative to the minimal threshold Cohen of 0.2, CT
differences were very-likely-to-almost-certainly trivial at all time points. SF differences
were likely-to-very-likely trivial, but the 90% CL at 53 and 113 min did not cover 0,
indicating a consistent, small positive effect of GF on SF.

	G¥	GF¥	Difference expressed as Cohen† (90% CL)	Chances of GF being higher, trivial, and lower relative to G‡	Interpretation
Table 5-3. Inferential statistics for stride parameters during the sub-maximal period					
CT right foot (sec)					
3 min	0.279	0.279	0.01 (-0.10, 0.11)	0%, 100%, 0%	Almost certainly trivial
53 min	0.288	0.288	0.00 (-0.09, 0.09)	0%, 100%, 0%	Almost certainly trivial
113 min	0.289	0.290	0.03 (-0.12, 0.17)	3%, 96%, 1%	Very likely trivial
SF (strides·sec^{-1})					
3 min	1.446	1.448	0.03 (-0.10, 0.15)	1%, 98%, 0%	Very likely trivial
53 min	1.437	1.448	0.13 (0.04, 0.21)	8%, 92%, 0%	Likely trivial
113 min	1.439	1.450	0.13 (0.02, 0.24)	15%, 85%, 0%	Likely trivial

¥Means prior to transformation. †Data were natural log-transformed. ‡Based on smallest worthwhile Cohen effect size of 0.2. Sample size n = 20.

Differences between G and GF for substrate oxidation, energy expenditure, and FS ratings are presented in **Table 5-4**. Carbohydrate oxidation was possibly lower at 5 and 117 min for GF, and conversely, fat oxidation was possibly higher at 5 and 117 min for GF. Energy expenditure differences were very likely trivial at both 5 and 117 min. FS ratings were possibly lower for GF at 5 min, but became possibly higher for GF at 50 and 110 min.

Table 5-4. Inferential statistics for other variables collected in proximity to stride parameters					
	G¥	**GF¥**	**Difference expressed as Cohen (90% CL)**	**Chances of GF being higher, trivial, and lower relative to G‡**	**Interpretation**
CHO oxidation (g·min⁻¹)†					
5 min	2.41	2.32	-0.19 (-0.44, 0.07)	0%, 52%, 47%	Possibly lower
117 min	1.91	1.83	-0.14 (-0.36, 0.08)	1%, 68%, 32%	Possibly lower
Fat oxidation (g·min⁻¹)†					
5 min	0.34	0.40	0.33 (-0.15, 0.80)	67%, 29%, 4%	Possibly higher
117 min	0.54	0.60	0.18 (-0.05, 0.41)	45%, 55%, 0%	Possibly higher
Energy expenditure (kcal·min⁻¹)†					
5 min	13.1	13.3	0.08 (-0.01, 0.18)	3%, 97%, 0%	Very likely trivial
117 min	13.1	13.3	0.08 (0.00, 0.17)	1%, 99%, 0%	Very likely trivial
FS (-5 to +5)*					
10 min	4.4	4.2	-0.23 (-0.54, 0.08)	1%, 42%, 57%	Possibly lower
50 min	3.7	3.9	0.19 (-0.10, 0.48)	48%, 50%, 2%	Possibly higher
110 min	2.3	2.6	0.16 (-0.13, 0.45)	41%, 56%, 2%	Possibly higher
¥Means prior to transformation. †Data were natural log-transformed. *FS at 10 and 50 min were percentile rank-transformed because of non-normal distribution with zero values. ‡Based on smallest worthwhile Cohen effect size of 0.2. Data for CHO/fat oxidation and energy expenditure unavailable for one participant. Abbreviations: CHO, carbohydrate.					

Differences between G and GF for treadmill velocity at miles 1.7 and 3.7 of the TT are presented in **Table 5-5**. While there was a 65% chance that GF resulted in at least 0.8% higher treadmill velocity at mile 1.7, there was also an 8% chance that GF resulted in lower treadmill velocity. Thus, the effect was deemed unclear despite an apparent trend towards higher velocity for GF.

Table 5-5. Inferential statistics for treadmill velocity during the time trial					
	G¥	GF¥	% difference (90% CL)†	Chances of GF being higher, trivial, and lower relative to G‡	Interpretation
Speed (m·sec⁻¹)					
mile 1.7	3.81	3.87	1.4 (-1.2, 4.1)	65%, 27%, 8%	Unclear
mile 3.7	3.95	3.96	0.2 (-2.2, 2.7)	34%, 42%, 23%	Unclear
¥Means prior to transformation. †Data were natural log-transformed. ‡Based on smallest worthwhile effect size of 0.8%. Sample size n = 18.					

Inferential statistics for stride parameters during the TT are presented in **Table 5-6**. All differences for stride parameters were likely-to-almost-certainly trivial, except for SL at mile 1.7, which had a 27% chance of being higher with GF, relative to a Cohen effect of 0.2.

	G¥	GF¥	Difference expressed as Cohen (90% CL)†	Chances of GF being higher, trivial, and lower relative to G‡	Interpretation
Table 5-6. Inferential statistics for stride parameters during the time trial					
CT right foot (sec)					
mile 1.7	0.262	0.261	-0.06 (-0.31, 0.18)	4%, 79%, 17%	Likely trivial
mile 3.7	0.259	0.258	-0.04 (-0.24, 0.16)	2%, 89%, 9%	Likely trivial
SF (strides·sec⁻¹)					
mile 1.7	1.476	1.475	-0.01 (-0.12, 0.09)	0%, 99%, 0%	Almost certainly trivial
mile 3.7	1.480	1.473	-0.08 (-0.19, 0.04)	0%, 96%, 4%	Likely trivial
SL (m)					
mile 1.7	2.587	2.635	0.13 (-0.08, 0.33)	27%, 72%, 1%	Possibly higher
mile 3.7	2.676	2.697	0.06 (-0.13, 0.25)	11%, 88%, 1%	Likely trivial

¥Means prior to transformation. †Data were natural log-transformed. ‡Based on smallest worthwhile Cohen effect size of 0.2. Sample size n = 18.

Discussion

The primary discovery of this investigation was that ingestion of a glucose-fructose beverage, relative to a glucose-only beverage, better maintained SF during endurance running, even when controlling for running velocity. The magnitude of this effect was quite small (Cohen = 0.13, 90% CL 0.04-0.21) and did not meet the oft recommended threshold for practical meaningfulness for physiological and biomechanical factors (Cohen = 0.2; Hopkins, 2004). The fact that there was any difference in SF between constant-velocity trials may be meaningful, however, given that stride parameters are heavily dependent on running velocity (Hoyt, Wickler, & Cogger, 2000). Due to the numerous potential physiological and psychometric effects of MTC, delineation of the exact mechanisms responsible for the difference in SF is not possible. We did measure substrate utilization and FS in proximity to stride parameters in an attempt to gain some insight, and the most substantial difference between G and GF

appeared to be for FS ratings. Moreover, the direction of differences (positive or negative) generally paralleled one another for SF and FS ratings at 53 and 113 min. However, this does not necessarily mean that greater FS ratings were the cause of higher SF *per se*, as reverse causality is a possibility. Indeed, previous work has shown that modifying SF without changing velocity can alter psychological affect during running (Messier et al., 1986). Consequently, the potential bi-directional relationship between SF and FS ratings prohibits making strong statements about mechanistic pathways, so future work will be needed to help delineate these findings.

Although the data tentatively supported the hypothesis that glucose-fructose ingestion would maintain SF, it did not seem to have an effect on treadmill CT. Previous work has shown that increasing SF, while keeping running velocity constant, results in decreased CT (Morin, Samozino, Zameziati, & Belli, 2007). Thus, we hypothesized that CT would decrease as a byproduct of increased SF. The reason for lack of difference in CT despite a difference in SF is unclear, but the discrepancy may be explained by the fact that participants in previous studies were instructed to alter SF, whereas in this study any change in SF was likely unintentional or subconscious.

Another finding of this study was that GF resulted in possibly greater SL at mile 1.7 of a 4-mile TT. Correspondingly, treadmill velocity for GF tended to be higher at mile 1.7 (3.87 vs. 3.81 m·sec^{-1}), and given the very likely trivial differences in SF and CT, SL likely accounts for the greater treadmill velocity. This finding concurs with the results from Williams et al. (1992), in which a high carbohydrate diet better maintained running velocity and SL during a 30-km treadmill TT. Moreover, a very strong negative correlation between SL and performance time was apparent in that study ($r = -0.94$). In contrast, Rollo and Williams (2009) found no difference in SF or SL when carbohydrate and placebo were ingested before and during 1-hour of self-paced running. That study, however, was underpowered with only 8 participants and provided minimal detail on the measurement of SF and SL, precluding statements about measurement sensitivity. Moreover, the running duration was significantly shorter compared to the present study and Williams et al. (1992), possibly contributing to the lack of difference.

Similar to running stride parameters, few studies have explicitly examined the effects of carbohydrate on running economy, none of which focused on MTC (Brisswalter et al., 2000; Sproule, 1998). Stride parameters and running economy are dependent on one another (Saunders et al., 2004), and consequently, measuring running economy could be informative regarding stride characteristics, even in the absence of direct stride evaluation. Brisswalter et al. (2000) did not find a significant difference in energy cost during 120 min of running with the consumption of a 5.5% carbohydrate solution versus placebo. However, carbohydrate delivery was only 30-40 g·hr^{-1} and the sample size of 10 did not allow for small effects to be detected. An additional study from Sproule (1998) concurred with these findings, but may have been too short (80 min) to deplete muscle glycogen and alter substrate use. Other studies have shown that oxygen consumption does not significantly differ between carbohydrate and placebo ingestion during prolonged running, but these studies did not specifically aim to evaluate running economy (Millard-Stafford, Sparling, Rosskopf, & DiCarlo, 1992; Nieman et al., 2003; Utter et al., 1999). In the current study, there did not appear to be any substantial differences in energy expenditure between the trials. Given the small number of studies and aforementioned limitations, further research is needed to make more conclusive statements regarding the effects of carbohydrate on stride parameters and running economy. Likewise, future studies examining MTC should consider measuring running economy and stride parameters in parallel.

This study has several strengths that build upon the MTC literature. The high camera frame rate employed (one frame = 0.0025 sec) allowed for small stride differences to be detected between conditions. Moreover, the constant-velocity task allowed for the direct comparison of beverage effects, which is important since self-pacing complicates interpretation due to the dependency of stride on velocity (Hoyt et al., 2000). The running duration was longer and sample size was larger compared to previous studies examining carbohydrate and stride parameters (Brisswalter et al., 2000; Sproule, 1998). Unlike the majority of previous MTC research, this investigation was double-blinded with data on the effectiveness of participant blinding. While several studies

115

reported single- (Hulston et al., 2009; Jeukendrup et al., 2006; Jeukendrup & Moseley, 2010; Lecoultre et al., 2010; Riddell et al., 2001) or double-blinding (Baur et al., 2014; Clarke et al., 2012; O'Brien & Rowlands, 2011; O'Brien et al., 2013; Pfeiffer et al., 2009; Roberts et al., 2014; Rowlands et al., 2012; Rowlands et al., 2008; Triplett et al., 2010), only two formally evaluated beverage flavor characteristics (Rowlands et al., 2008; O'Brien et al., 2013).

On the other hand, several limitations to this investigation are apparent. Treadmill running does not completely replicate over-ground running (Wank, Frick, & Schmidtbleicher, 1998), although at moderate velocities (3.3-4.8 m·sec^{-1}) and on horizontal surfaces (no incline) the differences in SL, SF, and CT appear to be small (Elliott & Blanksby, 1975; Nelson, Dillman, Lagasse, & Bickett, 1972). Regardless, the differences observed between G and GF should only be generalized to the studied velocities and further generalization is limited until studies are done using over-ground running. Additionally, we did not utilize a non-carbohydrate control in an effort to minimize the number of prolonged runs and maximize recruitment. Lastly, the effect sizes for SF and SL were quite small, which makes interpreting the practical relevance of the findings challenging.

Conclusions

In summary, this investigation demonstrated that ingestion of a glucose-fructose beverage, relative to a glucose-only beverage, better maintained SF during 120 min of constant-velocity running. Furthermore, ingestion of glucose-fructose possibly led to greater SL during a 4-mile TT, although the effect on running velocity was unclear despite tending to be faster with glucose-fructose. The magnitude of these effects was quite small, however, so studies with adequate sample sizes and sensitive measures will be required to further elucidate the effects of MTC on running stride parameters.

6

Dissertation Summary and Future Directions

The purpose of the dissertation was to address several limitations in the literature regarding MTC. Research on MTC has grown substantially over the past two decades, and as a result, food manufacturers, sport nutritionists, and researchers alike often recommend using foods and beverages with MTC in a wide-variety of sport settings. Despite the growing evidence, few studies have examined MTC while running, and given its popularity across the world, more research in this setting is urgently needed. Furthermore, no published study has quantified the use of MTC in a non-simulated setting, despite an abundance of laboratory-based cycling research. Athletes today have hundreds of carbohydrate supplements to choose from, and many of these products contain drastically different saccharide profiles. Previous literature seems to indicate that consuming glucose-fructose in a ratio of 1.2:1 to 1:1 is optimal for increasing exogenous carbohydrate oxidation and reducing GI distress. To what extent athletes choose foods and beverages meeting this criteria, however, has not been addressed in previous research. Additionally, it hasn't been addressed whether consumption of specific saccharides during non-simulated competition is associated with GI distress. Finally, previous studies largely failed to include women, as only 17 of 266 participants from 24 studies have been female. The findings of this dissertation related to these shortcomings are detailed below, organized by the Specific Aims addressed in Chapter 1.

Specific Aim 1 was to provide a quantitative description of saccharides used during an ultra-endurance triathlon and subsequently compare the estimates to recommendations from MTC literature (Chapter 3). In addition, it was hypothesized that glucose and fructose intake would be positively and negatively associated with GI distress during the run among participants consuming $\geq$50 g·hr^{-1} carbohydrate during the swim and bicycle. In general, the majority of foods and beverages used by relatively experienced triathletes did not meet the recommendation for saccharide composition, and the median glucose-to-fructose ratio ingested by participants was 2.9:1. Moreover, the vast majority of foods and beverages used (>90%) did not contain glucose and fructose in a ratio of 1.2:1 to 1:1, and over half contained greater than a 3:1 ratio. Practitioners and athletes can use the saccharide food and beverage profiles within this dissertation to

guide nutrition selection during competition. The data also showed that glucose intake during the swim and bicycle was associated with GI distress incidence during the run among participants consuming a high rate of carbohydrate. The association between fructose intake and GI distress was less clear, however, as the correlation was statistically insignificant when fructose from sucrose was included.

Specific Aim 2 was to examine the effects of MTC on metabolism, psychological affect, GI distress, and performance during prolonged endurance running (Chapter 4). It was hypothesized that glucose-fructose ingestion, in comparison to glucose-only, would result in better TT performance, less GI distress, greater blood lactate, greater total carbohydrate oxidation, and lower feelings of displeasure. The primary outcome, TT performance, was likely improved by at least 0.8% with glucose-fructose ingestion, with magnitudes of improvement ranging from 1.6-2.6% for men and women. In addition, glucose-fructose ingestion possibly reduced GI distress and possibly improved psychological affect. Despite these benefits, glucose-fructose ingestion did not increase blood lactate or result in higher end-exercise carbohydrate oxidation. These results apply to athletes consuming fluid and carbohydrate at relatively aggressive rates (500-600 ml·hr^{-1} and 1.0-1.3 g·min^{-1}) during prolonged running at 60-70% VO$_{2peak}$.

Specific Aim 3 was to examine the effects of MTC on ST, SF, CT, and SL during prolonged running (Chapter 5). It was hypothesized that that glucose-fructose ingestion, in comparison to glucose-only, would result in lower CT and higher SF during constant-velocity running lasting 120 min. Indeed, glucose-fructose ingestion better maintained SF during 120 min of constant-velocity running, although the magnitude of the effect was quite small. On the contrary, the data did not support the hypothesis that glucose-fructose ingestion would result in lower CT. Finally, ingestion of glucose-fructose possibly led to greater SL at mile 1.7 of a 4-mile TT.

This dissertation, in the grand perspective, builds substantially upon previous MTC research. The findings from Chapter 3 suggest that many athletes do not consume a balanced mix of glucose and fructose during ultra-endurance competition. This is likely due, in part, to the typical saccharide profile found in many of the products marketed and

sold as carbohydrate supplements. This suggests that athletes may need to pay closer attention to the saccharide composition of the products they use during competition. Likewise, more dissemination of knowledge may be needed to achieve greater awareness on the potential benefits and applications of MTC. Despite these findings, more research is needed to confirm that specific saccharides ingested during competition are associated with GI distress and performance. Although the data supports the notion that individuals consuming a high rate of carbohydrate predominantly as glucose may experience more GI distress, the analysis from Chapter 3 was of an exploratory nature meant to provide a framework for future research. Additional research in a variety of sport populations is needed to confirm these findings.

The findings from Chapters 4 and 5 markedly improve the literature on MTC ingestion during endurance running. As mentioned, only two previous studies have examined the effects of MTC during running, both of which showed no performance benefit. The sample size of 20 makes this the largest laboratory study investigating MTC during exercise, as only one field trial managed to achieve a larger sample. Moreover, the results are more practical and applicable in several respects. With the inclusion of women, this dissertation provides the first evidence that MTC can improve performance for men and women alike. Additionally, the beverage volume and carbohydrate concentration used, while still aggressive, were more realistic than many prior protocols. The fact that participants completed trials in a fed state also improves generalizability, as rarely do athletes begin competition after 10-12 hours of fasting.

Although this dissertation addresses several literature shortcomings, additional questions remain regarding the ingestion of MTC during training and competition. The data herein support the notion that glucose-fructose ingestion during endurance running is superior to glucose-only when carbohydrate intake is high (>1.0 g·min^{-1}), but future studies need to compare the ingestion of MTC to other strategies. For example, it is currently unknown whether ingestion of glucose-fructose at a high rate is superior to ad libitum intake. Since many individuals adjust their nutrition intake to minimize GI distress, it is plausible that some athletes will automatically choose a strategy that is

optimal for performance. Thus, recommending that a product contain a mix glucose-fructose when an athlete regularly consumes carbohydrate at $\geq$60 g·hr^{-1} is sound advice, but telling athletes that self-select lower intakes to increase intake to $\geq$60 g·hr^{-1} may not necessarily be advantageous. Several other questions regarding MTC need to be addressed, and while not meant to be a comprehensive list, areas for future research are outlined below:

1. Do GI disturbances lesson with repeated exposure to glucose-only feedings, thereby mitigating some of the proposed negative effects?

2. Do high-intensity, intermittent activities—such as basketball and soccer—benefit from MTC?

3. What are the mechanisms responsible for the improved psychological affect observed with MTC?

4. Do the performance benefits observed in the laboratory persist when tests are conducted in more ecologically-valid settings?

5. Does the form of carbohydrate (solid, semi-solid, liquid) alter the effectiveness of MTC?

6. Do minimally-processed foods with different saccharide profiles exhibit similar effects as the highly-refined ingredients used in previous work?

7. To what extent do athletes from other sports and competitions use foods containing MTC?

8. To what extent are athletes from other sports aware of the research and recommendations regarding MTC?

9. Does MTC ingestion, compared to glucose-only, result in improved adaptation to chronic training?

10. Given emerging evidence in sedentary populations, are there any health concerns for athletes frequently consuming fructose during exercise?

7

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8

Appendices

8.1 Institutional Review Board Approval Letter (Triathlon Data)

University of Minnesota

Twin Cities Campus	Human Research Protection Program	D528 Mayo Memorial Building
	Office of the Vice President for Research	420 Delaware Street S.E.
		MMC 820
		Minneapolis, MN 55455
		Office: 612-626-5654
		Fax: 612-626-6061
		E-mail: irb@umn.edu or ibc@umn.edu
		Website: http://research.umn.edu/subjects/

03/01/2013

Patrick B Wilson
UMD Recreational SportsD2
121   SpHC
Duluth, MN 55812

> RE: "Assessment of the Carbohydrate Sources Consumed during an Ultra-endurance
>   Triathlon."
>   IRB Code Number: **1302P28241**

Dear Mr. Wilson:

The Institutional Review Board (IRB) received your response to its stipulations. Since this information satisfies the federal criteria for approval at 45CFR46.111 and the requirements set by the IRB, final approval for the project is noted in our files. Upon receipt of this letter, you may begin your research.

IRB approval of this study includes the consent form received February 11, 2013.

The reviewer commends you on a well-written application.

The IRB would like to stress that subjects who go through the consent process are considered enrolled participants and are counted toward the total number of subjects, even if they have no further participation in the study. Please keep this in mind when calculating the number of subjects you request. This study is currently approved for 70 subjects. If you desire an increase in the number of approved subjects, you will need to make a formal request to the IRB.

For your records and for grant certification purposes, the approval date for the referenced project is February 28, 2013 and the Assurance of Compliance number is FWA00000312 (Fairview Health Systems Research FWA00000325, Gillette Children's Specialty Healthcare FWA00004003). Research projects are subject to continuing review and renewal; approval will expire one year from that date. You will receive a report form two months before the expiration date. If you would like us to send certification of approval to a funding agency, please tell us the name and address of your contact person at the agency.

As Principal Investigator of this project, you are required by federal regulations to inform the IRB of any proposed changes in your research that will affect human subjects. Changes should not be initiated until written IRB approval is received. Unanticipated problems or serious unexpected adverse events should be reported to the IRB as they occur.

The IRB wishes you success with this research. If you have questions, please call the IRB office at 612-626-5654.

Sincerely,

Christina Dobrovolny, CIP
Research Compliance Supervisor
CD/ks

CC: Stacy Ingraham

8.2 Institutional Review Board Approval Letter (Chapters 4 and 5)

UNIVERSITY OF MINNESOTA

Twin Cities Campus   ***Human Research Protection Program***   *D528 Mayo Memorial Building*
           Office of the Vice President for Research   *420 Delaware Street S.E.*
           MMC 820
           Minneapolis, MN 55455

Office: 612-626-5654
Fax: 612-626-6061
E-mail: irb@umn.edu or ibc@umn.edu
Website: http://research.umn.edu/subjects/

09/04/2013

Patrick B Wilson
UMD Recreational Sports
121   SpHC
Duluth, MN 55812

RE: "The Effects of Two Carbohydrate Sources on Metabolism and Performance during
       Endurance Running"
       IRB Code Number: **1308M40761**

Dear Dr. Wilson:

The referenced study was reviewed by expedited review procedures and approved on September 3, 2013. If you have applied for a grant, this date is required for certification purposes as well as the Assurance of Compliance number which is FWA00000312 (Fairview Health Systems Research FWA00000325, Gillette Children's Specialty Healthcare FWA 00004003). Approval for the study will expire one year from that date. A report form will be sent out two months before the expiration date.

Institutional Review Board (IRB) approval of this study includes the consent form dated August 9, 2013; and recruitment e-mail and recruitment flier, both received August 12, 2013.

The IRB would like to stress that subjects who go through the consent process are considered enrolled participants and are counted toward the total number of subjects, even if they have no further participation in the study. Please keep this in mind when calculating the number of subjects you request. This study is currently approved for 30 subjects. If you desire an increase in the number of approved subjects, you will need to make a formal request to the IRB.

The code number above is assigned to your research. That number and the title of your study must be used in all communication with the IRB office.

As the Principal Investigator of this project, you are required by federal regulations to inform the IRB of any proposed changes in your research that will affect human subjects. Changes should not be initiated until written IRB approval is received. Unanticipated problems and adverse events should be reported to the IRB as they occur. Research projects are subject to continuing review and renewal. If you have any questions, call the IRB office at 612-626-5654.

On behalf of the IRB, I wish you success with your research.

Sincerely,

Christina Dobrovolny, CIP
Research Compliance Supervisor
CD/ks

CC: Stacy Ingraham

8.3 High-performance Liquid Chromatography Sample Report

Final Report

MEDALLION LABS

9000 Plymouth Avenue North, Minneapolis MN 55427
1-800-245-5615 (763) 764-4453 Fax: (763) 764-4010

Completion Date: October 29, 2013
Date Submitted: October 18, 2013
Medallion Company ID: U_MINNESOTA07
Company Code: 15540

Patrick Wilson
University of Minnesota
School of Kinesiology
1900 University Avenue SE
Minneapolis, MN 55455
Email: wilso733@umn.edu

Library Number: 2013-MED-11304
PO Number: VISA

Fax:

Medallion Labs Sample ID: 2013-MED-11304-04   Apple Sauce
Customer Sample ID: 029

Assay Group	Test	Results	Test Date
Sample Handling Processing Level 1	Sample Process Fee	Sample Processed	10/18/13
Sugars	Fructose	7.09 %	10/25/13
	Glucose	4.45 %	
	Sucrose	1.45 %	
	Maltose	Less than 0.1 %	
	Lactose	Less than 0.1 %	
	Total Sugars	13.0 %	

Medallion Labs Sample ID: 2013-MED-11304-05   Coconut Water
Customer Sample ID: 030

Assay Group	Test	Results	Test Date
Sample Handling Processing Level 1	Sample Process Fee	Sample Processed	10/18/13
Sugars	Fructose	1.21 %	10/25/13
	Glucose	2.42 %	
	Sucrose	1.27 %	
	Maltose	Less than 0.1 %	
	Lactose	Less than 0.1 %	
	Total Sugars	4.90 %	

Medallion Labs Sample ID: 2013-MED-11304-08   Peanut Butter Bar
Customer Sample ID: 033

Assay Group	Test	Results	Test Date
Sample Handling Processing Level 1	Sample Process Fee	Sample Processed	10/18/13
Sugars	Fructose	1.62 %	10/25/13
	Glucose	10.7 %	
	Sucrose	4.03 %	
	Maltose	9.53 %	
	Lactose	Less than 0.1 %	
	Total Sugars	25.9 %	

Medallion Labs Sample ID: 2013-MED-11304-09   Powder Three
Customer Sample ID: 034

Assay Group	Test	Results	Test Date
Sample Handling Processing Level 1	Sample Process Fee	Sample Processed	10/18/13
Sugars	Fructose	32.6 %	10/29/13
	Glucose	32.2 %	
	Sucrose	32.9 %	
	Maltose	Less than 0.1 %	
	Lactose	Less than 0.1 %	
	Total Sugars	97.7 %	