

# **REVIEW PAPER**

# Ketogenic Diet and Sport Performance

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### Abstract

Many athletes are concerned about attaining or maintaining optimal body weight and composition for their sport. Athletes may want to reduce body weight to ensure optimal performance, to improve aesthetic appearance, or to compete in weight category sports. This leads to efforts to reduce body fat without losing muscle mass and often to nutritional practices that may have severe health consequences. A ketogenic diet is high in fat and low in carbohydrates (≤50 g d-1) and fairly high in protein. There are numerous randomized controlled studies showing that ketogenic diets effectively reduce body fat without causing excessive loss of lean body tissue. The crucial question is whether these diets influence sports performance and, if so, how. Many nutrition-exercise combinations have been studied in an effort to increase rates of fatty acid oxidation and attenuate the rate of carbohydrate utilization, thus potentially augmenting exercise performance. The evidence suggests that increased fat availability transfers into higher rates of both whole-body and muscle lipid utilization during standardized submaximal aerobic exercise. However, despite greater rates of fat oxidation, these diets consistently fail to improve endurance performance compared with a carbohydrate-rich diet, and little is known about the effect of a ketogenic diet on strength performance.

Keywords: ketogenic diet, physical exercise, endurance exercise, central fatigue, aerobic exercise

#### Introduction

The ketogenic diet (KD) is a nutritional approach consisting of high-fat and adequate protein content but insufficient levels of carbohydrates for metabolic needs (<20 g d-1 or 5% of total daily energy intake (Moscatelli et al., 2016; Paoli, Bianco, & Grimaldi, 2015; Phinney, Bistrian, Evans, Gervino, & Blackburn, 1983), thus forcing the body to use fat as a primary fuel source. The original KD was proposed as a 4:1 lipid:nonlipid ratio, with 80% of daily energy intake from fat, 15% protein, and 5% carbohydrate. Many modifications subsequently have been introduced to the original KD, for example, lowering the lipid: nonlipid ratio or no restrictions in daily energy (in kilojoules) intake with protein and fat. The majority of knowledge about the metabolic aspects of KD comes from studies conducted at the end of the 1960s (Owen et al., 1967; Owen, Felig, Morgan, Wahren, & Cahill, 1969); it has been shown that fasting ingesting (i.e., no or minimal amounts of food and caloric beverages for periods that typically range from 12 h to 3 wk) (Paoli et al., 2015) induces a particular metabolic state called "ketosis" (Chieffi et al., 2017).

Ketosis, the metabolic response to an energy crisis, is a mechanism to sustain life by altering oxidative fuel selection. Often overlooked for its metabolic potential, ketosis is poorly understood outside of starvation or diabetic crisis. Ketone body metabolism is a survival trait conserved in higher organisms to prolong life during an energy deficit or metabolic crisis. The advantages of ketone body metabolism during starvation are clear; providing an oxidizable carbon source to



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conserve precious glucose/gluconeogenic reserves while simultaneously satisfying the specific fuel demands of the brain. Ketone bodies, when present, act not only as respiratory fuels to power oxidative phosphorylation but as signals regulating the preferential oxidation and mobilization of fuel substrates (Moscatelli et al., 2015).

Many athletes are concerned about attaining or maintaining an optimal body weight and body composition for their sport (Kiens & Astrup, 2015; Messina et al., 2015). Athletes may want to reduce body weight to ensure optimal performance, to improve aesthetic appearance, or to compete in weight category sports. This leads to efforts to reduce body fat without losing muscle mass and often to nutritional practices that may have severe health consequences. The KD can be used by athletes to produce weight loss without impairing performance, especially strength performance. There are numerous randomized controlled studies showing that KD effectively reduces body fat without causing excessive loss of lean body tissue (Gibson et al., 2015; Viggiano et al., 2016). The crucial question is whether these diets influence sports performance. Many nutrition-exercise combinations have been studied in an effort to increase rates of fatty acid oxidation and attenuate the rate of carbohydrate utilization, thus potentially augmenting exercise performance.

The interaction between exercise-induced responses and nutrient availability has long been recognized (Hawley & Burke, 2010). It seems that altering the substrate supply during exercise can modify a training impulse, but it has not been clearly determined to what extent. Skeletal muscle energy status exerts profound effects on resting metabolism and fuel use during exercise, exercise capacity, regulation of cell signalling and gene expression, as well as numerous processes involved in training adaptation. Some of the more recent studies on nutrition and exercise metabolism have attempted to examine scientific evidence for the hypothesis that endurance training undertaken with low carbohydrate availability promotes greater adaptive changes compared to high carbohydrate availability (Hawley & Burke, 2010; Lambert, Hawley, Goedecke, Noakes, & Dennis, 1997; Monda et al., 2017; Volek et al., 2009; Zajac et al., 2014).

For example, athletes in endurance sports lasting one hour or more are constantly searching for new nutrition strategies to enhance performance. Knowledge about energy metabolism has placed the focus on dietary carbohydrates in the past three to four decades, with most athletes undertaking carbohydrate loading for different periods of time before competitions (Zajac et al., 2014). High-carbohydrate diets increase muscle and liver glycogen stores, improving endurance performance, yet simultaneously increase the rate of carbohydrate utilization during exercise. Having this in mind, scientists and athletes have begun experimenting with dietary procedures that would decrease the rate of carbohydrate utilization, while increasing fat metabolism during prolonged physical work. It seems that such an alternative in exercise metabolism can be induced by a high-fat, low-carbohydrate diet. Very low carbohydrate ketogenic diets have been used for years in fighting obesity and different common and rare disease states (Gibson et al., 2015).

## **Ketogenic diet and Endurance Exercise**

In an important study performed in endurance runners, KD promoted higher peak fat oxidation (Zajac et al., 2014). This finding has been attributed to increased fat oxidation capacity. In another investigation, exhaustive cycling performance was improved by nutritional ketosis (Cox et al., 2016). This might be a limitation of the human study, and a well-designed in vivo or in vitro experiment may validate this result. It was reported that in an experiment that lasted for 762 days, muscle mitochondrial volume was increased by KD (Parry et al., 2018). Other authors show that a 12-week KD combined with daily treadmill exercise induced higher gene expression in markers of fatty acid oxidation, as compared with the control diet combined with exercise (Shimizu et al., 2018). It was also reported that ketolytic metabolism and lipolytic metabolism were remodelled by an eight-week KD in mice, thereby enhancing their endurance (Ma et al., 2018). These results explain the partial mechanisms by which keto-adaption showed great potential in improving endurance exercise capacity. However, other researchers have reported that KD increased benefit in body composition and wellbeing but failed to enhance endurance capacity (Zinn, Wood, Williden, Chatterton, & Maunder, 2017).

Furthermore, a low-carbohydrate, high-fat diet impaired exercise economy and performance after intensified training in a group of elite race walkers (Burke et al., 2017). In an animal model, however, eight weeks of KD significantly enhanced the endurance capacity of C57/BL6 mice (Zinn et al., 2017); a correlation existed between body weight and running time until exhaustion with mice on heavier a KD running longer. This was attributed to keto-adaptation (Zinn et al., 2017). Since there was an inter-individual difference, the subjects possessing higher metabolic flexibility may prefer KD and reflect the weight change. After a two-month KD, the average weight of KD mice decreased by 30% compared with mice on a normal diet (Ma & Suzuki, 2019; Murtaza et al., 2019).

#### **Effects on Anaerobic Exercise**

Anaerobic exercise is a high intensity, low duration exercise that lasts less than 2 min. Energy demands are met by the phosphagen system and lactic acid system, which are highly dependent upon skeletal muscle glycogen. During anaerobic exercise, high contractile forces occur within the muscle, and muscle fibres become damaged. In addition to the replenishment of carbohydrates during the recovery period, adequate consumption of essential amino acids is necessary to support the protein synthesis required to repair and rebuild the muscle. In this regard, LC/KDs typically provide sufficient protein intake (~15% of daily calories) to avoid amino acid deficiency. However, due to the low carbohydrate intake, the increased reliance of amino acids toward gluconeogenesis and the impairment of glycogen-store restoration may adversely affect anaerobic performance. Several studies evaluated the effects of LC/ KDs on anaerobic performance, primarily assessing power or strength parameters, in various populations, including endurances athletes (McSwiney et al., 2018), Cross-Fit participants (Wilson et al., 2017), gymnasts (Paoli et al., 2012), and powerlifters (Greene, Varley, Hartwig, Chapman, & Rigney, 2018). Dietary interventions ranged from 6 weeks to 12 weeks and included normal training regimens typical of the populations studied. In general, consumption of the LC/KD did not result in strength or power measures that were significantly different from the control groups (Harvey, Holcomb, & Kolwicz, 2019). One study reported a significant increase in relative power, but not absolute power, which was due to the decreased body weight experienced by the subjects. In some studies, significant decreases in skeletal muscle thickness or lean body mass were noted. Moreover, muscle hypertrophy from resistance training may be blunted with the LC/KD (McSwiney et al., 2018). These studies demonstrate that the LC/KD diet is not an effective strategy to increase anaerobic performance in trained individuals or athletes, and it has the potential to negate the expected increases in lean body mass from anaerobic training (Harvey et al., 2019).

#### Effect on central fatigue

In addition to the aforementioned physiological changes in the muscle, the metabolic changes induced by long-term KD diets may also affect the central nervous system during exercise. The role of the central nervous system in the development of physical fatigue has long been recognized (Gandevia, 2001). Alterations in the metabolic fuel use during exercise after adaptation to an LCHF diet can affect cerebral amino-acid uptake, energy metabolism, and neurotransmission. The increased rate of fat oxidation during exercise after adaptation to a KD diet is likely to increase brain uptake of free tryptophan. This is the consequence of increased competition for binding to albumin by rising concentrations of non-esterified fatty acids (NEFA). Free tryptophan is the precursor of serotonin (5-hydroxytryptamine), a brain neurotransmitter associated with the feeling of lethargy and tiredness that may contribute to the loss of central drive and motivation (Davis & Bailey, 1997). Increased brain uptake of free tryptophan has been reported to favour cerebral serotonin synthesis and contribute to central fatigue (Chang, Borer, & Lin, 2017). The high protein content of KD diets also leads to elevated ammonia production during exercise (Chang et al., 2017). Ammonia is another factor that could induce central fatigue by altering cerebral energy metabolism and neurotransmission and also affect signalling pathways within the neural circuits (Secher, Seifert, & Van Lieshout, 2008). Subjects adapted to KD diets experienced higher plasma concentrations of NEFA and ammonia, two agents contributing to central fatigue, during exercise at various intensities (Ferreira et al., 2014). A pilot study with untrained adults consuming a hypocaloric KD diet for two weeks suggested that increased blood concentration of ketone bodies was associated with the feeling of fatigue and mood disturbance during submaximal exercise, which are indicators of central fatigue (Ferreira et al., 2014). There is currently a knowledge gap regarding the possible effect of long-term adaptation to LCHF diets on central fatigue in various types of exercise that is in need of additional research.

#### Conclusion

In modern sport nutrition, practitioners teach athletes to manipulate their eating practices to avoid unnecessary and excessive intakes of carbohydrates per se, to optimize training outcomes via modification of the timing, amount and type of carbohydrate-rich foods and drinks to balance periods of

#### Acknowledgements

There are no acknowledgements.

#### **Conflict of Interest**

The authors declare that there are no conflicts of interest.

Received: 08 November 2019 | Accepted: 25 December 2019 | Published: 01 February 2020

low- and high-carbohydrate availability and to adopt proven competition strategies that provide appropriate carbohydrate availability according to the needs and opportunities provided by the event and individual experience (Burke, 2015). It is important to consider insights from research and athlete testimonials to identify different scenarios in which one approach might offer advantages over another or to explain divergent outcomes, rather than insist on a single "truth" or solution. Indeed, although there is a continual cry to rid sports nutrition of "dogma" (Brukner, 2013), it would seem counterproductive if new ideas were as dogmatic as the old beliefs they seek to replace. This author and others continue to undertake research to evolve and refine the understanding of conditions in which low carbohydrate availability can be tolerated or actually beneficial (Jeukendrup, 2017). However, we also recognize that the benefits of carbohydrate as a substrate for exercise across the full range of exercise intensities via separate pathways, the better economy of carbohydrate oxidation versus fat oxidation (ATP produced per L of oxygen combusted) (Cole, Coleman, Hopker, & Wiles, 2014), and the potential CNS benefits of mouth sensing of carbohydrate (Burke & Maughan, 2015) can contribute to optimal sporting performance and should not be shunned simply because of the lure of the size of body fat stores. In other words, there should not be a choice of one fuel source or the other, or "black versus white", but rather a desire to integrate and individualize the various dietary factors that can contribute to optimal sports performance.

For endurance athletes, the literature supports LC/KDs as an effective strategy to reduce body weight and fat mass, particularly in a period of 3-12 weeks. Limited studies demonstrate a significant improvement in exercise performance at submaximal (~60%) intensities. However, exercise performance at higher intensities may actually be impaired. For athletes concerned with anaerobic power and strength, short-term consumption of LC/KDs does not negatively affect these performance parameters but may lead to unwelcomed decreases in lean body mass or blunted skeletal muscle hypertrophy. Therefore, the literature does not support the use of LC/KD as an effective dietary strategy to increase athletic performance. Ketone body supplements, including KS and KE, are commercially available and gaining popularity in the exercise community. However, since supplements are not evaluated or approved by the Food and Drug Administration (FDA), consumers must pay careful attention to the components of the supplements. Compared to KS, KE supplements appear to be more effective at inducing ketosis; however, there are limited studies demonstrating improvements in the exercise performance of trained athletes. Moreover, the benefits of KE supplementation in non-athletes is unknown. Although recent research findings lend support to targeting ketone body metabolism for the treatment of cardiac dysfunction, obesity, diabetes, and exercise performance, further research is needed before dietary interventions or supplementation is implemented.

#### References

- Brukner, P. (2013). Challenging beliefs in sports nutrition: Are two "core principles" proving to be myths ripe for busting? Br. J. Sports Med., 47, 663-664. doi:10.1136/bjsports-2013-092440.
- Burke, L.M. (2015). Re-Examining High-Fat Diets for Sports Performance: Did We Call the 'Nail in the Coffin' Too Soon?. Sports Med., 45, 33–49. doi:10.1007/s40279-015-0393-9
- Burke, L.M., & Maughan, R.J. (2015). The Governor has a sweet tooth Mouth sensing of nutrients to enhance sports performance. Eur. J. Sport Sci.,

15(1), 29-40. doi:10.1080/17461391.2014.971880.

- Burke, L.M., Ross, M.L., Garvican-Lewis, L.A., Welvaert, M., Heikura, I.A., Forbes, S.G., Mirtschin, J.G., Cato, L.E., Strobel, N., Sharma, A.P., & Hawley, J.A. (2017). Low carbohydrate, high fat diet impairs exercise economy and negates the performance benefit from intensified training in elite race walkers. J. Physiol., 595(9), 2785-2807. doi:10.1113/JP273230.
- Chang, C.K., Borer, K., & Lin, P.J. (2017). Low-Carbohydrate-High-Fat Diet: Can it Help Exercise Performance? J. Hum. Kinet., 56, 81-92. doi:10.1515/ hukin-2017-0025.
- Chieffi, S., Messina, G., Villano, I., Messina, A., Valenzano, A., Moscatelli, F., Salerno, M., Sullo, A., Avola, R., Monda, V., Cibelli, G., & Monda, M. (2017) Neuroprotective Effects of Physical Activity: Evidence from Human and Animal Studies. *Front. Neurol.*, 8,188. doi: 10.3389/fneur.2017.00188
- Cole, M.J., Coleman, D.A., Hopker, J.G., Wiles, J. (2014). Improved Gross Efficiency during Long Duration Submaximal Cycling Following a Short-term High Carbohydrate Diet. *International journal of sports medicine*, 35(3), 265-269. doi:10.1055/s-0033-1348254
- Cox, P. J., Kirk, T., Ashmore, T., Willerton, K., Evans, R., Smith, A., Murray, A.J., Stubbs, B., West, J., McLure, S.W., King, M.T., Dodd, M.S., Holloway, C., Neubauer, S., Drawer, S., Veech, R.L., Griffin, J.L., & Clarke, K. (2016). Nutritional Ketosis Alters Fuel Preference and Thereby Endurance Performance in Athletes. *Cell Metab.*, 24(2), 256-68. doi:10.1016/j. cmet.2016.07.010.
- Davis, J.M., & Bailey, S.P. (1997). Possible mechanisms of central nervous system fatigue during exercise. *Medicine and Science in Sports and Exercise*, 29(1), 45-57. doi:10.1097/00005768-199701000-00008.
- Ferreira, G.A., Osiecki, R., Lima-Silva, A.E., De Angelis-Pereira, M.C., & De-Oliveira, F.R. (2014). Effect of a reduced-CHO diet on the rate of perceived exertion curve during an incremental test. *Int. J. Sport Nutr. Exerc. Metab.*, 24(5), 532-542. doi:10.1123/ijsnem.2013-0248.
- Gandevia, S.C. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiol. Rev.*, *81*, 1725–89.
- Gibson, A.A., Seimon, R.V., Lee, C.M.Y., Ayre, J., Franklin, J., Markovic, T.P., Caterson, I.D., & Sainsbury, A. (2015). Do ketogenic diets really suppress appetite? A systematic review and meta-analysis. *Obes. Rev.* doi:10.1111/obr.12230.
- Greene, D.A., Varley, B.J., Hartwig, T.B., Chapman, P., & Rigney, M. (2018). A low-carbohydrate ketogenic diet reduces body mass without compromising performance in powerlifting and olympic weightlifting athletes. J. Strength Cond. Res., 32(12), 3373-3382. doi: 10.1519/ JSC.00000000002904.
- Harvey, K.L., Holcomb, L.E., & Kolwicz, S.C. (2019). Ketogenic Diets and Exercise Performance. *Nutrients*, *11*, 2296. doi:10.3390/nu11102296.
- Hawley, J.A., & Burke, L.M. (2010). Carbohydrate availability and training adaptation: Effects on cell metabolism. *Exerc. Sport Sci. Rev.*, 38(4), 152-160. doi:10.1097/JES.0b013e3181f44dd9.
- Jeukendrup, A.E. (2017). Periodized Nutrition for Athletes. Sport. Med., 47(Suppl. 1), 51–63. doi:10.1007/s40279-017-0694-2.
- Kiens, B., & Astrup, A. (2015). Ketogenic Diets for Fat Loss and Exercise Performance: Benefits and Safety? *Exerc. Sport Sci. Rev.*, 43(3), 109. doi:10.1249/JES.00000000000053.
- Lambert, E.V., Hawley, J.A., Goedecke, J., Noakes, T.D., & Dennis, S.C. (1997). Nutritional strategies for promoting fat utilization and delaying the onset of fatigue during prolonged exercise. J. Sports Sci., 15(3), 315-324. doi:10.1080/026404197367326.
- Ma, S., Huang, Q., Tominaga, T., Liu, C., & Suzuki, K. (2018). An 8-Week Ketogenic Diet Alternated Interleukin-6, Ketolytic and Lipolytic Gene Expression, and Enhanced Exercise Capacity in Mice. *Nutrients.*, 10(11), 1696. doi:10.3390/nu10111696.
- Ma, S., & Suzuki, K. (2019). Keto-Adaptation and Endurance Exercise Capacity, Fatigue Recovery, and Exercise-Induced Muscle and Organ Damage Prevention: A Narrative Review. Sports, 7(2), pii: E40. doi:10.3390/ sports7020040.
- McSwiney, F.T., Wardrop, B., Hyde, P.N., Lafountain, R.A., Volek, J.S., & Doyle, L. (2018). Keto-adaptation enhances exercise performance and body composition responses to training in endurance athletes. *Metabolism*, *81*, 25-34. doi:10.1016/j.metabol.2017.10.010.ž
- Messina, G., Zannella, C., Monda, V., Dato, A., Liccardo, De Blasio, S., Valenzano, A., Moscatelli, F., Messina, A., Cibelli, G., & Monda, M.

(2015). The Beneficial Effects of Coffee in Human Nutrition. *Biology and Medicine*, 7(4), 1-5. doi:10.4172/0974-8369.1000.

- Monda, V., Valenzano, A., Moscatelli, F., Salerno, M., Sessa, F., Triggiani, A.I., et al. (2017). Primary Motor Cortex Excitability in Karate Athletes: A Transcranial Magnetic Stimulation Study. *Front. Physiol.* 8, 695. doi:10.3389/fphys.2017.00695.
- Moscatelli, F., Messina, G., Valenzano, A., Petito, A., Triggiani, A.I., Ciliberti, M.A.P., Monda, V., Messina, A., Tafuri, D., Capranica, L., Cibelli, G., & Monda, M (2015). Relationship between RPE and Blood Lactate after Fatiguing Handgrip Exercise in Taekwondo and Sedentary Subjects. *Biol. Med.*, 1, S3008. doi:10.4172/0974-8369.1000s3008
- Moscatelli, F., Messina, G., Valenzano, A., Monda, V., Viggiano, A., Messina, A., et al. (2016) Correction: Functional Assessment of Corticospinal System Excitability in Karate Athletes. *Plos One*, *11*(7), e0159846. https://doi. org/10.1371/journal.pone.0159846
- Murtaza, N., Burke, L., Vlahovich, N., Charlesson, B., O' Neill, H., Ross, M., Campbell, K., et al. (2019). The Effects of Dietary Pattern during Intensified Training on Stool Microbiota of Elite Race Walkers. *Nutrients*, *11*(2), 261. doi.org/10.3390/nu11020261
- Owen, O.E., Felig, P., Morgan, A.P., Wahren, J., & Cahill, G.F. (1969). Liver and kidney metabolism during prolonged starvation. J. Clin. Invest., 48(3), 574-583. doi:10.1172/JCI106016.
- Owen, O.E., Morgan, A.P., Kemp, H.G., Sullivan, J.M., Herrera, M.G., & Cahill, G.F. (1967). Brain metabolism during fasting. J. Clin. Invest., 46(10), 1589-1595. doi:10.1172/JCI105650.
- Paoli, A., Bianco, A., & Grimaldi, K.A. (2015). The Ketogenic Diet and Sport: A Possible Marriage? *Exerc. Sport Sci. Rev.*, 43(3), 153-62 doi:10.1249/ JES.00000000000050.
- Paoli, A., Grimaldi, K., D'Agostino, D., Cenci, L., Moro, T., Bianco, A., et al. (2012). Ketogenic diet does not affect strength performance in elite artistic gymnasts. J. Int. Soc. Sports Nutr., 9(34). doi:10.1186/1550-2783-9-34.
- Parry, H.A., Kephart, W.C., Mumford, P.W., Romero, M.A., Mobley, C.B., Zhang, Y., et al. (2018). Ketogenic diet increases mitochondria volume in the liver and skeletal muscle without altering oxidative stress markers in rats. *Heliyon*, 4(11), e00975. doi:10.1016/j.heliyon.2018.e00975.
- Phinney, S.D., Bistrian, B.R., Evans, W.J., Gervino, E., & Blackburn, G.L. (1983). The human metabolic response to chronic ketosis without caloric restriction: Preservation of submaximal exercise capability with reduced carbohydrate oxidation. *Metabolism*, 32(8), 769-776. doi:10.1016/0026-0495(83)90106-3.
- Secher, N.H., Seifert, T., & Van Lieshout, J.J. (2008). Cerebral blood flow and metabolism during exercise: Implications for fatigue. J. Appl. Physiol., 104, 306–314 doi:10.1152/japplphysiol.00853.2007.
- Shimizu, K., Saito, H., Sumi, K., Sakamoto, Y., Tachi, Y., & Iida, K. (2018). Shortterm and long-term ketogenic diet therapy and the addition of exercise have differential impacts on metabolic gene expression in the mouse energy-consuming organs heart and skeletal muscle. *Nutr. Res., 60*, 77-86. doi:10.1016/j.nutres.2018.09.004.
- Viggiano, E., Monda, V., Messina, A., Moscatelli, F., Valenzano, A., Tafuri, D., et al. (2016). Cortical spreading depression produces a neuroprotective effect activating mitochondrial uncoupling protein-5. *Neuropsychiatr. Dis. Treat.*, 12, 1705–10. doi:10.2147/NDT.S107074.
- Volek, J.S., Phinney, S.D., Forsythe, C.E., Quann, E.E., Wood, R.J., Puglisi, M.J., et al. (2009). Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. *Lipids*, 44(4), 297-309. doi:10.1007/s11745-008-3274-2.
- Wilson, J.M., Lowery, R.P., Roberts, M.D., Sharp, M.H., Joy, J.M., Shields, K.A., et al. (2017). The Effects of Ketogenic Dieting on Body Composition, Strength, Power, and Hormonal Profiles in Resistance Training Males. J. Strength Cond. Res. doi:10.1519/jsc.000000000001935.
- Zajac, A., Poprzecki, S., Maszczyk, A., Czuba, M., Michalczyk, M., & Zydek, G. (2014). The effects of a ketogenic diet on exercise metabolism and physical performance in off-road cyclists. *Nutrients*, 6(7), 2493-508. doi:10.3390/nu6072493.
- Zinn, C., Wood, M., Williden, M., Chatterton, S., & Maunder, E. (2017). Ketogenic diet benefits body composition and well-being but not performance in a pilot case study of New Zealand endurance athletes. J. Int. Soc. Sports Nutr., 14(22). doi:10.1186/s12970-017-0180-0.