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The Impact of the Ketogenic Diet on Depression and Psychological Well-being: A Randomised Controlled Trial with Integrated Qualitative Analysis

by

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Abstract

Background and aims:
There is evidence to suggest that a ketogenic diet (KD) may help to alleviate psychiatric symptoms, including depression, but this has not been studied extensively or compared directly to the impact of the more common low carbohydrate diet (LCD). The aim of this research was to understand the impact of a non-calorie-restricted low carbohydrate diet and ketogenic diet on depression and aspects of psychological well-being in those with either mild to moderate depressive symptoms or low or no depressive symptoms.

Materials and methods: In a randomised control trial with quasi experimental design, participants with mild to moderate depressive symptoms and low depressive symptoms were randomised into either a LCD, a KD, or a control diet (diet as usual) generating a total of 6 participant groups. The dietary interventions (LCD and KD) were delivered through an online education platform for 12 weeks, followed by 12 weeks of unsupported continued diet. The control diet was maintained for a total of 6 weeks. Examinations at baseline (T0), day 1, week 6, week 12, and week 24 included questionnaires and psychological measures stress, anxiety, mental well-being, positive and negative affect, depression, self-compassion, social support, and body appreciation. Demographical data was also collected and analysed. Attrition rates were explored post intervention, and a qualitative thematic analysis was carried out on participants interview data following the KD to better understand their experience of the dietary intervention.

Results: From study 1, the KD group saw no improvements in psychological well-being. The LCD group reported significant improvements in stress, anxiety, and negative affect after 12 weeks and in depressive symptoms after 24 weeks compared to the KD and control group. Significant improvements in positive affect, mental well-being and depressive symptoms were found in those with lower levels of body appreciation compared to those with higher levels, regardless of diet type. From study 2, dropout rates peaked during the 12-week intervention compared to post intervention and the end of the study at 24 weeks. Those with depressive symptoms were less likely to drop out of the study compared to those who were 'healthy'. From the qualitative study 3, participants in the KD group experienced both physical and mental health improvements. They lost weight and experienced an increase in confidence, energy, and self-esteem. Some reported a renewed meaning and purpose in life.

Conclusion:
The ketogenic diet did not improve quantitatively measured depressive symptoms or aspects of psychological well-being from self-reported questionnaires. However, from interview data, improvements were experienced by those on the ketogenic diet suggesting that the diet worked for some. Reasons for this contradiction are explored and may be explained in part, by reviewing the intervention design. A low carbohydrate diet was found to improve some aspects of psychological well-being in those with mild to moderate depressive symptoms over 24 weeks. Adverse events experienced were mild and temporary, but retention of participants was challenging. Further well-designed randomised control trials are warranted to identify whether a ketogenic diet would improve psychological well-being in those with more severe depression akin to antidepressant efficacy.

Declaration

I declare that this work has been composed entirely by myself, and that it has not been submitted, in whole or in part, in any previous application for a degree. Except where explicitly stated otherwise by reference or acknowledgment, the work presented is entirely my own.

Erin Louise Bellamy

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Chapter 1: Introduction and Literature Review

1.1 Ketogenic Diets

Ketogenic Metabolic Therapy is a dietary approach in which the macronutrients of meals, fat, carbohydrates, and proteins, are distributed in such a way as to put the body in a ketogenic metabolic state whereby it creates ketones. The diet itself is more commonly known as the ketogenic diet (KD). In order to reach this metabolic state, a daily macronutrient breakdown of low carbohydrate, moderate protein and high fat is followed. The usual percentage breakdown per day is 60% fat, 30% protein and 5-10% carbohydrates, as long as carbohydrates are kept below 50g, and ideally 20g per day (Masood et al., 2022). There are many types and versions of a KD which will be explored and discussed in this section. The KD is the only diet closest to fasting that can be safely followed long-term that presents similar therapeutic outcomes (Desli et al., 2022). The difference between the KD and a low carbohydrate diet (LCD) is the amount of carbohydrates consumed per day. A LCD is commonly defined as between 90 and 130 grams of carbohydrates per day (Goldenberg et al., 2021). This is not low enough to produce ketones which are generally produced at around 50 grams of carbohydrates per day or less (Wylie-Rosett et al., 2013).

Though the benefits of a KD have been known and used medically for over 100 years to treat epilepsy (Wheless, 2008) and fasting for much longer, this way of eating has not been supported until recently for other illnesses. A small number of research groups have started to investigate the benefits of this dietary intervention within other areas of health with interesting findings. Recent research on the KD has been focused on cognition, weight loss, obesity

management, and type 2 diabetes (T2D) (Castellana et al., 2020; Chinna-Meyyappan et al., 2022; Saslow et al., 2017; Westman et al., 2018). This change in attitude towards carbohydrate consumption has led to increasing awareness for the need to further investigate the possible physical and mental health benefits of lowering carbohydrates in the human diet.

1.1.1 Ketosis

Following a KD and restricting calories are both ways to mimic the effects of fasting, a chosen period of time without food. This process switches the body from a sugar and glucose burning metabolic state into a fat and ketone burning state called "ketosis" (Paoli, 2014). Ketosis is a natural metabolic state and can be prevented in adults with approximately 50g of carbohydrates per day (Bier et al., 1999). Ketosis is a metabolic state where molecules called ketone bodies are elevated in the blood, breath and urine and are used as energy for the body when glucose reserves are low. They are made from hydrogen, carbon, and oxygen (Scott & Deuster, 2017) and the body can make then when sleeping, fasting, restricting calories (to induce ketosis), or following a ketogenic diet. There are three ketone bodies, acetoacetate (AcAc), acetone (ACE) and beta-hydroxybutyrate (BHB). There are always some ketones present, but at relatively low levels in the body, particularly when the recommended daily amount of carbohydrates is at least 200g per day, or 50% of overall energy intake (Macdonald, 1999). Interestingly, ketones are also found in pregnant women and newborn infants (Akram, 2013).

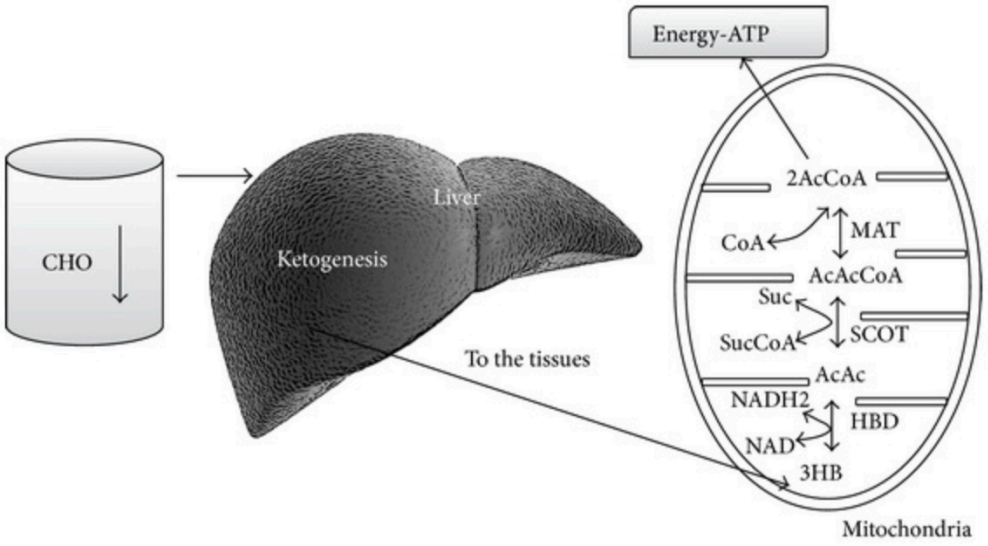

Figure 1.1: An illustration of ketone production from Paoli et al. (2014). *Abbreviations are as follows, carbohydrates (CHO), 3-hydroxybutyrate (3HB), nicotinamide adenine dinucleotide (NAD), nicotinamide adenine dinucleotide hydrogen (NADH2), hydroxybutyrate dehydrogenase (HBD), acetoacetate (AcAc), 3-CoA transferase (SCOT), succinyl-CoA (SucCoA), acetoacetyl-CoA (AcAcCoA), methylacetoacetyl-CoA thiolase (MAT), coenzyme A (CoA), Acetyl coenzyme A (2AcCoA), adenosine triphosphate (ATP) (This source is open access which permits reproduction in any medium provided it is properly cited)*

Once carbohydrates are reduced to a level that initiated ketosis (<20g/day) either through a KD or fasting, the body will utilise the glucose in the blood for energy followed by glycogen stores from the muscles and liver; providing approximately 2000kcals worth of energy (Adeva-Andany et al., 2016). This process can be maintained for approximately three days before the body needs to sequester extra energy (Batch et al., 2020).

Once the body has used the glycogen stores it turns to the liver to metabolise fat into ketones (ketogenesis) which are then sent to the mitochondria and converted into energy (ATP) to fuel the body (see Figure 1.1). This ATP energy from ketones is cleaner, produces less oxidative stress as a by-product of converting into ATP and is more efficient than ATP created from glucose (Prince

et al., 2013). Then gluconeogenesis begins, a process where the body produces its own glucose in order to maintain blood sugar while the body switches to its alternative fuel source, 'ketone metabolism'.

Fat and ketones are used as energy instead of carbohydrates and sugar (Masood et al., 2022). This fat is used as energy by most organs in the body apart from the brain and the liver which use the ketone bodies. Ketone bodies provide this energy to the brain by crossing the blood-brain barrier (Jensen et al., 2020).

The molecule AcAc is metabolised from the fat and the ketone BHB and molecule acetone are created from AcAc. ACE is measured in the breath and is a by-product of fat metabolism. This can be measured with a breath monitor and makes a person's breath smell sweet. AcAc is excreted in the urine and can be tested using urine dipsticks. This is the most popular way to test for ketones and is used in most medical centres and hospitals. The ketone BHB is measured in the blood, and it appears that BHB is the most interesting molecule when it comes to the KD's therapeutic effects on the body. Following a standard western diet high in carbohydrates, levels of ketone bodies are usually less than 0.5mmol/L as measured in the blood by a blood ketone monitor (Omori et al., 2023). Ketosis, also known as 'nutritional ketosis' has been reached once blood ketone levels increase to 0.5mmol/L and above. Therapeutic levels of ketones are found above 0.5mmol/L but for many diseases such as epilepsy, seizure control is exhibited at levels between 1-3mmol/L or higher (Anderson et al., 2021; Omori et al., 2023). Ketosis can be reached via three methods, fasting, the ketogenic diet, and taking exogenous ketones, commercially known as ketone salts, medium chain triglycerides (MCTs), and ketone esters which are

products that are ingested alongside any diet that increase ketone levels exogenously.

1.1.2 Fat adaption and metabolic flexibility

After 12-16 hours of fasting, BHB blood ketone levels begin to rise, and they reach 1-2mmol/L after 48 hours of fasting. BHB will continue to increase to 6-8mmol/L with prolonged fasting but will stop rising around 8mmol. Levels above 2mmol/L can also be reached using a KD which mimics fasting (Newman & Verdin, 2014).

Alongside this, as the body moves over from burning glucose and sugar to fat and ketones as a primary fuel, the body becomes more sensitive to certain hormones such as insulin and leptin. Insulin is a hormone responsible for maintaining normal blood glucose levels by making sure that the cells take the glucose in from the blood stream. It is responsible for growth and is released by the pancreas (Wilcox, 2005) and decreases on a KD. Leptin is a hormone responsible for balancing food intake and energy expenditure and is important for appetite regulation, along with another hormone called ghrelin (Gruzdeva et al., 2019).

After a period of four to six weeks, sometimes longer, following a KD, and being in a state of ketosis, the body becomes 'fat adapted'. The body recognises that it is using fat and ketones as the primary fuel and therefore has become more efficient at using this energy source. Energy levels should become stable, blood sugar regulated, mental focus increased, and athletic performance output balanced or even improved (Phinney et al., 1983; Phinney et al., 1980). The KD can then be maintained for as long as necessary as long as the individual meets

their nutritional recommendations for all essential fatty acids, amino acids, vitamins, and minerals. It is possible to follow a very low to zero carbohydrate diet and still get adequate nutrients if you include vegetables or organ meats in your diet (Mcclellan & Du Bois, 1930; Westman et al., 2007) and this is because there is no such thing as an essential carbohydrate, only essential proteins, and fats through amino and fatty acids (Bier et al., 1999).

1.2 Types of Ketogenic Diet and Ketone Enhancing Products

According to the research, fasting has been used as a treatment for epilepsy since the Hippocratic era (D'Andrea Meira et al., 2019; Kim, 2017). In 1911 the first research study on fasting in epilepsy was published (Guelpa, 1911). As fasting could not be maintained indefinitely, Dr Wilder at the Mayo Clinic created a high fat KD that mimicked the effects of fasting by increasing ketones and called it the KD because of its ketones producing effects (Kim, 2017).

In 1921 the 'Classic" ketogenic diet was introduced for the treatment of drug resistant epilepsy (Wilder, 1921) with introduction to clinical practice in 1925. This form of the ketogenic diet has a ratio of 4:1 of fat to protein plus carbohydrates, or 90% fat and 10% protein plus carbohydrates. This is extremely difficult to maintain over time and is mainly reserved for intense treatment of severe illnesses such as epilepsy or brain tumours, specifically glioblastoma (D'Andrea Meira et al., 2019; Klein et al., 2020).

Since 1921 the classic KD has been adapted for the treatment of other illnesses as well as for general day to day use with a variety of more relaxed ratios. There are over seven different types of the KD and for those following a KD solely to improve general health, the ratios can be modified to suit the individual's lifestyle

and goals. For example, for those wanting to lose weight, they may follow an Atkin's approach with more standard ketogenic macronutrient percentages such as 60% fat, 30% protein, and 10% carbohydrates. See Table 1.1 and 1.2 for an overview of the most popular types of KD compositions and KD dietary programs (see Tables 1.1 and 1.2).

During this decade we have seen the production of products that can enhance and improve the adherence to a KD such as MCT oil, ketone salts, and exogenous ketones. Research into exogenous ketones is underway to explore the benefits of these products for brain diseases (Wang et al., 2023). All these products increase the levels of ketones in the body, either by increasing endogenous production or through exogenous consumption (Omori et al., 2023). This helps the individual to reach levels of ketones that once might have needed a stricter dietary approach with the inclusion of intermittent or prolonged fasting. Many of these supplements are classified as generally regarded as safe (GRAS).

Table 1.1: Macronutrient composition in ratios and percentage of popular ketogenic diets and their purpose

Name	*Source*	*Year*	*Ratio*	*Fat*	*Protein*	*Carbohydrates*	*Purpose*
Classic Ketogenic Diet (CKD)	Wilder (1921)	1921	4:1	90%	6%	4%	Childhood Epilepsy
Modified Ketogenic Diet (MKD)	Multiple Reviews by Wirrell (2008) and Hee Seo et al. (2007)	1924 - 1960	3:1 2:1 1:1	87% 82% 70%	10% 12% 15%	3% 6% 15%	Children who require higher amounts of protein or carbohydrate. Easier for outpatient implementation
MCT Oil Supplement	Huttenlocher et al. (1971)	1971	1:9:1	*50%/21% (MCT/LCT)	19%	10%	Medium chain triglyceride oil is included with each meal. Allows more carbohydrates in the diet and is easier to follow for Epilepsy
Low Glycemic Index Treatment (LGIT)	Pfeifer et al. (2005)	2005	2:3	60%	28%	12%	Choosing carbohydrates with glycemic indices of less than 55. Improved tolerability and easier for outpatients with Epilepsy
Modified Atkins Diet (MAD)	Kang et al. and Kossoff et al. (2007; 2006)	2007 2006	0:8:1	65%	29-32%	3-6%	Improved tolerability and easier implementation for childhood Epilepsy
Standard Ketogenic Diet (SKD)	Bueno et al. and Kirkpatrick et al. (2013; 2019)	2013 2019	-	70-75%	20%	5-10%	Long term weight loss, obesity management, and cardiometabolic risk factors
Well Formulated Ketogenic Diet (WFKD)	Phinney et al. (1983)	1983	-	No restriction	10-30%	5-10% Less than 50g total daily	To avoid side effects and adverse events for anyone following a ketogenic diet

Table 1.2: Macronutrient composition in grams of popular ketogenic dietary programs

Name	*Source*	*Year*	*Fat*	*Protein*	*Carbohydrates*	*Purpose*	*Links and Footnotes*
Atkin's Diet	Astrup et al. (2004)	Since 1972	No restriction	No restriction	<30g	Weight loss	-
Virta Health Program	Veazie et al. (2020)	Since 2019	No restriction	1.5g/kg LBM	3–5 servings non-starchy vegetables <30g	Weight loss, T2D improvements, general health	https://www.virtahealth.com/
Low Carb Program	Diabetes.co.uk	Since 2015	No restriction	No restriction	<130g	Weight loss, T2D improvements, general health	https://www.lowcarbprogram.com/
Paleolithic Ketogenic Diet (PKD)	Clemens et al. (2018)	Since 2013	Varied paleolithic diet, animal meat and fat based	Personalised	<20g	Chronic internal diseases such as cancer, autoimmune, Crohn's and arthritis among others	https://www.paleomedicina.com/
Wahls Protocol	Irish et al. (2017)	Since 2011	Varied paleolithic diet, animal meat and fat based	50-70g/day	3 cups of raw greens <20g	Multiple Sclerosis (MS)	https://terrywahls.com/

1.3 Side Effects, Safety, and Efficacy of the Ketogenic Diet

As with any dietary initiation, there is a period of adjustment with implementation. Some people may experience side effects when starting the diet, but they are temporary and pass after a few days up to two weeks once the individual adjusts to the state of ketosis. In common terms, this phase is referred to as 'keto flu' (Batch et al., 2020; Bostock et al., 2020). Symptoms will vary and it has been noted that the severity and intensity of these side effects may differ from person to person (Bostock et al., 2020; Shalabi et al., 2021). The severity of the symptoms depends on a wealth of factors including the amount of carbohydrates consumed in the run up to starting the diet. If the diet is followed and implemented correctly, most, if not all, of these symptoms can be prevented or alleviated.

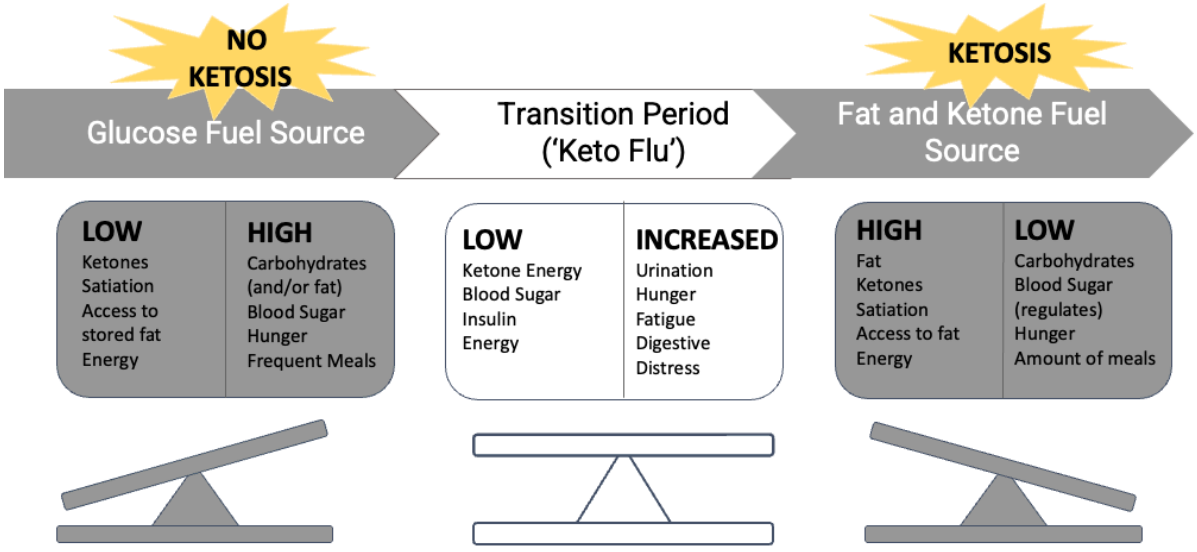

Figure 1.2: Illustration of the transition period from glucose metabolism to fat and ketone metabolism

As the body moves from burning glucose as fuel to fat and ketones for fuel there is a period where the body is in limbo without enough glucose to use for energy and unable to properly metabolise fat (see Figure 1.2). Until ketones are produced, this can leave the body feeling lethargic and fatigued. However, this resolves itself once the body is in a state of ketosis and blood glucose levels regulate. This can take anything from 24 hours to a week or two depending on the individual and their daily carbohydrate intake and fasting experience (Sethi & Ford, 2022).

Some common side effects experienced by individuals beginning to implement the diet are, temporary fatigue (Schmidt et al., 2011), temporary constipation (Schmidt et al., 2011), muscle cramps, bad breath, and heart palpitations (Bostock et al., 2020; Shalabi et al., 2021). Research suggests that the main cause of these side effects is the lack of optimal hydration and the imbalances of essential minerals and electrolytes, magnesium, potassium, and sodium (Bostock et al., 2020). When insulin is low, the body does not hold on to its glycogen stores or water. Instead, it releases it, and research shows that when the body is moving into ketosis there is an increase in micturition and a loss of body salts from the body (Rabast et al., 1981). This is called natriuresis, the loss of sodium in the urine (Kackley et al., 2022). Salting foods to taste and topping up with a supplemental electrolyte drink can help alleviate any symptoms of dehydration and electrolyte imbalance such as headache, fatigue, and muscle cramps (Bostock et al., 2020).

Long term side effects have been studied too. Long term side effects depend on the type of KD an individual is following. There are long term side effects

reported for those following the classic 4:1 ratio KD for treatment resistant epilepsy and other severe illnesses. This is because by following a 4:1 ratio, it is very difficult to reach full nutritional adequacy (Zupec-Kania & Spellman, 2008). Strict adherence to the high fat levels in the diet are needed to prevent seizures and the individuals are also unwell.

Looking at the literature on the KD for diseases that don't need the very high fat levels, and that benefit from carbohydrate restriction and ketone production, long term side effects are rare. Very few long term side effects have been reported for T2D, polycystic ovarian syndrome (PCOS), non-alcohol fatty liver disease (NAFLD) (Volek et al., 2005), and no significant side effects were found following a KD long term for those with obesity (Dashti et al., 2004, 2006). In contrast, the KD has been shown to improve all these diseases and its long term efficacy has been reported (Kossoff & Rho, 2009; Volek et al., 2005).

With regards to less common side effects, in some individuals, a rash can occur on the trunk of the body (Aberer et al., 2022; Xiao et al., 2021). There is limited research to show the reasons and biological mechanisms for this, but it has been hypothesized that up until fat adaptation, the body excretes ketone bodies through the breath (ACE) and through the urine and sweat (AcAc) and therefore, when the sweat dries on the skin, the acetone that is present causes inflammation and a rash on the skin (Aberer et al., 2022; Xiao et al., 2021).

Evidence suggests that the diet is well tolerated, especially if following a well formulated ketogenic diet which includes a variety of fats, fibres, and proteins (Danan et al., 2022). With regards to the safety of the KD it is important to note

here that the term ketosis is different to ketoacidosis which is a life-threatening condition experienced by those with type 1 diabetes, poorly managed T2D, and possibly postnatally during lactation according to some recent case studies (Ward et al., 2023). It has been stated that nutritional ketosis is safe and as ketone levels increase, glucose levels decrease and stabilise (Courchesne-Loyer et al., 2017; Ludwig, 2020). With ketoacidosis, ketone levels increase alongside elevated glucose levels which are also accompanied by an acidotic blood pH which is not seen in nutritional ketosis (Masood et al., 2022).

As a result of this, there are some people who should not follow a KD. There are some absolute contraindications for the diet such as those with inherited fat or ketone metabolism disorders (Masood et al., 2022), people taking SGLT-2 inhibitors for T2D or cardiovascular disease (CVD) (Mistry & Eschler, 2021), pregnancy (Tanner et al., 2021), breastfeeding (Alawi & Falhammar, 2018; Alawi et al., 2018; Liu & Bertsch, 2021; Osborne & Oliver, 2022) and anorexia nervosa, where weight is not currently stable. There are case series and a case report on the positive impact of a KD on weight stable anorexia nervosa (Calabrese et al., 2022; Norwitz et al., 2023; Scolnick et al., 2020). Overall, research suggests that the administration of a KD for long periods of time is safe (Dashti et al., 2004).

1.4 Ketogenic diets in Physical Health

Over the years, research has investigated the effect of ketogenic diets in many areas from sports performance (Paoli & Bianco et al., 2015), and diseases such as cardiovascular disease (Mohammadifard et al., 2022), to type 2 diabetes

(Daly et al., 2006; Gower & Goss, 2015; Westman et al., 2018; Wong et al., 2021; Yancy et al., 2005) and cancer (Poff et al., 2019; Poff et al., 2013; Weber et al., 2020). Some of these studies have measures aspects of psychological well-being as a secondary measure and found positive effects in areas such as mood and depressive symptoms (Adams et al., 2022).

However, the majority of the literature investigating the KD has been for physical health conditions, with first use for treatment resistant epilepsy in children in the 1920s. Since then, research has branched out to other diseases with the focus in recent years on the benefits of a KD for T2D. As many physical and mental illnesses share symptoms, reviewing the available literature here may help us to better understand the potential impact the KD may have on overall health.

As stated earlier, therapeutic ketosis has been used to control epilepsy (Neal et al., 2008) and put prediabetes and T2D into remission (Poplawski et al., 2011). Improvements in PCOS, NAFLD, and obesity have also been reported (Mavropoulos et al., 2005; Paoli, 2014; Tendler et al., 2007) which is expected as T2D, prediabetes, PCOS, obesity, and NAFLD are all associated with features of metabolic syndrome. Metabolic syndrome overall improves with a KD too (Volek et al., 2005).

Taking a closer look at the biological actions of the KD for these diseases, blood sugar levels have been shown to reduce (Yancy et al., 2005) along with weight loss (Volek & Westman, 2002). What is interesting about the KD, is that because it regulates appetite hormones, it also reduces cravings (Gibson et al., 2015),

and reduces hunger (McClernon et al., 2007) by reducing expression of ghrelin the hunger hormone (Grigolon et al., 2020) and it increases satiety and fullness after meals, keeping one fuller for longer (Paoli, 2014).

Positive impacts on gut biosis and gut dysregulation have also been noted (Cabrera-Mulero et al., 2019; Genedi et al., 2019; McFarland et al., 2017; Mörkl et al., 2020; Xie et al., 2017; Zagórska et al., 2020), as well as alleviation of colitis (Kong et al., 2021), relief from irritable bowel syndrome (IBS) symptoms and reduced heartburn (Austin et al., 2009; Austin et al., 2006). Improvements in CVD and subsequently a reduction in cardiovascular risk have been reported (Noakes et al., 2006; Sharman et al., 2002) alongside a normalisation of blood pressure (Daly et al., 2006; Gardner et al., 2007) and a reduction in blood triglycerides (fat molecules) when compared to low fat diets (Aude et al., 2004; Parks et al., 1999).

Looking at neurological illnesses, improvements have been observed in traumatic brain injury (TBI) (Prins et al., 2005), autism spectrum disorder (ASD) (Evangeliou et al., 2003) Parkinson's disease, and Alzheimer's disease (Paoli et al., 2014) along with improve memory (Krikorian et al., 2012), increased cognitive performance (Xu et al., 2010) and protection against cognitive impairment (Davidson et al., 2013). There are also positive reports on the KD for multiple sclerosis (Storoni et al., 2015) due to the diets immunomodulating effects (Brenton et al., 2022).

The KD has been shown to sensitize cancer cells to standard treatment by depriving the cells of glucose which is the predominant fuel source for many

cancers (Mundi et al., 2021; Seyfried et al., 2012; Tan-Shalaby, 2017; Weber et al., 2020). Finally, improvements in acne have been found (Paoli et al., 2012) and the KD has been proven to reduce systemic inflammation in the body, and pain (Ruskin et al., 2009). Overall, what can be understood from this is that the KD has many biological pathways, of which some can improve symptoms of disease and even the disease outcomes themselves.

1.5 Ketogenic Diets, the Brain, and Psychological Illness

Since the KD hit the mainstream diet market in 2016, individuals have been following this way of eating predominantly to lose weight (Basolo et al., 2022). Many of those who followed the diet to lose weight experienced the benefits mentioned in the previous section but also began to experience improvements in their mood, and anxiety levels (see Tables 1.4 and 1.5) (Cucuzzella et al., 2017; Dietch et al., 2023). It appears in recent years that the research into KD's has broadened beyond physical illnesses and there is literature being published regularly now on the impact of the KD for psychiatric conditions (Bostock et al., 2017; Danan et al., 2022; Norwitz et al., 2020, 2023).

Research in recent years has focused more so on the possibility of ketogenic dietary applications for psychiatric and mood disorders. It has been suggested that ketogenic dietary therapy (KDT) should be considered as an intervention for treatment resistant mood disorders (Brietzke et al., 2018). However, strong randomised controlled trials are yet to be published, although there are some clinical trials underway.

Table 1.3: Ketogenic diet trials in animal models of anxiety, depression, schizophrenia, and autism spectrum disorder

Author	*Model*	*Sample (n)*	*Type of KD*	*Duration*	*Ketone Test*	*Result*
Ari et al. (2016a)	Anxiety	Rats (n=80)	Standard diet + exogenous ketone supplements	83 days and 7 days	Yes	Reduced anxiety behaviours
Hollis et al. (2018)	Anxiety	Rats (n=99)	Standard diet + MCT supplementation	15 days	Yes	Reduced anxiety behaviours
Murphy et al. (2004)	Depression	Rats (n=20)	4:1 ketogenic diet	3 weeks	Yes	Diet had antidepressant effects
Sussman et al. (2015)	Depression and Anxiety	Mice (n=20)	4:1 ketogenic diet fed in utero followed by standard diet postnatally	30 days	Yes	Reduced susceptibility to anxiety and depression, neuroprotective
Kraeuter et al. (2015)	Schizophrenia	Mice (n=6)	Ketogenic diet of 77.9% fat where 93% of total energy is from lipids	3 weeks	Yes	Normalized pathological behaviours in schizophrenia-linked behaviours
Castro et al. (2017)	Autism Spectrum Disorder	Mice (n=8)	Ketogenic diet with 0g of carbs	70 days	No	Improvements in social behaviours
Ahn et al. (2014)	Autism Spectrum Disorder	Rats (n=6)	6:1 ketogenic diet	10 days	Yes	Diet improved mitochondrial respiration and aspects of bioenergetic dysfunction
Mychasiuk et al. (2017)	Autism Spectrum Disorder	Mice (n=27)	6:1 ketogenic diet	14 days	Yes	Improvements in brain region deficits associated with ASD
Ruskin et al. (2017)	Autism Spectrum Disorder	Mice (n=50)	75% fat ketogenic diet	21 days	Yes	Significant relief of autism-linked symptoms
Olivito et al. (2023)	Autism Spectrum Disorder	Mice (n=16)	67.70% fat, 15.90% protein, 1% carbohydrate	5 weeks	No	Reduces inflammation, remodels gut-brain axis and reduces cognitive and social deficits

Table 1.4: Ketogenic diet trials in human models with schizophrenia, autism spectrum disorder, and persistent mental illness

Author	*Condition*	*Sample (n)*	*Type of KD*	*Design*	*Duration*	*Result*
Pacheco et al. (1965)	Schizophrenia	19-63 year old females (n=10)	Unknown possibly 4:1 ratio	Pilot study	2 weeks	Decrease in symptoms after two weeks and then an increase in symptoms in 70% of sample 1 week after discontinuing diet
Yancy et al. (2009)	Overweight participants, no mental health diagnosis	Randomised to Keto Diet and Low-Fat Diet (n=119)	<20g carbs per day	Randomised trial comparing Keto diet to Low Fat diet	24 weeks	Health Related Quality of Life (HRQOL measure) improved more in the Keto Diet group compared to the Low-Fat group
Campbell et al. (2019)	Bipolar disorder	Those with bipolar disorder (n=274)	KD, omega-3 enriched, or vegetarian diet	Observational analytic study of online comments about mood effects of dietary interventions	Months and years	Reported mood stabilization and remission of symptoms were higher for the KD than for other diets. Many improvements lasting years.
Evangeliou et al. (2003)	Autism Spectrum Disorder	Children (n=30)	71% fat ketogenic diet	Pilot prospective study	24 weeks with intermittent diet free intervals	60% of children improved. Improved concentration and learning
Herbert et al. (2013)	Autism and Epilepsy	Child (n=1)	1.5:1 ketogenic diet	Case report	Years / Ongoing	Improved from Severe Autistic to Non-Autistic and IQ increased 70 points
Danan et al. (2022)	Persistent mental illness (MDD, bipolar disorder and schizoaffective disorder)	Adults (n=31)	<20g carbs per day	Retrospective analysis	6-248 days	All participants achieved clinically important difference in severity of illness. 43% achieve clinical remission. 79% of participants reduced medication or it was unchanged

Table 1.5: Case Reports of the ketogenic diet in psychiatric conditions and their outcomes

Author	*Condition*	*Sample (n)*	*Type of KD*	*Ketone Levels*	*Noted Change*	*Result*
Cox et al. (2019)	T2D and MDD for 26 years	65 year old female	65% fat, 25% protein, 10% carbs	Blood between 0.5-2.0mmol/L	Reviewed at 12 weeks	PHQ-9 dropped from 17 (moderately severe) to 0 (no symptoms reported), 75% reduction in SSRI medication
Kraft et al. (2009)	Schizophrenia, paranoia, and hallucinations for 63 years	70 year old female	<20g carbs per day		Increased energy and psychotic symptom decrease at 7 days	Increased energy, complete remittance of auditory and visual hallucinations maintained for over a year and ongoing
Palmer et al. (2019)	Schizophrenia, hallucinations, and paranoia for 65 years	82 year old female	Unknown	Unknown	Results apparent after two weeks	Lost 150lbs weight, mood improved, hallucinations and paranoia disappeared, stopped all antipsychotic medications, no psychotic symptoms
Palmer et al. (2019)	Depression, anxiety, anorexia nervosa, schizophrenia, hallucinations, and paranoia for 20 years	39 year old female	Unknown	Unknown	Results apparent after one month	Resolution of all psychotic symptoms within one month, lost 70lbs in weight, came off all antipsychotic medications and free from all psychotic symptoms
Saraga et al. (2020)	Bipolar disorder, mania, and depression with psychotic symptoms for 26 years	60 year old female	Noted as similar to Phelps et al. (2013)	Urine between 0.05 and 0.4 g/L	'After starting the diet…'	Reduced anxiety and maintenance of euthymia, stopped medications, resolution of manic episodes
Gilbert-Jaramillo et al. (2018)	Schizophrenia for 8 years and 4 years	22 year old twins (n=2)	3:1 ratio	Urine	Reviewed at 6 weeks	Female: PANSS dropped from 101 to 91, but increased to baseline 2 weeks after stopping the diet Male: PANSS dropped from 82 to 75
Phelps et al. (2013)	Bipolar Depression Type 2 for 44 years and 17 years	69 and 30 year old females (n=2)	70% fat, 22% protein, 8% carbs	Maintained urine ketones for 7 months	One saw symptoms resolve within 2-3 days of ketosis	Both stopped all mood stabiliser medications and experienced improved mood and a greater feeling of calm. Maintained diet for 2 and 3 years
Yaroslavsky et al. (2002)	Bipolar depression rapid cycling	49 year old female	4:1 ratio	No urine ketones noted	No changes noted at 4 weeks	No urinary ketones and no clinical improvements

1.5.1 Ketosis and the brain

There are many proposed theories for how the KD might improve psychiatric conditions and many of these actions can be seen later in this chapter in Table 1.6.

While using the KD to treat epilepsy, it was observed that attention, cognition, and mood improved in some cases (Murphy et al., 2004). The KD appears to have mood stabilising effects (Brietzke et al., 2018; Campbell & Campbell, 2019; Norwitz et al., 2020). When ketones are present in the blood, there is a reduction in neuronal excitability and anticonvulsant effects are observed (Masino & Rho, 2012). The anticonvulsant drugs prescribed for epilepsy treatment (e.g., lithium), are also prescribed for mood stabilisation in mood disorders such as bipolar disorder suggesting that epilepsy and bipolar disorder share some aetiology (Qaswal, 2020). These mood stabilisers reduce intracellular sodium levels and decrease excitatory neurotransmission (Bojja et al., 2022; Huang & El-mallakh, 2007). A KD also elicits this effect without needing to administer the anticonvulsant drug and in some cases can exceed the levels of mood stabilization achieved with medications (Phelps et al., 2013). Phelps et al. (2013) found these results in two women with bipolar disorder who followed a KD for two and three years respectively. Carbohydrates were kept below 20g per day and improvements were related to their state of ketosis.

There is ample evidence to show that it is the ketone molecules that act as a mood stabilizer and mimic the biological mechanisms of mood stabiliser medications (El-Mallakh & Paskitti, 2001; Sánchez-Villegas et al., 2013; Yu et al., 2023). Mood stabilisation appears to occur by reducing intracellular sodium

in bipolar disorder type 2 (Phelps et al., 2013). Lithium, one of the most common mood stabiliser treatments used in bipolar for mania and depression, sensitizes insulin and insulin signalling (Campbell et al., 2022; Malhi et al., 2017). An RCT carried out by Calkin et al found significant improvements in bipolar in those given metformin, a blood glucose lowering drug which also sensitizes insulin (Calkin et al., 2022). Metformin has also been found to promote anxiolytic and anti-depressant like effects in mice fed a high fat diet (Zemdegs et al., 2019). El Mallakh et al. (2001) suggests that there are many other reasons as to why the KD may work aside from the anticonvulsant and cellular effects. The KD exhibits some of the same effects as lithium and metformin, reducing and regulating blood sugar, promoting anxiolytic and anti-depressant like effects, and improving insulin sensitivity (Kovács et al., 2018; Murphy et al., 2004; Skow & Jha, 2023).

Glombik et al. (2020) noted that in depression, impairments in brain energy and metabolism are reported. Improvements in these areas are found by those following a KD (El-Mallakh, 2001). Mula (2017) also reported that depression is associated with an increased risk of epilepsy. Across all mood disorders, it has been suggested that there is significant metabolic dysfunction including impaired mitochondria, reduced glucose metabolism and increased insulin resistance (Campbell & Campbell, 2020; Ernst et al., 2016). Mitochondria are organelles found in nearly every cell in the body. They are responsible for many functions in the body but most importantly, for creating energy and storing it as ATP for the body to use when needed. Their importance for human survival has

traditionally given them the nickname, the 'powerhouse of the cell' (McBride et al., 2006; Wills, 1992).

Poor mitochondrial function and inflammatory cytokines are present in many psychiatric disorders (Li Liu et al., 2023). Volek et al. (2005, 2009) have shown that the KD can exhibit significant improvements in metabolic health, including improving mitochondrial function and health and supporting mitochondrial biogenesis (Hasan-Olive et al., 2019). Ketones have also been shown to be anxiolytic, neuroprotective, and anti-inflammatory as reported in Table 1.3.

Therefore, the theoretical basis for using a KD in psychiatric conditions is that the ketones provide critical energy (ATP) to the brain, and it regulates many biological processes that have become impaired due to biological or psychological factors.

1.5.2 Ketogenic diets in the psychiatry literature

It is important to note that to date, no RCTs have been published on the ketogenic diet for psychiatric disorders. There are clinical trials in progress globally, however the results have not yet been reported in the literature. There are animal studies, a handful of case studies in humans, and some small trial data (see Tables 1.3, 1.4 and 1.5). So far, the biological mechanisms of the KD for psychiatric conditions have not yet been realised and are not yet fully understood (El Karkafi et al., 2023).

Looking at the research that is available, Varaee et al. carried out a systematic review and meta-analysis of eight studies and found no significant association between a LCD and improvements in either depression or anxiety (Varaee et al.,

2023). To add to this, a recent systematic review on the efficacy of low carb and ketogenic diets for mood and anxiety disorders states that there are no high-quality studies on the evidence for these dietary interventions, although some studies suggested positive effects (Dietch et al., 2023). Finally, Sindler et al. (2023) carried out a systematic review of RCTs looking at the effects of low carbohydrates diets on psychological outcomes. They included 16 RCTs and identified four variables, quality of life, mental health, mood, and fatigue. They found that the KD had the same impact on psychological well-being as any other diet in those without health issues. In other words, the KD didn't improve psychological well-being in those who were already healthy. However, in stage 2 and 3 cancer patients and those with Alzheimer's disease, improvements in quality of life and mental health were found compared to control diets. They reported that following a Low Carbohydrate Ketogenic Diet (LCKD) does not negatively impact psychological well-being and they recommend an intervention of 12 weeks or longer for the best chance of improvements. Overall, it is clear that more research is needed specifically in mental health populations to truly determine if the KD can be used as a novel therapeutic intervention to improve psychiatric symptoms.

1.6 Ketosis and Affect

Compared to other psychiatric illnesses, much less is known about the KD and depression in humans. Until recently there have been no studies with depression as a core focus (Bostock et al., 2017) and instead the effects of ketones on mood and depressive symptoms have mainly been a secondary measure. To date there are still no human studies looking at the effect of the KD on depression but

suggestions of the potential biological mechanisms of the KD have been suggested to include energy metabolism, oxidative stress, and immune and inflammatory processes (Kraeuter et al., 2020).

Reviewing the research further in specific disease groups, depressive symptoms have been found to improve in those with T2D following a digitally administered carbohydrate restricted (ketogenic diet <30g/day) diet over two years (Adams et al., 2022). A case study by Cox et al. (2019) found that markers of clinical depression, self-efficacy and T2D normalised in a 65 year old female who presented with T2D and clinical depression after being treated with 12 weeks on a KD, with high intensity interval training (HIIT) training and some psychotherapy sessions.

In those without disease, Halyburton et al. (2007) found that a low carbohydrate, high fat diet produced weight loss and improved mood after following an online intervention. Mental aspects of Health-related quality of life (HRQOL) improved more in participants following an LCKD than an LFD, possibly resulting from the LCKD's composition, lack of explicit energy and calorie restriction, higher levels of satiety or metabolic effects (Yancy et al., 2009). Finally, at week two of a six week study, a group following a KD with additional supplemental ketone salts exhibited lower depression scores compared to the low fat, ketogenic and placebo group, perhaps due to the elevated ketone levels beyond that which is seen on a standard ketogenic diet without supplementation (Kackley et al., 2022). As ketone levels of 4-6mmol/L exhibit neuroprotective benefits (Fedorovich et al., 2018), this suggests that higher, more therapeutic

levels of ketones may be necessary to reduce depression scores and replicate these findings.

However, there are some studies that show no improvements in depression or mood. No significant improvement in depression was found in those following a KD for Parkinson's disease, however, then mean ketone levels reported were 0.5mmol/L which confirms nutritional ketosis but not the therapeutic levels needed for neuroprotective benefits. The sample also continued to suffer from Parkinson's disease which may have biased the outcomes (Tidman, 2022).

Other outcomes like anxiety have been measured in some of these studies. Anxiety is tied closely to mood and is often measured in studies focused on depression. In the same study by Tidman et al. (2022) participants with Parkinson's disease found improvements in anxiety after 12 weeks of following a KD with <16g carbohydrates per day. From this, it appears that diets high in 'healthy' fat is anxiolytic while diets high in sugar may have more anxiogenic characteristics (Murphy & Mercer, 2013).

There are many studies using rodents and mice that have studied how the ketogenic diet may alleviate depressive symptoms (see Table 1.3). De Almeida Rabello Oliveira studied the effect of a short term and long-term KD compared with a control diet on the cortical spreading of depression in young rodents. They found that short term KD's had a positive effect in decreasing brain cerebral excitability (de Almeida Rabello Oliveira et al., 2008). In another study with rodents (n=40) fed a KD (4:1) compared to a control diet (.082:1), those on the

KD spent less time immobile and were less likely to exhibit 'behavioural despair', suggesting the diet may have antidepressant properties (Murphy et al., 2004).

Several rodent studies indicate that some biological factors of the KD specifically the role of ketone bodies, may improve mental health symptoms such as anxiety (Ari et al., 2016). A study using exogenous ketone supplementation plus standard diet compared to standard diet alone in rats found that those being administered the ketone supplements experienced reduced anxiety related behaviour (Ari et al., 2016). Following on from this, in a similar experiment, rats were given a MCT oil supplemented diet or a control diet for two weeks, and they found that those on the MCT supplemented diet also exhibited reduced anxiety like behaviours (Hollis et al., 2018). Finally, a study by Sussman in 2015, looked at the behaviour of 8-week-old rodents fed a KD in utero and a standard diet postnatally compared with rodents fed a standard diet prenatally and postnatally and found that rodents fed a KD in utero were less likely to develop anxiety and depression and that they were more likely to be physically active compared to the standard pre and post-natal group (Sussman et al., 2015). Not all studies found long term improvements, however. Though the KD decreased brain cerebral excitability in young rats compared to a control diet over ten days, no significant effect was found after seven weeks (de Almeida Rabello Oliveira et al., 2008).

Altogether, these findings demonstrate some potential role for the KD in managing symptoms of depression and anxiety. There are many biological factors of ketones that may alleviate symptoms of depression or even protect and prevent the onset of psychiatric illness. There is even research to show that

producing ketones, either through prolonged fasting or a KD can help alleviate anxiety (Kesl et al., 2016; Murphy & Mercer, 2013) and that this may be due to the ketones anti-inflammatory characteristics (Ruskin et al., 2009). Aside from the modulation of inflammatory markers, other pathways include the regulation of hormones (Patrick & Ames, 2015) and changes in neurotransmission (McNally & Hartman, 2012). Though this is encouraging, the research available is limited. There are some other suggested pathways that ketones may improve depressive symptoms which will be reviewed further in section 1.6.5.

1.6.1 Depression

More than 1 billion people globally, live with a diagnosable mental health condition (Rehm & Shield, 2019). Of diagnosed mental health disorders, depression is the leading cause of poor health and disability worldwide (Friedrich, 2017; Husain et al., 2020). This figure is calculated based on years of life lost from premature death and years of life lived in less than full health (World Health Organization, 2004). Depression has a lifetime prevalence of 10-12% (El Karkafi et al., 2023; Rose et al., 2022), with around 6% of the world's population at any one time point suffering from this disorder which is approximately 322 million individuals (Bromet et al., 2011; Patel et al., 2016). The number of people living with depression rose by almost 20% in the ten years between 2005 and 2015 (World Health Organization, 2017) and in addition to this, 264 million people are living with anxiety disorders, which is an increase of 15% between 2005 – 2015.

According to the World Health Organisation (WHO) and a systematic review published in 2021, depressive and anxiety disorders increased by more than 25% during the COVID-19 pandemic with extra demand on mental health

services (Santomauro et al., 2021; World Health Organization, 2022). Furthermore, over 75% of individuals diagnosed with either anxiety, mood, or substance use disorders in low- and middle-income countries do not receive treatment (Evans-Lacko et al., 2018) and this treatment gap for high income countries is approximately 35-50% (World Health Assembly, 2012).

This suggests that there are many barriers to receiving care. Factors such as social stigma, lack of trained health professionals, lack of investment in mental health services and awareness, low perceived need for treatment, lack of personal financial means in some cases, and long care waiting lists have all been shown to disrupt the ease of accessing care in times of need (Coêlho et al., 2021; Coombs et al., 2021; Luitel et al., 2017). Of those who can access treatment, at least one third of those living with depression are treatment resistant and have been diagnosed with treatment resistant depression. This means that they have tried at least two medications without improvement (Husain et al., 2020).

In addition to this, both anxiety and depression have been shown to be risk factors for both the development and worsening of other illnesses such as diabetes, cardiovascular disease, hypertension, chronic respiratory disorders, arthritis, autoimmune disorders, and substance use disorders (Arnaud et al., 2022; Steffen et al., 2020). The co-occurrence of depression and anxiety disorder is also common in primary care (Hirschfeld, 2001).

Mood disorders are split into two categories, depressive disorders, and bipolar disorders according to the Diagnostic Statistical Manual (DSM) (Sekhon & Gupta,

2022). To diagnose an individual with depression, individuals must present with least five of the following symptoms alongside a depressed mood or anhedonia (a reduced ability to experience pleasure in things) over the previous two weeks; persistently low mood, anhedonia, lack of interest in pleasurable activities, feelings of guilt or worthlessness, a lack of energy, a significant increase or decrease in appetite, reduced concentration, agitation, disrupted sleep by oversleeping or experiencing insomnia, or suicidal ideation (Hasin et al., 2018).

Depression is also an umbrella term for a diagnosis that includes many additional factors called specifiers. According to the fifth version of the DSM (DSM-5), depression has six specifiers that can be added to the depression diagnosis to provide more details about the individual's condition. Specifiers for depression are, chronic, catatonic features, melancholic features, postpartum onset, seasonal pattern, and atypical features (American Psychiatric Association, 2013). Melancholia is a specifier of depression, in other words it is not a standalone mood disorder, although there are many researchers and clinicians in the field who are calling for it to be declared as such (Parker et al., 2010). If an individual is diagnosed with melancholia, they have a diagnosis of depression with melancholic features such as weight loss, loss of appetite and feelings of guilt or shame (Kennedy, 2008).

1.6.2 Biological mechanisms of depression

Thought the exact pathophysiology of depression is not clear and there may be many pathways through the specifiers mentioned above, from the research, depression appears to be associated with psychosocial experiences, such as trauma or adversity (Li Liu et al., 2023; O'Neil et al., 1986). Negative life events

change affect, and this can be mediated by alterations in hormones, specifically serotonin in some cases (Cowen & Browning, 2015). Serotonin has a role in sleep, hunger, mood, learning, and memory (Bakshi & Tadi, 2022). Though for many years it was understood that serotonin levels were associated with depression, a recent systematic review of the literature stated that there is no evidence to show that altered serotonin levels are associated with depression (Moncrieff et al., 2022).

Either way, the impact of these negative experiences, or the negative environment, and subsequent depressive symptoms have been argued to be associated with several biological factors. Research has proposed that there are many biological mechanisms of depression such as energy imbalances, for example stress is associated with dysregulated glucose metabolism (Tian et al., 2023), mitochondrial dysfunction, dysregulation in neurotransmitters, gut dysbiosis, and inflammation among others (Marx et al., 2021; Erjavec et al., 2021; Penninx et al., 2013).

Dysregulation of the gut microbiota through dysbiosis and gut permeability can be improved with the supplementation of probiotics, symbiotics and faecal transplants, along with a Mediterranean diet. Those with depression were found to have an increased level of Bacteroidetes and Proteobacteria and a reduction in Firmicutes alongside other dysregulated species (Varesi et al., 2023). The research into this area is still in its infancy which makes it difficult to extrapolate cause and effect.

The mechanistic pathway with the most research published over the past few decades is inflammation. Depression is associated with chronic low-grade inflammation, and it is a pathway to both risk and neuroprogression (Berk et al., 2013). It has been found that in those with diagnosed physical illnesses, who have chronic inflammation, they also show symptoms of depression. This depression may result from long standing inflammation in the body (Dantzer, 2017). A recent study by Bekkevold found that C-Reactive Protein (CRP), a marker of inflammation, along with Interleukin 6 (IL-6) a pro-inflammatory cytokine, increased anxiety, and depression symptoms, measured by the Hospital Anxiety and Depression Scale (HADS) in a sample of over 68,000 participants (Bekkevold et al., 2023).

Abdominal obesity, or increased waist measurements beyond ideal reference ranges, are also associated with increased levels of inflammation, measured by CRP, and metabolic syndrome (MetS) (Keller & Lemberg, 2003). Abdominal obesity is also the main characteristic of metabolic syndrome alongside insulin resistance, inflammation and T2D (Després & Lemieux, 2006). Both obesity and MetS are accompanied by low grade inflammation (Saltiel & Olefsky, 2017). MetS is defined by a combination of central obesity or increased waist circumference, high blood pressure, low levels of high (‘good’) density lipoprotein (HDL) cholesterol, elevated triglycerides, hyperglycaemia, and increased fasting glucose (Huang, 2009).

Research from Sen et al (2021) states that MetS which can also be called ‘insulin resistance’ along with other metabolic disorders such as T2D increase the risk of depression, and vice versa. Systematic reviews and meta-analyses show that

T2D, obesity and MetS can be prevented and put into remission by following a low carbohydrate or ketogenic diet (Goldenberg & Johnston, 2021; Meng et al., 2017; Westman et al., 2018).

A systematic review on the association between adverse childhood experience (ACE) and inflammation in depression suggests that depression and ACE subpopulations have elevated levels of IL-6 compared to depression only and healthy controls. Therefore, perhaps depression -ACE subgroups are more likely to respond to anti-inflammatory treatment interventions (Gill et al., 2020). The depression-ACE group did not present with elevated CRP although some presented with increased Tumor Necrosis Factor Alpha (TNF-α) (Gill et al., 2020).

Taking a closer look at the biological mechanism of inflammation in mood disorders, there are a couple of inflammatory markers and factors that are present in some cases of depression and bipolar disorder. It was found that in those with depression and bipolar disorder, some individuals exhibit higher blood levels of IL-6 the pro-inflammatory cytokine. As a pro-inflammatory cytokine, it exerts direct pro-inflammatory actions on other cells. These higher IL-6 levels are correlated with suicidality and non-responsiveness to antidepressant drugs (Enache et al., 2019).

TNF-α is another inflammatory marker that is increased in depression (Enache et al., 2019). A meta-analysis found that TNF-α, IL-6 and inflammatory marker Interleukin-1 receptor antagonist protein (IL-1Ra) levels were significantly increased in acute cases of schizophrenia, bipolar mania and depression compared to healthy controls (Goldsmith et al., 2016). Strawbridge et al. found

that in those deemed as non-responders to treatment, persistently high TNF-α levels were found along with higher baseline inflammation levels compared to healthy controls (Strawbridge et al., 2015). Many other pro inflammatory cytokines are released (IL-1beta, IL-18 and IL-33) when the NOD-like receptor protein 3 (NLRP3) inflammasome is activated. The NLRP3 inflammasome is important for the immune system and protection against viruses, bacterial and fungal infections, but can contribute to serious health conditions when activated by its stimuli leading to mitochondrial dysfunction and the production of reaction oxygen species (ROS) (Kelley et al., 2019). The NLRP3 inflammasome activation is linked to depressive behaviours and therefore it has been suggested that the use of NLRP3 inhibitors could be potentially therapeutic for many neuroinflammatory disorders (Bhattacharya & Jones, 2018). A recent study stated that high glucose or blood sugar levels activate the NLRP3 inflammasome and that inhibiting it, for example through a ketogenic diet, can alleviate T2D induced depression (Su et al., 2023).

1.6.3 Current treatments for depression

Treatment for depression, like other psychiatric conditions, includes a variety of different interventions, some more intrusive and intensive than others, depending on the severity of the illness.

For depression, guided self-help, talk therapy, and cognitive behavioural therapy (CBT) are first line treatments recommended by the National Institute for Health and Care Excellence (NICE) guidelines (NICE, 2022). However, antidepressants are frequently prescribed, and they come with many negative side effects (Kirsch, 2014). The most common side effects are sexual dysfunction,

drowsiness, weight gain, insomnia, anxiety, dizziness, headache, dry mouth, blurred vision, nausea, rash, and tremor (Sheffler et al., 2023). Alongside this, many antidepressants have unfavourable metabolic side effects and increased risk of MetS. Metabolic syndrome covers a group of symptoms, weight gain mainly in the stomach area, obesity, insulin resistance, hypertension, dysfunctional glucose metabolism, diabetes, hyperinsulinemia, and other lipid irregularities (Chokka et al., 2006; Crichton et al., 2016; Gramaglia et al., 2018; Hiles et al., 2016; Scheen, 2023). Many antidepressants and antipsychotics also block dopamine, which in turn reduces motivation for the individual making it more challenging to stay motivated (Ichikawa & Meltzer, 1995; Kapur, 2004; Leggio et al., 2008; Molitch, 2020).

Antidepressant therapy is commonly prescribed for those with classic depression that is moderate to severe in nature and is primarily used for symptom relief (DeRubeis et al., 2008). There are many different types of antidepressants, introduced clinically in the 1950's, and each are prescribed at different levels of treatment resistance (Lopez-Munoz & Alamo, 2009). Examples of these are:

- Selective serotonin reuptake inhibitors (SSRIs). For example, Sertraline and Citalopram
- Serotonin-norepinephrine reuptake inhibitors (SNRIs). For example, Duloxetine and Venlafaxine
- Serotonin modulators. For Example, Trazodone and Nefazodone
- Atypical antidepressants. For example, Mirtazapine and Bupropion
- Tricyclic antidepressants (TCAs). For example, Amitriptyline and Clomipramine

- Monoamine oxidase inhibitors (MAOIs). For example, Phenelzine and Moclobemide
- Other medications including mood-stabilizers and antipsychotics

Other treatments for depression that will not be reviewed in detail in this thesis are:

- Electroconvulsive Therapy (ECT) which is the gold standard therapy for treatment resistant MDD, however it only works short term (Abbott et al., 2013)
- Transcranial Magnetic Stimulation (TMS) which can improve the severity of symptoms in MDD (Sonmez et al., 2019)
- Vagus Nerve Stimulation (VNS), the mechanisms of action of which are still unclear, shows improvements in treatment resistant depression over three to 12 months (Carreno & Frazer, 2017)
- Esketamine used in tandem with antidepressants in treatment resistant depression (Sheffler et al., 2023)

Sometimes a combination of antidepressants and talking therapy is prescribed. Talking therapies such as cognitive behavioural therapy (CBT) and counselling are used for mild to moderate depression that is not improving (Leavisso et al., 2020; Teasdale et al., 1984). The most prominent program of treatment in the UK is the Improving Access to Psychological Therapies (IAPT) service, available on the NHS, which aims to increase the availability of talking therapies to those with a depression or anxiety diagnosis (Clark, 2011). The combination of antidepressants and talking therapy has been shown to be more effective than

medication alone according to a meta-analysis of randomized trials (Cuijpers et al., 2014).

However, when it comes to antidepressants efficacy, approximately 15% of individuals with depression experience a substantial antidepressant effect beyond that of placebo. A 'large response' is classified as a 10 or more point improvement on the 7-item Hamilton depression rating scale (range 0–52 points) (HAMD-7). This is based on a review of 232 randomised double-blind placebo-controlled trials of antidepressants for depression. Researcher in this study also stated that the number needed to treat to improve one patient was seven (Stone et al., 2022). This means that six other individuals would experience the side effects of antidepressants without any clinical improvement in their symptoms, and while they are taking the antidepressants, they are experiencing the poor metabolic side effects, with no perceived benefit to their mental state.

The effect size of antidepressants in those with depression is 0.30 which suggests a modest improvement (Khan & Brown, 2015). These findings were supported by a large systematic review and meta-analysis of 522 trials, reviewing 21 antidepressant drugs for the treatment of depression in adults suggesting that antidepressants are modestly better than placebo in the short term (Cipriani et al., 2018). However, responses to this large systematic review and meta-analysis reanalysed the data and reviewed the methodology, accounting for the biases that were missed in the original study. It was concluded that the 'modest' improvement stated, should in fact be 'very low' as the mean difference between antidepressants and placebo as measured on the HAMD-7

was only 2 points on the 52-point scale (Munkholm et al., 2019). Stone et al., confirmed this by stating that though antidepressants have greater efficacy over placebo, the difference is very small (Stone et al., 2022). Though statistically significant, the effects of antidepressants may not have clinical significance. Though treatment for depression is primarily the prescription of antidepressants, those with depression with atypical features have poorer responses to SSRIs and tricyclical antidepressants (Sen et al., 2021).

Overall, current treatments approaches for depression are significantly ineffective for large numbers of sufferers. Most treatments are based on the serotonin theory and aim to increase serotonin levels, but these don't work for everyone. With the exact pathophysiology of depression still unknown, along with highly variable antidepressant effects, biologically based alternatives are necessary (Smolensky et al., 2023).

1.6.4 Nutritional interventions and treatments for psychiatric disorders

A meta-analysis of 21 studies carried out by Li et al. (2017) showed that the Western dietary pattern is associated with an increased risk of depression. However, there are many dietary interventions that are said to improve depression and the severity of symptoms. The results of a meta-analysis of randomised control trials looking at the effects of dietary improvement on depression and anxiety symptoms were encouraging and stated that diet can play a role in the treatments of depressive symptoms (Firth et al., 2019). These dietary interventions will be reviewed.

Anti-Inflammatory

According to a systematic review on anti-inflammatory diets as a potential intervention for depressive disorders, it has been suggested that those who eat a pro-inflammatory diet have a 1.4 increased chance of depression as opposed to those following an anti-inflammatory diet (Tolkien et al., 2019). Diets with a low dietary inflammatory index (DII) have been shown to be associated with lower levels of depression (Fond et al., 2020).

Whole Foods Approach

Certain foods such as olive oil, fish, fruits, vegetables, nuts, legumes poultry, dairy and unprocessed meat have been suggested to improve depressive symptoms by acting on the gut brain circuit (Lang et al., 2015). This dietary approach aims to eliminate ultra-processed and refined foods.

A diet focused on vegetables, fruit, meat, fish, and whole grains was associated with lower risk of depression and anxiety whereas a western diet of ultra-processed and refined foods and sugars was associated with more psychological symptoms of these illnesses (Jacka et al., 2010).

Mediterranean

Frith et al. found that the Mediterranean diet is associated with better mental health outcomes compared to those following a Western diet (Firth et al., 2020). They also suggested that the Mediterranean diet can reduce inflammatory markers whereas the Western diet in known to increase inflammation. Following a Mediterranean diet appears to protect against depression in some

observational studies according to a systematic review of healthy dietary indices and risk of depression outcomes (Lassale et al., 2019).

The SMILES trial and the Healthy Eating for Life with a Mediterranean Diet (HELFIMED) trial both reported reductions in depressive symptoms in those following a Mediterranean diet (Jacka et al., 2017; Marx et al., 2021; Parletta et al., 2019). The SMILES trial found that over 12 weeks, remission from depression was found in 32% (n=10) of participants in an intervention group with a reduction in the depression rating scale (MADRS) score of more than 10 points (Jacka et al., 2017). Much work has been done in this area and it has been suggested that diet could be an amenable factor for depression and other psychiatric illnesses. This research field has been coined 'Nutritional Psychiatry' by Professor Felice Jacka at Deakin University in Australia (Marx et al., 2017).

Plant Based Vegan and Vegetarian Diets

Vegan and vegetarian diets focus most to all their dietary intake on items from the plant kingdom only. A meta-analysis carried out to look at the vegetarian diet and depression scores found that vegetarians had higher depression scores than non-vegetarians based on a sample of nearly 50 thousand participants (n=49,889) (Ocklenburg & Borawski, 2021). In keeping with these findings another systematic review and meta-analysis stated that vegan or vegetarian diets were related to higher risks of depression (Iguacel et al., 2021). However, the most recent systematic review found that there was conflicting evidence that there was an association between these diets and depression (Jain et al., 2022).

It has also been shown that those with lower intake of meat, or non-consumers, had significantly higher levels of depression, anxiety, and self-harm (Dobersek, Wy, et al., 2021) and experienced twice as many depressive episodes as those who ate meat (Kohl et al., 2023).

Carnivore Diet

A Carnivore diet is a diet that consists of only animal products and excludes most or all plant foods. In a meta-analysis of the data, it was found that meat consumption was associated with lower levels of depression and anxiety compared to those following a vegan diet (Dobersek, Teel, et al., 2021). Taking a closer look at those following a Carnivore diet, 100% of diabetics came off their injectable medications, 92% came off insulin therapy, 84% came off oral medications and CRP decreased significantly in a group of over 2000 individuals (n=2029) (Lennerz et al., 2021). This may be due to improvements in MetS and the anti-inflammatory effects of ketones alongside the removal of ultra-processed inflammatory foods. This diet has become popular in recent years (Lennerz et al., 2021), but more rigorous research studies still need to be carried out. However, the results and impact of this diet are promising and to be expected as in some ways, the diet is similar to a low carbohydrate and ketogenic diet.

Nutritional Deficiencies

Supplementing vitamins and minerals that may not be adequately absorbed or ingested due to gut permeability or dietary preference is another way to approach psychiatric conditions. There are many vitamin deficiencies that have been associated with psychiatric conditions (Dogan et al., 2008; Hutto, 1997;

Young, 2007). A recent case study reported that a 75 year old woman was admitted to an inpatient psychiatric unit while presenting with symptoms of schizophrenia such as hallucinations and delusions. She had first experienced this when she was 68 years old. A blood test found that she had mild anaemia and vitamin B12 (cobalamin) deficiency. She was treated with an antipsychotic medication and vitamin b12 supplements and within five days she no longer experienced delusions and hallucinations diminished a week later when she was discharged in full remission (Teodoro, 2023).

When it comes to vitamins and other supplements, a systematic review showed that though micronutrients supplementation can improve psychiatric symptoms in some children, the dosages available in market bought supplements are not concentrated enough to improve symptomatology (Rucklidge et al., 2014).

From this it can be assumed that unless high doses of vitamins or minerals are prescribed or administered by a medical professional, it will not be the food in the dietary change that will reverse or alleviate the depressive symptoms present because the nutrients will not be strong enough. There is no need to query whether it is the Omega 3, the removal of gluten, toxins or heavy metals that might alleviate these symptoms. Therefore, the remaining factor that may alleviate these depressive symptoms is ketones. In conclusion, there is some research to suggest that making the above mentioned changes can have a positive effect on the risk of depression but by understanding that the change in nutrients may not be strong enough to alter the depression pathway, looking towards a combination approach or beyond the food is essential. This research

will focus on the less studied potential role of ketones in the pathophysiology of depression.

Fasting

There is research to suggest that fasting improves some symptoms of psychiatric conditions (Fond et al., 2013) and fasting as a practice has been used as far back as 500BC (Wheless, 2008). However, fasting can be extremely difficult to implement into daily life in society, especially for those who are living with a psychiatric illness. Therefore, finding a diet that mimics the effects of fasting, with optional stages of intermittent fasting may improve adherence and consequently, possible improvements in mental health outcomes.

The Fasting Mimicking Diet (FMD) was researched and formulated by biologist, Professor Valter Longo, from the University of Southern California. The FMD promotes many of the same biological improvements as fasting, but while eating specific foods (Brandhorst et al., 2015). Research states that this diet can only be followed periodically for five days, at maximum, once per quarter year (Brandhorst et al., 2015; Rangan et al., 2022; M. Wei et al., 2017). The FMD was shown to reduce neuroinflammation in a mouse model (Rangan et al., 2022) and improve levels of inflammation measured by CRP in humans (Wei et al., 2017). It has been suggested that it can also suppress the inflammatory process in arthritis (Venetsanopoulou et al., 2019). In a FMD dietary study of 220 participants over a three-month period, depressive symptoms were significantly reduced (Maniaci et al., 2020).

Protein Sparing Modified Fasting

In a study of very low-calorie diets (400kcal per day) that followed a Protein Sparing Modified Fasting (PSMF) approach, which is comprised of low daily calories specifically coming from protein, significant reductions in anxiety were observed by week four and in depression were observed by week three (Wadden et al., 1985). Again, as the body is put into the fasted state through low caloric intake, ketones are produced by the liver and would therefore be present in these individuals which may be the pathway by which this approach works.

Low Carbohydrate Diets

Low Carbohydrate Diets and Ketogenic Diets are precursors to fasting. They mimic some of the effects fasting produces in the body as they can both put the body in a state of 'ketosis'. Usually, a LCD consists of more carbohydrates compared to a KD, so much so that a low carbohydrate should not put the individual into ketosis. However, there are many factors and situations that are difficult to control where an individual on an LCD could be in ketosis without realising, and therefore reaping the possible benefits of the KD which may bias the outcomes of a study.

A recent meta-analysis and systematic review of eight studies in the literature (n=576) found that there was no significant association between a low carbohydrate ketogenic diet and the risk of depression and anxiety (Varaee et al., 2023). However, the limitation of this study is that the articles included in the study had a wide range of macronutrients and calories which makes it very difficult to measure and compare whether there is an improvement in depression and anxiety or not. The low carbohydrate literature therefore cannot be relied

on as the dietary composition varies from study to study and in some cases the literature states it is low carbohydrate when in fact it is ketogenic. Ultimately, it is difficult to identify which studies are truly low carbohydrate, and their impact on depression, anxiety, and other psychiatric conditions. However, there is some encouraging research that suggests that a KD that induces therapeutic ketosis may improve symptoms of depression and other aspects of psychological well-being such as anxiety (Dietch et al., 2023; El Karkafi et al., 2023; Niepoetter et al., 2019; Tidman, 2022).

1.6.5 Relationship between biological factors of depression and ketones

When reviewing the literature on the biological pathways of depression and of ketones in disease management, many overlaps have been identified. Some biological roles of ketones appear to counteract those of depression in an overall positive direction. Though this does not mean that the KD will counteract all biological factors of depression, it is at least a start and a convincing argument for studying the KD for psychiatric conditions such as depression. In Table 1.6 there is a non-exhaustive list of biological factors of depression and their related ketone effect.

Table 1.6: Biological factors of depression and their related ketone effects

	Depression Biological Factor	*Related Ketone Effect*
1	A positive association between depressive disorder and insulin resistance (Pearson et al., 2010)	Insulin resistance can be prevented and put into remission (Goldenberg & Johnston, 2021; Meng et al., 2017; Westman et al., 2018a).
2	Increased levels C-reactive protein (CRP) inflammatory marker (Howren et al., 2009)	Reducing inflammation through activation of peroxisome proliferator-activated receptors (PPARs)(Cullingford, 2008; Jeong et al., 2011)
3	Impaired insulin sensitivity (Weber et al., 2000)	Improves insulin sensitivity (Skow & Jha, 2023b)
4	Increase in fasting blood glucose levels which impact glucose metabolism (Peng et al., 2017)	Normalisation of blood glucose levels (Stafstrom & Rho, 2012)
5	Energy metabolism dysfunction (Zuccoli et al., 2017)	Normalization of abnormal energy metabolism (Stafstrom & Rho, 2012)
6	Mitochondrial dysfunction caused by oxidative stress alters intracellular metabolism and can damage mtDNA (Tobe, 2013)	Stimulates mitochondrial biogenesis, resulting in stable synaptic function (Bough et al., 2006; Maalouf et al., 2009a). Increases antioxidant effects, reduces oxidative stress, increase mitochondrial respiration (Greco et al., 2016; Maalouf et al., 2009; Pinto et al., 2018; Youm et al., 2015)
7	An association between metabolic syndrome and depression suggesting depression is a metabolic disease (Dunbar et al., 2008; Lang & Borgwardt, 2013)	Carbohydrate restriction improves aspects of metabolic syndrome (Volek et al., 2009)
8	A causal pathway from inflammation to depression suggesting depression is an inflammatory disease (Lang & Borgwardt, 2013; Valkanova et al., 2013)	Carbohydrates and sugar promote inflammation. KD lowers inflammation (Gasior et al., 2006a) and decreases the inflammatory mediators in cells (Maalouf et al., 2009a)
9	Depression as a neurodegenerative disease (Lang & Borgwardt, 2013)	Ketones can decrease oxidative damage, increase mitochondrial biogenesis, and bypass the complex 1 activity in some neurodegenerative diseases (Paoli et al., 2014)
10	Impairment in central monoaminergic function and activity (Brigitta, 2002)	Regulates neurotransmitters and metabolites of monoamines (Brietzke et al., 2018; Sethi & Ford, 2022)
11	An upregulation of inflammation decreases production of monoamines, serotonin, histamines, melatonin, and dopamine (Moylan et al., 2013)	A KD therapeutically changes the dopaminergic system (Church et al., 2014)
12	Increased cortisol (Stetler & Miller, 2011)	KD helps to regulate blood sugars which can be an issue for those with long term stress and high cortisol. It also significantly decreases cortisol levels (Polito et al., 2021; Yancy et al., 2005)
13	Decreased metabolism of norepinephrine, increased activity of tyrosine hydroxylase (Charney & Manji, 2004)	Increases endogenously produced norepinephrine (Operto et al., 2020; Weinshenker, 2008)

Table 1.6 (Continued)

	Depression Biological Factor	*Related Ketone Effect*
14	Increased levels of pro-inflammatory markers IL-1α, TNF-a, IL-1, and IL-6, damage the central serotonin system (Dantzer et al., 2008; Howren et al., 2009)	Inhibits inflammatory mediators such as interleukins and TNF-a and suppresses IL-6, and IL-8, among others (Forsythe et al., 2008; Maalouf et al., 2009a) Positive regulation by anti-inflammatory factors rather than proinflammatory (Campbell et al., 2014)
15	Abnormalities in serotonin 1a receptors (Drevets et al., 1999)	Addition of omega 3's and fatty acids increases serotonin (Patrick & Ames, 2015)
16	P2X7-NLRP3 inflammasome pathway releases the pro-inflammatory cytokine -IL1β (Bhattacharya & Jones, 2018)	Beta-hydroxybutyrate inhibits the NLRP3 inflammasome (Pinto et al., 2018; Shippy et al., 2020; Storoni et al., 2015)
17	Levels of dopamine are reduced (Lambert et al., 2000)	Suppresses appetite (Gibson et al., 2015a) and reduces psychological cravings increased by dopamine functions (C. K. Martin et al., 2011).Associated with dopaminergic and serotonergic modulation (Brietzke et al., 2018; Dahlin et al., 2012)
18	Reduction in dopamine neurotransmission (Meyer et al., 2001)	Addition of BHB in mice protects from the dopaminergic neurodegeneration (McDonald & Cervenka, 2018; Norwitz et al., 2019)
19	Hippocampal volume loss (Hasler et al., 2007) Elevated glucocorticoid levels, lead to hippocampal atrophy (Christoffel et al., 2011)	BHB protects the hippocampal neurons from beta amyloid toxicity (Kashiwaya et al., 2013) Glutathione increases in hippocampal cells (Napolitano et al., 2020)
20	Decreased neurotrophic factors are responsible for brain volume loss (Hasler, 2010)	Increase in activity of neurotrophic factors (Maalouf et al., 2009a) which can protect brain against injury
21	Decreases in hippocampal brain derived neurotrophic factor levels (BDNF) (Hasler, 2010)	BHB increases BDNF (Chen et al., 2017; Sleiman et al., 2016)
22	Decreased GABA in the prefrontal and occipital cortex of the brain (Hasler, 2007)	Increases GABA levels and regulates GABA function (McDaniel et al., 2011; Ricci et al., 2020; Yudkoff et al., 2005; Yudkoff et al., 2004) Alters the GABA:Glutamate ratio (Włodarczyk & Cubała, 2019)
23	Dysfunction of the glutamate neurotransmitter system (Hasler, 2010)	Ketone bodies regulate neurotransmission balance (inhibiting glutamate transporters and increasing inhibitory neurotransmitters) (McNally & Hartman, 2012) Mitochondria are responsible for neurotransmission, neuronal plasticity, and cellular resistance. Improvement in mitochondrial function and a decrease in cell death (Gano et al., 2014; Gasior et al., 2006; Kovács & Dobolyi, 2013; Maalouf et al., 2009)
24	Abnormal glutamate levels (Hasler et al., 2007)	Inhibits glutamate decarboxylase and decreases activity of stimulates the synthesis of GABA (Brietzke et al., 2018)
25	Shortened REM latency (Hasler, 2010)	REM latency increases (St-Onge et al., 2016)
26	Altered and dysregulated HPA axis (Carroll et al., 1976; Hasler, 2010; Smolensky et al., 2023; Stetler & Miller, 2011)	Positive impact on the HPA axis (Polito et al., 2021)

Table 1.6 (Continued)

	Depression Biological Factor	*Related Ketone Effect*
27	Deficiency of monoamines and disturbed transmission (Hasler, 2010; Smolensky et al., 2023)	Regulates neurotransmitters and associated with dopaminergic and serotonergic modulation (Brietzke et al., 2018; Sethi & Ford, 2022)
28	Neurotoxic and neurotrophic processes (Hasler, 2010)	Astrocyte ketogenesis is a neuroprotective pathway (Guzmán & Blázquez, 2004)
29	High levels of ROS are closely linked to neuronal death (Popa-Wagner et al., 2013)	Reduces levels of reactive oxygen species (ROS) which are carcinogenic, through its effect on uncoupling proteins and increased energy ATP availability (McDaniel et al., 2011; Stafford et al., 2010; Sullivan et al., 2004). Induces expression of mitochondrial uncoupling proteins which reduces ROS production (Bough et al., 2006; Do Young Kim et al., 2010; Seyfried et al., 2005)
30	Reduced ATP production (Gardner & Boles, 2008)	Enhances ATP production (Maalouf et al., 2009b; Masino & Geiger, 2008; Storoni et al., 2015)
31	Impaired oral glucose tolerance (Weber et al., 2000)	Ketones produced can be used as an alternative source of fuel in the setting of impaired or absent glucose metabolism (Owen et al., 1967; Storoni et al., 2015)
32	Lower GSH glutathione levels (Godlewska et al., 2015)	Increases levels of glutathione synthesis through its inhibitory action on histone deacetylases and activation of the Nrf2 pathway (Jarrett et al., 2008; Milder & Patel, 2012; Storoni et al., 2015)
33	Increased apoptotic stress (Shelton et al., 2011)	Protection from apoptosis and decreased activity of pro-apoptotic factors (Maalouf et al., 2009; Sullivan et al., 2004)
34	Impaired UCP expression and (Hermes et al., 2016)	Promote UCP activity, specifically the UCP2, UCP4, and UCP5 (Storoni et al., 2015)
35	Imbalanced metabolism of the kynurenine pathway (Xi-Cong Liu et al., 2017)	Increases kynurenic acid (KYNA) in the brain which is an endogenous neuroprotectant (Urbańska et al., 2014; Żarnowski et al., 2012)
36	Decreased adenosine signalling (Elgün et al., 1999)	Increases adenosine signalling in the brain which has anti-inflammatory effects (Boison, 2017; Chan et al., 2007; El-Mallakh & Paskitti, 2001; Lusardi et al., 2015; Masino et al., 2011; Masino & Geiger, 2008)
37	Elevated intracellular sodium concentrations (Huang & El-Mallakh, 2007)	Reduces blood pH causing mild acidosis which reduces intracellular sodium concentrations (El-Mallakh & Paskitti, 2001; Phelps et al., 2013) Exchanges extracellular protons (acid) with intracellular sodium, regulating levels (El-Mallakh & Paskitti, 2001)
38	Impaired glucose metabolism and tolerance (Hennings et al., 2012)	Upregulates mitochondria to use ketone bodies and beta-oxidation of fatty acids as fuel to the body, both of which bypass glycolysis if glucose metabolism is impaired (Lutas & Yellen, 2013a). Glycolysis is reduced in the presence of BHB (Achanta & Rae, 2017)
39	Associated with a reduction in glucose utilisation (El-Mallakh & Paskitti, 2001)	Changes fuel from glucose to ketone utilisation (Sethi & Ford, 2022)

Table 1.6 (Continued)

	Depression Biological Factor	*Related Ketone Effect*
40	Positive association between depressive disorder and insulin resistance (Pearson et al., 2010)	Decreases need and production of insulin (Boden, 2005)
41	The status of histone acetylation levels is used as a biomarker for depression (Park et al., 2021)	BHB has a direct, dose-dependent inhibitory activity on class I histone deacetylases (HDACs) including HDAC1, HDAC3, and HDAC4 (Achanta & Rae, 2017; Storoni et al., 2015)
42	Mitochondrial respiratory chain dysfunction (Fernström et al., 2021; Rezin et al., 2009)	Preserves ATP levels in the event of mitochondrial respiratory chain dysfunction (Storoni et al., 2015)
43	Mitochondrial permeability transition pore (mPTP) when open due to stress, leads to ATP decrease and cell death (Elustondo et al., 2016; Yang et al., 2022)	Open ATP channels on the inner mitochondrial membrane prevents the formation of mitochondrial permeability transition pores (MPTPs) (Storoni et al., 2015). AcAc and BHB increase the limit for calcium induced MPTP formation (Do Young Kim et al., 2007)
44	Associated with low levels of ATP production (J. Allen et al., 2018)	BHB attenuates the decrease in ATP production (Gano et al., 2014; Gasior et al., 2006; Kovács & Dobolyi, 2013; Maalouf et al., 2009a; Sullivan et al., 2004; Tieu et al., 2003)
45	6-hydroxydopamine indues anxiety and depression (Beppe et al., 2015; Santiago et al., 2014)	Protects dopaminergic neurons against 6-hydroxydopamine neurotoxicity in a rat model (Cheng et al., 2009)
46	Synaptic mechanisms are dysregulated, and the connectivity between brain regions becomes unbalanced (Christoffel et al., 2011)	Stimulates mitochondrial biogenesis, which results in stable and regulated synaptic function (Bough et al., 2006) Restoration synaptic activity in succinic semialdehyde dehydrogenase deficient (disorder of GABA metabolism) mice (Nylen et al., 2009)
47	Increased Aβ in the bilateral frontal lobes of the brain (Chung et al., 2015)	Decreased amounts of β-amyloid deposition (Van der Auwera et al., 2005)
48	Decreased AMPK activity (Lee et al., 2020)	Increased AMPK activity (McDaniel et al., 2011; Youm et al., 2015)
49	Increased DNA methylation (Sales et al., 2021; Zhu et al., 2023)	Decreased DNA methylation (Lusardi et al., 2015)
50	Decreased sirtuin activity (Hou et al., 2022; Lo Iacono et al., 2015; Song & Kim, 2016)	Increased sirtuin activity (Maalouf et al., 2009a)
51	Decreased glutamate and glutamine (Son et al., 2018)	Increased glutamine (Yudkoff et al., 2005)
52	H3k9bhb reduced in mice (Chen et al., 2017)	Reverses reduction of H3k9bhb (Chen et al., 2017)
53	Increased microglia activity and inflammatory activation (Enache et al., 2019; Guan et al., 2020)	Cessation of microglial changes and activity (Grigolon et al., 2020)

Though this table explores the biological pathways by which ketones and ketosis may counteract factors of depression and improve depressive symptoms, the reasons why or how ketones exhibit these effects is still unknown and beyond the scope of this work. For detailed metabolic and biochemical reviews of the current literature, see Masino (2022) and Kossoff et al. (2020).

However, there is unmistakable evidence at the biochemical level that show the potential benefits of the KD on depression. So far, as seen earlier in the chapter, there is only a small amount of evidence to show that lowering carbohydrates in the diet can improve depressive symptoms or other mental health issues in humans at the dietary intervention level. However, evidence summarised in Table 1.6 demonstrates multiple pathways of action suggestive of a clear role for a KD in improving depressive symptoms and therefore it should be trialed as a potential treatment or adjunctive treatment to standard care.

1.6.6 Proposed pathways for ketones on depression

As seen in the biological factors table, Table 1.6, there are many plausible pathways by which ketones may have antidepressant effects and decrease symptoms of depression. Reducing inflammation, neurotransmitter regulation, energy balance, mitochondrial biogenesis, and improvement in gut permeability are all actions whereby ketones could decrease depressive symptoms.

Inflammation is the body's way of defending itself (Chen et al., 2018; Freire & Van Dyke, 2013). It is beneficial and necessary in acute circumstances, however, too much inflammation over a long period of time leads to chronic inflammation. Chronic inflammation is associated with many illnesses such as CVD, cancer,

T2D, neurodegenerative diseases among others (Furman et al., 2019). There is research to support the association between depression and this chronic low-grade inflammation (Berk et al., 2013; Lang & Borgwardt, 2013; Valkanova et al., 2013). It has been reported that depression and inflammation have a bidirectional relationship (Kiecolt-Glaser et al., 2015). Inflammation is identified by increased levels of many inflammatory markers in some people with a depression diagnosis (Chin Fatt et al., 2023; Howren et al., 2009; Shelton & Miller, 2010).

Table 1.7: Studies of depression with dysregulated or increased inflammatory markers

Author	*Date*	*Inflammation Markers*	*Outcomes*
Valkanova	(2013)	Increased CRP, IL-6	Increased depressive symptoms even after adjusting for demographic factors
Jeenger et al.	(2017)	Increased CRP	Increased depression severity
Kiecolt-Glaser et al.	(2015)	IL-6, TNF-α, IL-1β, IL-2, IL-1RA and CRP	Higher in those with depression compared to controls
Pérez-Sánchez et al.	(2018)	IL-12, IL-13, and IL-15	Higher in those with depression compared to healthy adolescents
Beurel et al.	(2022)	Increased IL-6, CRP, TNF-α, IL-10, IL-13, IL-18, IL-12, IL-1RA	Dysregulated levels of inflammatory markers in depression
Howren et al.	(2009)	CRP, IL-1, IL-6	All positively associated with depression
Raison et al.	(2006)	Increased IL-6, CRP, IL-1β, TNF-α	Increased risk for depression, reduced responsiveness to antidepressants
Chamberlain et al.	(2019)	CRP	Higher in those with treatment resistant depression
Petralia et al.	(2020)	IL-12 and IL-18	Increased in those with depression
Miller et al.	(2009)	IFN-γ	Increased in those with depression

Dysregulated levels of inflammatory markers have been reported in many systematic reviews and meta-analyses on depression and anxiety (Beurel et al., 2020; Dantzer, 2017; Hiles et al., 2012). See Table 1.7 for an example of studies that show elevated inflammatory markers and their associations with depression.

In current standard treatment for depression, nearly all antidepressant medications appear to have anti-inflammatory properties (Maes, 2008; Tomaz et al., 2020). If antidepressants have anti-inflammatory effects, and work in some cases, then it could be proposed that anti-inflammatory processes such as drugs or dietary interventions may have antidepressant effects (Troubat et al., 2020). From the literature, it has also been shown that ketones lower rates of inflammation in the body (Gasior et al., 2006) and decrease the inflammatory mediators in cells (Maalouf et al., 2009). This approach could be potentially helpful for those who are treatment resistant and do not respond to the current standard treatment. A recent study that investigated this relationship found that individuals with high levels of inflammation are less likely to respond to antidepressants (Cattaneo et al., 2016) and may be used as markers of treatment resistance, for example those with high CRP and IL-6 (Petralia et al., 2020; Chenghao Yang et al., 2019). Therefore, if some of the underlying biological factors of depression are based on inflammation then perhaps the anti-inflammatory effects of a KD on the body (Gasior et al., 2006; Jeong et al., 2011) may alleviate some depressive symptoms and improve declining metabolic health, a side effect of the medications used.

Depression is also mediated by pro-inflammatory cytokines which activate the HPA axis and impairs the central serotonin and neurotransmission system (Dantzer et al., 2008). Depression is associated with epilepsy (Mula & Schmitz, 2009) and in those with epilepsy the KD regulates the neurotransmitter levels of serotonin and dopamine (Dahlin et al., 2012). In depression, levels of serotonin and dopamine are altered (Belujon & Grace, 2017) so if epilepsy has been treated with a KD since the 1920s, perhaps this dietary approach may also help alleviate depressive symptoms.

The health of the body's mitochondria is also important as they are responsible for creating energy (ATP). Impaired mitochondria have been associated with psychiatric disorders and the implementation of a KD appears to improve mitochondrial health and energy balance and reduce mitochondrial dysregulation (Niepoetter et al., 2019).

Calarge et al. showed that the severity of depression was associated with increased intestinal and gut permeability in 41 women. Their work suggests that this may activate the innate immune system which promotes the development of depression (Calarge et al., 2019). Research shows there is a clear relationship between gut dysregulation and depression. The KD has a positive impact on gut biosis and gut dysregulation (Cabrera-Mulero et al., 2019; Genedi et al., 2019; McFarland et al., 2017; Mörkl et al., 2020; Xie et al., 2017; Zagórska et al., 2020), and it alleviates colitis (Kong et al., 2021), IBS and heartburn (Austin et al., 2009; Austin et al., 2006).

1.6.7 Potential role of ketones and the ketogenic diet in the context of depression

In a systematic review and meta-analysis, it was found that a pro-inflammatory diet was independently associated with an increased risk of depression (Wang et al., 2018). The standard Western diet has been shown to be highly inflammatory. Therefore, it is warranted to follow an anti-inflammatory style diet in order to reduce these levels. The KD has been shown to exhibit greater anti-inflammatory and anti-depressant properties in many diseases compared to other diets, and this is predominantly due to the function of the ketone molecule, BHB (Grigolon et al., 2020; Jeong et al., 2011; Maalouf et al., 2009; Masino & Geiger, 2008; Ruskin et al., 2009). Research suggests that BHB can cross the blood brain barrier (Augustin et al., 2018) and therefore the state of ketosis has been shown to protect the neurons in the brain from neuronal injury (Davidson et al., 2013; Maalouf et al., 2009). In addition to the antidepressant, neuroprotective and anti-inflammatory effects of ketones in the KD, the diet can also improve metabolic health as stated earlier (Newman & Verdin., 2014; Sullivan et al., 2004; Volek et al., 2005).

When it comes to depression, there appear to be two schools of thought. The first being that consuming a Western diet with high levels of ultra-processed foods leads to MetS which is then associated with a higher risk of depression. The second being that the presence of depression leads to an increased consumption of ultra-processed foods due to elevated hunger levels in some people which then increases the prevalence of MetS. There is research to support both arguments (Contreras-Rodriguez et al., 2023; Simmons et al., 2016).

However, research has shown that some people can improve and even eliminate their MetS with food, specifically a low carbohydrate ketogenic approach (Volek et al., 2005, 2009), and some can reduce their depressive symptoms and improve their mental health with food (Jacka et al., 2017; Marx et al., 2021; Parletta et al., 2019). Depression has been coined a metabolic disease because of this association between MetS and depression (Dunbar et al., 2008). This suggests that food may be the driver for some cases of depression, and therefore the KD may improve depressive symptoms through its anti-inflammatory and neuroprotective actions. It has been suggested that using a KD to reach therapeutic levels of BHB in the blood may be a novel approach for the treatment of depression, especially treatment resistant depression (Kovács et al., 2019).

1.7 Defining Psychological Well-being

Food is used by many people to regulate their mood, mainly to improve their negative mood state or emotions. Wurtman et al. (1995) reported that low mood increases the desire for carbohydrates and consuming carbohydrates can improve a depressed mood. However, studies carried out also suggest that removing the carbohydrates and sugar from the diet result in a reduction of depressive symptoms and the reintroduction of these foods cause the return of depressive symptoms (Christensen, 1993).

The term mood is often used to state an overall feeling based on a combination of factors that make up psychological well-being. Psychological well-being is an umbrella term consisting of a few different aspects. In this thesis, the aspects chosen to create the term psychological well-being were stress, depression,

anxiety, mental well-being, self-compassion, and positive and negative affect. Each of these will be discussed in more depth in the next chapter.

1.8 Limitations to Previous Research

There is no such thing as an essential carbohydrate, but there are essential fatty acids and amino acids from protein (Bier et al., 1999). There are no essential carbohydrates, yet the current dietary guidelines advise an average of 260 grams of carbohydrates daily (Buttriss, 2000). Carbohydrate intake is associated with an increased risk of metabolic syndrome (Liu et al., 2019) of which more than 31% of individuals, including 3% of children and 5% of adolescents live with globally (Engin, 2017; Noubiap et al., 2022). So, although this level of carbohydrates can be tolerated by some people, it is not tolerated by those with metabolic syndrome or those at risk of developing metabolic syndrome, such as those taking psychiatric medications.

There are many limitations to the current literature and studies on ketogenic diets for psychiatric conditions. Many of the studies on KD and psychiatric conditions have focused on mechanisms of action in rodents and mice, and less so in humans. This makes it difficult to extrapolate and generalise the results to humans. Though this preclinical work is necessary to better understand biological mechanisms and finer details that cannot be tested in humans, human studies are imperative before a treatment recommendation can be offered. Therefore, now that there is a large amount of rodent and mouse literature in support of this potential intervention, human trials are an important next step.

Many of the dietary intervention studies have poor adherence and high attrition levels. Working with a sample of individuals living with a psychiatric condition can make it more difficult to adhere to a new diet or take part in a research study. Therefore, more studies with larger sample sizes are needed to test the intervention. Outcome measures also vary across studies with some using standardised measures and others using subjective measures. There is no consistency between studies even when looking at the same disease.

The tracking of ketones has also not been consistent across the literature. There is one way to determine whether an individual has reached a state of ketosis, and that is by measuring ketones in the blood, breath, and urine. Frequent testing and reporting of ketones in research studies has not been consistent and therefore makes it difficult for researchers and clinicians to determine whether the participants results were due to ketosis or not.

To date, the sample size of dietary intervention studies in low carbohydrate and KD research has varied. Some are small with samples as little as N=31 (Meckling et al., 2004), N=32 (Danan et al., 2022) and N=58 (Sheffler et al., 2023) and others larger, with sample sizes up to N=132 (Samaha et al., 2003). However, even larger, and longer studies are required, alongside the gold standard, randomised control trials to better understand the role, impact, mechanisms, and efficacy of a ketogenic diet on psychological well-being and depression (Bostock et al., 2017; Hariton & Locascio, 2018).

In terms of study structure and design, the most encouraging study in recent years (Danan et al., 2022) was carried out in a hospital inpatient setting and did

not include a control group. Though the results were extremely positive, the patients were not blind to their intervention, and it is unclear whether the findings could be replicated in a real world, outpatient setting. Though significant clinical benefits were observed, researchers were unable to determine which psychosocial aspects or biological factors of following the KD worked for the patients. The biggest limitation in this research is the variations across KD studies in terms of their macronutrient and caloric approaches to diet. Some studies use total daily carbohydrates of 5% and others up to 20%. Some studies are calorie controlled and others are ad libitum, some with supplemental MCTs and others without. As stated earlier, there are many types of KD composition, but the studies published so far, differ in this regard making it very difficult to compare studies and outcomes. There are no protocols set on how exactly to administer the diet. As discussed earlier, ketosis can be reached via many routes which adds a level of complexity to the generalisability of research. A consensus and universal set dietary protocol is needed to ensure consistency across all research studies, and ultimately to patients if found to be beneficial.

1.9 Advancement and Originality of This Research

El Karkafi et al. (2023) state that the literature now has many case studies to support the KD's mood stabilising and anxiolytic effects but that the main void is large human studies that can increase understanding of the diet's effects on behaviour and on the disorders themselves (El Karkafi et al., 2023). These published case studies are a result of the clinical work that some psychiatrists are carrying out in private practice where they are implementing the ketogenic

diet alongside the current standard of care with encouraging results (Danan et al., 2022; Palmer, 2017).

There are some clinical trials registered on the clinicaltrials.gov register looking at the improvements of neural network instability in schizophrenia via the ketogenic diet (recruiting), the impact of the KD on obesity and metabolic abnormalities in bipolar disorder (not yet recruiting), the KD for psychotic disorders (recruiting), and a pilot study of the KD in bipolar disorder (results pending).

To the researcher's knowledge this current thesis will be the first randomised control trial of a LCD and KD on depressive symptoms and psychological well-being in humans. This dietary approach may be developed as an adjunct to current psychiatric and psychotherapeutic therapy and medication for which are known to have severe debilitating side effects (Correll et al., 2015).

1.10 Rationale and Aims of this Program of Research

More is known about the KD and its biological mechanisms than any other dietary intervention. Fasting has been used for millennia and the KD was created to mimic the effects of fasting but with food. There is over 100 years' worth of literature available on the KD and how it works on the biological level for diseases (Guelpa., 1911; Wilder., 1921).

There is now growing evidence that the UK government's healthy eating guidelines (World Health Organization, 2015) based on the 'Eatwell Plate' are not supported by high quality research (Harcombe et al., 2015). According to a systematic review and meta-analysis, the evidence and literature available at

the time of guideline creation did not support what was proposed (Harcombe et al., 2016). If this is true, perhaps there are alternative ways of eating that can improve our physical and mental health.

As mentioned above and seen in Tables 1.4 and 1.5, there is research to suggest that the KD affects well-being, albeit through secondary or indirect measures, (Adams et al., 2022; Halyburton, 2007; Cox et al., 2019; Tidman, 2022; Yancy et al., 2009) it can be proposed that KD intervention programs are very likely to impact affect and well-being when tested as a primary measure.

If antidepressants are only marginally more effective than placebo and come with many negative side effects, perhaps trialling a KD which has little to no adverse side effects would be beneficial. The KD is well tolerated, especially compared to the side effects of antidepressants and other medication used for psychiatric conditions. Even if individuals don't see improvements in their mental state while on a KD, they would at least know that their metabolic health would be improved which could counteract the negative metabolic effects of many psychiatric medications.

From the evidence it is clear that the KD produces significant metabolic changes in the body that influence mood and depressive symptoms (see Tables 1.4 and 1.5). The current work will investigate the impact of the KD on well-being outcomes and will use a low carbohydrate dietary intervention that does not reach a state of ketosis, along with a control group to compare outcomes.

1.10.1 Study 1 – Quantitative

This research study is intended to be the first randomised control study of a KD on depressive symptoms and psychological well-being in an otherwise healthy cohort of humans. The purpose of this study is to compare a KD, to a low carbohydrate diet (LCD) in those with and without depressive symptoms in a medium sized sample of human participants. Individuals will follow an online dietary intervention program for 12 weeks, followed by 12 weeks independently without the online program. This study is a quantitative, double blind randomised control trial with quasi experimental mixed design elements.

The KD produces metabolic changes that increase levels of ketones which have been linked to potential mood elevated effects in mice and rodents (Ari et al., 2016; Hollis et al., 2018; Kraeuter et al., 2020; Murphy et al., 2004; Olivito et al., 2023) so it is predicted that these effects will be replicated in study 1.

There is currently no literature comparing the effects of a KD to a LCD with this population sample. In this study it is predicted that participants in the KD group will show significant improvements in affective state (depression, anxiety, positive and negative affect), stress and mental well-being compared to those in the LCD group. This is because the LCD does not produce the metabolic changes that increase the levels of ketones in the body because mechanistically it does not drop ketones low enough to initiate the state of ketosis (Wylie-Rosett et al., 2013). However, by following a LCD, most high glycemic carbohydrates and sugars are removed from the diet. It is predicted that participants in the LCD will show some improvements in affective state (depression, anxiety, positive and negative affect), stress and mental well-being compared to those

in a control group, but perhaps not as much as the KD diet. With dietary interventions, affective changes may be multifactorial and positive changes may be related to factors outside of the diet, for example weight loss, or program engagement and support.

In addition, psychosocial barriers and facilitators may influence the participants experience of the dietary intervention (Sheridan et al., 2020). Therefore, baseline characteristics such as current health and mental health status, social support, body appreciation and self-compassion will also be measured. Predictions for these measures will be covered in Chapter 2.

1.10.2 Study 2 – Qualitative

A qualitative study of participants who followed the ketogenic dietary intervention will be added to complete this program of research. The aim of the study is to develop a greater understanding of the participants journey through the ketogenic dietary intervention and to identify any common themes across their accounts.

There are limitations to online questionnaires like those sent to participants in study 1. Knowledge is limited by the questions asked and participants may have oversimplified their answers. This qualitative segment will add experience and nuance to the data collected by questionnaire in study 1.

This will provide a qualitative narrative to support the quantitative results from the previous study. Thematic analysis will be used to explore the accounts of participants who are randomised to the ketogenic dietary intervention in study 1 captured via semi structured one to one interview.

Chapter 2: Study 1 - Ketogenic Diet vs Low Carbohydrate Diet Randomised Trial

2.1 Introduction

2.1.1 Overview

The Ketogenic diet has been used since the 1920's to treat treatment resistant epilepsy in children. The medications used to treat epilepsy are often the same medications used to treat types of depression, e.g., bipolar disorder and lithium (Curran & Ravindran, 2014). As the ketogenic diet has been clinically researched, tested, and used for over 100 years, we know more about the pathophysiology of the ketogenic diet than any other diet, including the Mediterranean diet. There is ample research to suggest that psychological well-being may improve when following a ketogenic diet, specifically in those with depressive symptoms, and perhaps even a subsample of these who identify or may have inflammation or metabolic derangement through mitochondrial dysfunction as the root cause of their illness. This chapter will explore how following different types of dietary interventions, specifically low carbohydrate, and ketogenic diets, may alleviate depressive symptoms, and alter other aspects of psychological well-being.

2.1.2 Online dietary interventions

Online interventions are a new and novel way for patients to access treatment and care in their own time. Online dietary interventions give patients the agency to take responsibility for their health and have access to treatment and care in real time, wherever they are. The introduction of dietary interventions shows

promise to reach those in the community who need help the most but who may not have access to the care they need for many reasons.

Patients may feel that their doctor is not supportive, that they have tried conventional dietary approaches and they haven't worked. They also may be busy and don't have the time to attend face to face meetings. Specifically in a post pandemic world, the use and potential benefits of online dietary interventions are high. However, it is important to understand the effectiveness of online interventions with regards to dietary behaviour change.

An early systematic review of the online (eHealth) intervention literature by Norman et al. (2007) found mixed results when it came to the effectiveness of online interventions for physical activity and dietary behaviour change designed for a population with Diabetes and cardiovascular disease. Of the 13 dietary behaviour eHealth intervention studies reviewed, seven favoured the eHealth intervention for dietary behaviour change, five studies did not have enough evidence, and one studied favoured a face to face intervention approach. It is to be noted that the online interventions reviewed were of desktop applications, emails and websites and did not include mobile devices, apps, or messaging (Norman et al., 2007).

When looking specifically at online weight loss interventions, self-tracking and educational lessons as tools led to significant weight loss in a 12-week online program (Ross & Wing, 2016) and those who also included automated feedback on their progress for 12 weeks lost more weight overall compared to those using educational tools for weight loss only (Thomas et al., 2014). A systematic review

and meta-analysis of 18 studies (N=5700) by Neve et al., looking at the effectiveness of online interventions for weight loss in overweight and obese individuals found that although many studies resulted in weight change, it is difficult to determine the effectiveness of the interventions themselves due to the variety of study designs and reporting strategies. They suggested that online interventions with extra features such as personalization through feedback or tailoring information to the individual and providing chat rooms or forums achieved higher weight loss compared to those with education alone (Neve et al., 2010). This is consistent with the findings of Thomas et al. (2014). From the literature it is clear that online interventions can work for weight loss if designed with the participant in mind. If these interventions can work for weight loss, perhaps they can work for other health goals and outcomes.

An encouraging meta-analysis carried out in 2017 to review the effects of 18 technology mediated type 2 diabetes prevention programs on weight (N=2774) found that they can result in clinically significant improvements in diabetes health markers as well as weight loss (Bian et al., 2017). In recent years, the Virta Health Program has shown impressive results. Virta is an online platform that delivers a ketogenic diet (<30g carbohydrates) intervention alongside education, data-tracking, peer support and coaching for those with T2D. In their published studies, their intervention group (N=262) lost 12% at 1 year, compared to those in the control group (N=87) who did not lose weight at 1 year (Hallberg et al., 2018). The intervention group also put their diabetes into remission by reducing diabetes health markers and reducing or even eliminating diabetic prescription medication, including insulin therapy. Remission rates

increased from 12%-54% in the intervention group but decreased in the control group, 16%-9% (Veazie et al., 2020). Further research by Strombotne et al., analysed the medical records of patients who took part in an online telehealth and coaching intervention using a ketogenic diet under the Virta Health program. Over five months, they found that a ketogenic diet program was associated with clinically meaningful reductions in diabetic related health markers and costs, diastolic blood pressure, and BMI (Strombotne et al., 2021). So far, it is clear that online interventions can work for a number of health-related outcomes. What is different about the Virta Health Program is that their prescribed dietary intervention is a very low carbohydrate, ketogenic plan. This dietary approach, either face to face or online may achieve better health outcomes compared to other diets.

To explore this further, research carried out by Saslow et al., in 2017 found that individuals assigned to a very-low carbohydrate ketogenic diet online intervention (20-50g carbohydrates per day) through the Low Carb Program at Diabetes.co.uk (DCUK), alongside behavioural support, achieved better health outcomes compared to those in the control group who followed the American Diabetes Associations' "Create Your Plate" Diet which is a low-fat diet. A limitation of this study however is that the control group did not receive the same level of behavioural support as the intervention group, so it is unclear whether it was the behavioural support, the low carbohydrate ketogenic dietary intervention, or the combination of both that made the difference (Saslow et al., 2017). In another study investigating the outcomes of the The Low Carb Program, the online intervention was followed by 1000 participants who reduced

carbohydrates based on a visual plate method and increased their intake of green vegetables, fats, and low Glycemic Index (GI) fruits. Carbohydrates were reduced over the duration of the program to less than 130g per day, which is considered low carbohydrate but not ketogenic. The program was followed for 10 weeks and consisted of weekly automated emails, educational videos, data-tracking, and access to a discussion board. Participants who completed all 10 weeks (n=528, 52%) had a clinically meaningful reduction in weight and showed reductions in other diabetes related health markers. However, unlike the previous study, this study did not have a control group, so it is unclear whether the intervention caused the outcome (Saslow et al., 2018). The limitations in the study designs of many of these studies (e.g., not including control groups) makes it difficult to determine whether the improvements in health were due to the care interventions (coaching and peer support) or the diets themselves but it suggests that utilising a platform like this which focuses on developing a community run, service user led, peer support site may create a new way in which to research across communities.

Using this and other literature as a guideline, the low carbohydrate dietary intervention in this chapter will recommend a daily total carbohydrate intake of 90-130g to ensure a state of ketosis is not reached (<0.5 mmol/L blood ketone levels). This carbohydrate range is significantly higher than what research suggests is low in carbohydrates or 'low-carb'. However, the literature is not clear on the exact carbohydrate parameters for a low carbohydrate diet, there is a lot of variation across studies (Bravata et al., 2003). This range (90-130g) was given to ensure that participants assigned to this group do not accidently

drop their carbohydrate intake low enough to enter ketosis. However, for most participants, total carbohydrate intake levels above 50g per day are enough to keep out of a state of ketosis, when tested with a blood ketone monitor (<0.5 mmol/L blood ketone levels) as stated in more recent meta-analysis papers (Hashimoto et al., 2016). The ketogenic dietary intervention will recommend a much lower total carbohydrate intake of 20-50g per day to ensure a state of ketosis is reached (≥0.5 mmol/L blood ketone levels). By limiting daily carbohydrates to this range, ketosis will be realised in almost all cases without the need to test blood ketones, as long as participants stick to the dietary plan.

2.1.3 The effects of low carbohydrate and ketogenic diets on depression

There appear to be many common pathophysiological changes in the development of depression. Ketone molecules have been shown to alter neurotransmitter levels, inflammasomes and mitochondria expression, amongst other mechanisms, as mentioned in Chapter 1: Literature Review of this document.

Recent research suggests that both dietary and supplemental ketogenic interventions can modulate and ameliorate some of these negative changes to produce positive therapeutic effects (Kovács et al., 2019). The ketone body beta-hydroxybutyrate (BHB) which is produced when carbohydrates are reduced below 50g per day and the body moves into ketosis has anti-inflammatory properties. It has been shown that BHB treatment has an antidepressant like effect in both rat and mice models of anxiety and depression (Chen et al., 2017; Yamanashi et al., 2017).

Prenatal exposure to the ketogenic diet reduces the susceptibility to anxiety and depression in mice, even if a standard diet is followed postnatally. Positive anatomical changes in brain volume, in regions such as the cortex and cerebellum, are observed in mice on a ketogenic diet. It is suggested that this is due to the neuroprotective effects of ketones compared to mice not exposed to the ketogenic diet in utero (Sussman et al., 2015). Many of these studies are still to be replicated in humans.

A review of the status of the ketogenic diet in psychiatry in 2017 stated that to the best of the authors knowledge, there were no studies examining the effects of the ketogenic diet on depression in humans (Bostock et al., 2017) but that there is enough research to support human trials as the next step. In 2023, this is still the case.

2.1.4 Rationale for investigating variables

There is a growing area of research and evidence to suggest that the ketogenic diet can reduce depressive symptoms in at least a subsample of those with depression. However, it is still a relatively new research area and gold standard randomised control trials are needed to truly understand the impact of this approach on depressive symptoms and other aspects of psychological well-being. An overview of the variables investigated in this chapter are seen below: depression, affect, mental well-being, anxiety, and stress. The details of the additional measures - social support, body appreciation and self-compassion - can be seen in Chapter 3.

Depression and Depressive Symptoms

In rodent studies, a decline in depression was reported in mice who demonstrated high levels of ketones (Gumus et al., 2022) and therapeutic effects of a ketogenic diet were found on depressive-like behaviours (Guan et al., 2020).

From the human literature available there is a case study that showed the amelioration of clinical depression via the ketogenic diet after 12 weeks in a subject with T2D. The Patient Health Questionnaire (PHQ9) scores decreased from 17 to 0, showing an improvement from moderately severe levels of depressive symptoms to minimal depressive symptoms (Cox et al., 2019). The PHQ-9 has also assessed the severity of depression symptoms while following the ketogenic diet for the treatment of post-concussion syndrome (Rippee et al., 2020).

More recently, Danan et al., found 100% of individuals (N=23), with serious, persistent and poorly controlled mental illness such as major depressive disorder, bipolar disorder, and schizoaffective disorder, following a ketogenic diet of <20g total grams of carbohydrates per day saw a significant improvement in their depression scores as measured by both the Hamilton Depression Rating Scale (HAM-D) and the Montegomery-Asberg Depression Rating Scale (MADRS) (Danan et al., 2022).

Affect

Research suggests that some individuals consume certain foods to improve their negative affect or mood, particularly high carbohydrate foods in the form of simple sugars and refined carbohydrates. However, research carried out in the 1990's suggests that this improvement and lifting of depression is short lived and is followed by increased fatigue and lowered energy, contributing to long term negative affect (Christensen, 1993). Further evidence indicates that the removal of these simple carbohydrates altogether can produce long term cessation of the negative affect.

Positive affect has been associated with an increase in desire to take part in healthy activities such as selecting healthier food options (Griffin et al., 1993). It has been suggested that when positive affect is increased, individuals may make healthier food decisions overall (Jeffers et al., 2020). Individuals show they can resist temptation in favour of a long term health goal (Fedorikhin & Patrick, 2010). However, negative affect has been associated with an increased intake of high fat, sugar, and carbohydrate food (Yang et al., 2019) and the amount of carbohydrates consumed also increases negative affect in response to stress. The higher the intake, the higher the negative affect (Wouters et al., 2018).

Many treatments for depression focus on reducing negative affect. However, recent research suggests it may be the improvement of positive affect that leads to better depression outcomes (Oren-Yagoda et al., 2018).

In this thesis, affect will be measured to see if either of the ketogenic or low carbohydrate dietary interventions could improve deficits in positive affect and/or reduce negative affect in participants.

Mental Well-being

Significant improvements in mental well-being were found in those who completed an online weight loss and health promotion program which included following a low carbohydrate diet (Walker et al., 2021). In another study, those who diagnosed themselves with food addiction took part in online psychoeducational programs for 10-14 weeks. The online group intervention focused on addiction and food quality and required participants to follow a low carbohydrate diet. Significant improvements in mental well-being were found at the end of the study (Unwin et al., 2022).

Anxiety

A reduction in anxiety has been observed in many studies where rodents demonstrated increased levels of ketones, specifically Betahydroxybutyrate (BHB) (Bostock et al., 2017; Gumus et al., 2022). In humans, participants (N=16) with Parkinson's disease following a ketogenic diet for 12 weeks and reported statistically significant reductions in the symptoms of anxiety as measured by the Parkinson's Anxiety Scale (PAS) (Tidman et al., 2022). The ketogenic and low carbohydrate dietary interventions may also show a reduction in the symptoms of anxiety for populations outside of Parkinson's disease.

Stress

It is difficult for those under stress to follow healthy behaviours (Griffin et al., 1993). However, the initiation of low carbohydrate and ketogenic diets have been seen to reduce anxiety by producing anxiolytic effects, calming the brain in a way (Włodarczyk et al., 2020). A ketogenic diet has also been shown to reduce levels of stress in rodents (Brownlow et al., 2017). By measuring stress in this study, it will be identified whether a low carbohydrate diet and ketogenic diet may produce the same outcomes in a human sample.

In summary, this study will explore whether depressive symptom levels change depending on which dietary intervention is followed. As this study uses both a low carbohydrate and more restrictive ketogenic diet, perhaps an improvement in mental well-being, symptoms of anxiety and stress as well as affect will also be found.

2.1.5 Aims and hypotheses

Through a double-blind randomised control trial design, this study will investigate the idea that the ketogenic diet may alleviate depressive symptoms and improve psychological well-being in both healthy adults and those with depressive symptoms compared to controls. This study will compare psychological well-being outcomes following a KD intervention, a LCD intervention, and a wait list control group. Outcome variables as discussed above - stress, anxiety, depressive symptoms, affect and mental well-being - will be measured.

It is expected that those that follow both the KD, and LCD will show greater improvements overall compared with the wait list control group in both the healthy adults and depressive symptoms groups.

Although this study will not examine the specific biological mechanisms linking changes in ketone levels to psychological well-being, it is also proposed that the KD will have a positive impact on core psychological states. Participants in both healthy and depressive symptoms groups that are following a KD may show greater improvements in their psychological well-being measures compared with the LCD possibly due to the presence of ketones bodies or other mechanisms specific to the state of ketosis in the ketogenic diet.

There are three main hypotheses for this study.

- Lowering carbohydrate intake to initiate ketosis will improve psychological well-being in people with mild to moderate symptoms of depression.
- Lowering carbohydrate intake without initiating ketosis will improve psychological well-being in people with mild to moderate symptoms of depression.
- The ketogenic diet will show greater improvements in psychological well-being in those with mild to moderate depressive symptoms compared with a low carbohydrate diet. The ketogenic diet will have a greater impact because of the ketones that are produced which are not present in the low carbohydrate diet.

2.2 Method

2.2.1 Design

This study was a 2x3x4 quantitative, double blind randomised control trial with quasi experimental mixed design elements. It was not a full experimental design as the researcher was not in control of which psych health group participants were allocated to (e.g., depressive symptoms group or healthy group). Participants were allocated to a psych health group based on their responses to the baseline Patient Health Questionnaire (PHQ-9) measure.

The between group factors in this study were initial mental health status or psych health (healthy and depressive symptoms conditions) and diet type group (Ketogenic Diet (KD), Low Carbohydrate Diet (LCD) and Control). The within groups factor was time, with the online intervention lasting for a total of 12 weeks for the LCD and KD groups followed by 12 weeks without intervention, and a total of six weeks for the wait list control group. Participants in all groups were blind to this allocation. Wait list control group participants were told that recruitment was ongoing and that they would start the intervention once recruitment was complete. This was set at six weeks to reduce the severity of drop out if they were asked to wait any longer. Data was collected at baseline as screening (T0), day 1 – beginning of intervention (T1), six weeks – end of wait list control group participation (T2), 12 weeks – end of the online intervention (T3), and 24 weeks – end of study (T4).

Variables and Time points Measured

Table 2.1: Variables and when they were measured

Variable	*Time point Measured*
Age	T0
Location	T0
Body Mass Index (BMI)	T0
Diabetic Status	T0
Physical Health Status	T0
Pregnancy Status	T0
History of Recent Weight Loss	T0
History of Using a Low Carbohydrate Diet	T0
Partaking in Trial Status	T0
Depression Diagnosis Status	T0
Mental Health Diagnosis Status	T0
Severe Depression - High Risk Status	T0
Regular Medication Status	T0
Anti-depressant Medication Status	T0
Gender	T0
Height	T0
Level of Education	T0
Ethnicity	T0
Waist	T0, T1, T2, T3
Weight	T0, T1, T2, T3
Patient Health Questionnaire (PHQ-9)	T0
Berlin Social Support Scale (BSSS)	T1
Body Appreciation Scale (BAS-2)	T1
Perceived Stress Scale (PSS)	T1, T2, T3, T4
Positive and Negative Affect Scale (PANAS)	T1, T2, T3, T4
Warwick Edinburgh Mental Well-being Scale (WEMWBS-S)	T1, T2, T3, T4
Generalised Anxiety Disorder (GAD-7)	T1, T2, T3, T4
Centre for Epidemiological Studies Depression (CESD)	T1, T2, T3, T4
Self-Compassion Scale (SCS-SF)	T1, T2, T3, T4

All variables were measured through online questionnaires. They were sent via email from Diabetes.co.uk (DCUK) to each participant when they reached each time point until the end of the study at 24 weeks.

2.2.2 Participants

Collaborators – Diabetes Digital Media Ltd.

Since 2007, Diabetes Digital Media Ltd. (DDM) have been providing health platforms and patient-support networks online through Diabetes.co.uk (DCUK). DCUK is one of the health platforms created by DDM and it is currently the largest online community for type 2 diabetes (T2D) and health management in the world (About Us - DCUK, n.d.). It is the world's most active online support forum with over 1.8m members. At the time of collaboration, there were 600,000 members. DDM and DCUK do not receive any external funding and they make profits through advertising on their website for diabetes related products. The platform DCUK reinvests all profits earned into improving current educational programs and developing new courses and interactive tools for the international community.

Rationale for Using This Platform

DCUK provide a user-friendly online forum and educational interactive app so that individuals can track their daily food intake, mood, and other biomarkers such as weight and waist measurements. Biological markers such as ketone levels can also be measured for those on the KD. Individuals can also engage

with other members of the community from their phone, iPad, or laptop. This provides the individual with a support network anywhere, at any time.

This platform was chosen for this program of research because to the researcher's knowledge at the time of proposal, this was the only online health platform that provided education and dietary intervention programs to the public that included a strong support network in the UK.

Recruitment

For this study, 5070 participants were recruited and clicked on the study link to begin the screening questionnaire (see Figure 2.1). Of these, 2491 completed the screening questionnaire at baseline (T0) and 1074 were eligible to take part (see Table 2.2). These participants were randomly assigned to a diet intervention. Interventions in this study were the Ketogenic diet program (KD) and the Low Carbohydrate Diet program (LCD). There was also a group named 'wait list control'. The wait list control group served as a control group for the purpose of this study.

To recruit participants, an incentive of two years free membership, worth £139 to DCUK online digital health resources was promoted on recruitment posters. Potential participants were told that the study involved following a set amount of carbohydrates each day for 12 weeks and completing some questionnaires throughout the study (see Appendices K to O).

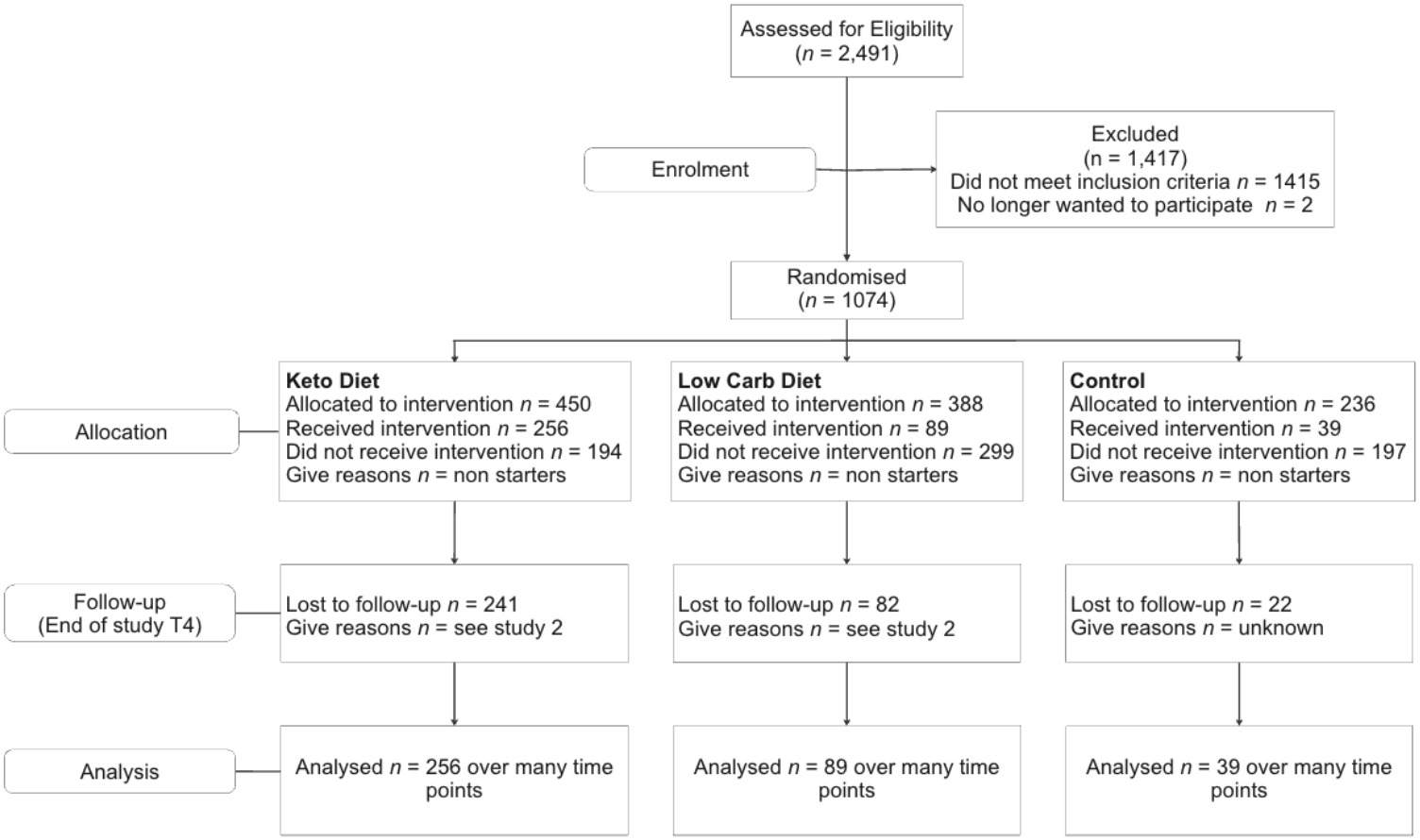

Figure 2.1: CONSORT flow diagram of recruitment, allocation, follow-up and analysis of all participants, and their groups

Participants were recruited through Diabetes.co.uk's online network, online forums, and the DCUK online community. Those who had signed up to DCUK's network or programs independently were sent information about the study and invited to sign up with the incentive if interested. The study was also promoted in their weekly newsletter and emails were sent to all subscribed individuals. Though the inclusion criteria stated that participant's must be non-diabetic to take part (see Table 2.3), the number of potential participants that could be contacted directly from DCUK was vast, and consisted of those with all types of diabetes, but also those without. Individuals on the DCUK email list were also aware of the company, and of the online program which may have made it easier to recruit even non-diabetic participants for this research.

Further recruitment was carried out via social media (Twitter, Instagram, and Facebook) using recruitment posters specifically for the study (see Appendix G). Recruitment columns were added to the newsletters of for-profit and not-for-profit organisations such as Ketosource (www.ketosource.co) and the Public Health Collaboration UK (www.phcuk.org).

Sample Size

For this study, the researcher aimed to recruit as many participants as possible within the timeframe. Previous research in this area was limited with sample sizes varying from N=31 (Meckling et al., 2004) to N=132 (Samaha et al., 2003). A higher recruited sample would allow for assumed attrition rates.

A total of 1074 participants were entered into the study and sent the questionnaire at time point 1 (T1), see Table 2.2.

Table 2.2: Breakdown of participants in each diet type and psych health condition

Diet Type Group	*Psych Health Condition*	*T1*
Ketogenic	Healthy	301
	Depressive Symptoms	149
Low Carbohydrate	Healthy	267
	Depressive Symptoms	121
Control	Healthy	170
	Depressive Symptoms	66
Total		1074

Of the 1074 participants eligible to take part in the study, the final sample consisted of 414 participants overall. A total of 384 participants completed a time point.

Screening and Inclusion Criteria

The baseline screening questionnaire (T0) assessed eligibility for the current research program, by addressing the inclusion and exclusion criteria, seen in Table 2.3.

Those who were found to be eligible were then divided into 'healthy' and 'depressive symptoms' based on their score from the PHQ-9 which was presented at the end of the screening questionnaire. A score of less than 20 allocated participants to the healthy group and a score of 20 or more, allocated participants to the depressive symptoms group. All participants were then randomly assigned by a team member at DCUK via an algorithm to one of three groups, the low carbohydrate diet group, the ketogenic diet group, or the wait list control group.

Table 2.3: Criteria of inclusion and exclusion for eligibility

Criteria	*Included*	*Excluded*
Age	19-65	<19, >65
Location	UK	Outside the UK
Body Mass Index (BMI)	>18.5kg/m^2	<18.5kg/m^2
Diabetic Status	Non-Diabetic	Pre-Diabetic, T1D, T2D
Physical Health Status	No Physical Health Issues	Physical Health Issues
Pregnancy Status	Not pregnant and no plans in next six months	Pregnant or planning pregnancy in next six months
History of Recent Weight Loss	Less than two stone	Two stone or more
History of Using a Low Carbohydrate or Ketogenic Diet in last two years	No History	History
Partaking in Trial Status	Not currently partaking in trial on diet or exercise	Partaking in other trial on diet or exercise
Mental Health Diagnosis Status	Depression and anxiety only	Any other mental health diagnosis
Severe Depression - High Risk Status Question 'Recently have you had thoughts that you would be better off dead or of hurting yourself in some way?'	Answered 'No'	Answered 'Yes' and referred to mental health support services
Antidepressant Medication Status	Taking Antidepressants for more than three weeks	Taking Antidepressants for less than three weeks
Patient Health Questionnaire (PHQ-9)	Scores of less than 20	Scores of 20 or greater

Severe mental health issues were controlled for by including a question that identified whether someone did or did not have the mental capacity to take part. Those without capacity were excluded from taking part.

The researcher also excluded those whose scores suggest that they may have severe depression. Participants were identified through the scoring of the PHQ-9. Scores of 20 or above represent severe depression and therefore posed a high risk for taking part in the study. There were three potential participants identified during the recruitment phase who met this criterion. These participants were provided with the details of external mental health crisis helplines that they could contact if they felt necessary. They were thanked for their interest and time in completing the questionnaire.

Table 2.4: Breakdown of participants recruited, eligible, started and completed part of the study

Status	*No. of Participants*	*%*	*Explanation*
Recruited	5070	100	Total
Completed Screening Questionnaire	2491	49.13	% Completed of total recruited
Eligible and Sent T1	1074	43.12	% Eligible of completed screening
Completed a Time point	384	35.75	% Completed a Time point

Study Attrition

Table 2.5: Breakdown of number of participants in each diet type and psych health condition who completed a questionnaire at each time point through until the end of the study at T4

Diet Type Group	*Psych Health Condition*	*Completed T1*	*Completed T2*	*Completed T3*	*Completed T4*
Ketogenic	Healthy	177	39	12	9
	Depressive Symptoms	76	14	6	6
Low Carb	Healthy	57	15	10	5
	Depressive Symptoms	29	3	1	2
Control	Healthy	18	11	-	-
	Depressive Symptoms	13	6	-	-
Total		370	88	29	22

Of the 384 participants who completed a time point there were 324 females (84.4%) and 56 males (14.6%). Age ranged from 19 to 65 years (M= 48 years, SD = 9.02). Three hundred and thirty-two participants (85.7%) identified as white ethnicity and 242 (63%) had completed an undergraduate degree or higher. Weight measurements ranged from 48kg to 141kg with a mean weight of 83.6kg (SD=16.12). With regards to psychological health, 50 participants (13%) said they had received a diagnosis of depression or anxiety, of which 38 (76% of 50 participants) said they were taking antidepressant medication. The most common antidepressants being taken by participants were Sertraline, N=15 (39.5%) and Fluoxetine, N=10 (26.3%). These participants were kept in the study as they had been taking antidepressants for more than three weeks and therefore considered stable. This may have impacted research outcomes and is discussed later in section 2.4.5.

For the mental health factor, participant groups were defined by scores on the Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001), which measures the severity of experienced depressive symptoms. Those with little or no depressive symptoms (<5 on the PHQ-9) were included as the 'healthy adults' sample (N=263) and those with mild to moderate depressive symptoms (5-19 on the PHQ-9) were included as the 'depressive symptoms' sample (N=121). The group was termed ‘depressive symptoms’ for the purposes of the study method - but this was not communicated to the participants at any point.

Participants were allocated to either the KD (N=256), or LCD (N=89) diet group for 12 weeks or the wait list control group (N=39), for six weeks. For the wait list control participants, they were told that they had been accepted to the program, but that they had to wait a few more weeks until recruitment was complete before they could start the study. Participants were asked to continue their diet as normal while they waited, to use the online program platform where they could set up an online profile and begin to track their food and other health markers. They were also asked to complete the questionnaires that were emailed to them over the waiting period. They did not have access to the educational videos or the full program until six weeks had passed and they completed their final questionnaire for the study at T2. Once they had completed their time as a wait list control participant, they were debriefed on the whole study and were granted free access via the use of a voucher code to a diet program of their choice, separate to this study.

The KD and LCD interventions were identical, aside from the amount of carbohydrates they were encouraged to follow. Participants were randomly

assigned by a team member at DCUK to keep the allocation blind for the researcher. All participants were blinded as to which group, they were allocated to.

It was possible to keep the group allocation blind from the participants as they were not informed of the primary aims of the study in the information sheet. They were told that the purpose of the study was to learn about how diet affects mood (see Appendix I). It was explained to them that they would be following a diet that reduced the amount of carbohydrates they ate to a set daily amount. They were not informed of this amount until they had been allocated to an intervention and had started the program and educational videos. They were not informed that there were two intervention groups with varying carbohydrate allowances, nor that one would create a state of nutritional ketosis in most cases, while the other would not for most people. Over the duration of the study, it may have become apparent to the participant what diet they had been asked to follow, but it was not explicitly explained to them until after the study was complete. It was not possible to objectively assess if ketosis had been achieved.

2.2.3 Materials and measures

DCUK - Low Carb Program

Through the DCUK health platform for T2D there are a range of educational programs available. Individuals are educated on their illness and learn how to personalise their diet and lifestyle with the aim of reducing their symptoms and improving their health outcomes. These programs are designed to work alongside conventional care provided by primary health physicians, overall improving the rate of remission T2D (Summers et al., 2021).

The most popular program available through the DCUK platform is the Low Carb Program. This is a 10-week online education program aimed at those with T2D. It provides individuals with the tools to make lifestyle changes mainly through a dietary approach.

The NHS has approved the safety of this program (*Commission the NHS-Approved Low Carb Program*, n.d.). Healthcare teams and General Practitioners can prescribe the Low Carb Program to patients through the NHS and give their patients the choice of long term medications or lifestyle intervention. The Low Carb Program app is featured in the list of online tools approved by NHS Digital.

Interestingly, the Low Carb Program is not only for those with T2D, though this was the initial intended audience. Anyone can join the Low Carb Program if they wish to learn how to improve their health through lifestyle change. As of February 2022, a total of 466,000 members have completed the Low Carb Program, 30% of which do not have T2D. The Low Carb Program has shown to be of benefit to both those with T2D, as well as those with polycystic ovarian syndrome, non-alcoholic fatty liver disease, prediabetes, and obesity (*Low Carb Program - Sustainable Weight Loss and Blood Glucose Control*, n.d.).

Intervention Design

The two intervention programs used in this research study, KD, and LCD, were both adapted versions of the current Low Carb Program from DCUK. Although the Low Carb Program was initially developed for those with T2D, the LCD and KD interventions were adapted for the study and references to T2D were

removed from the programs where possible. The researcher worked with DCUK to adapt the programs to suit the research study.

The interventions for both diet groups were run online through the DCUK platform and included dietary recommendations, educational videos, methods to track progress and supportive forums run by the DCUK community. Moderators were present in the online forums. These individuals moderated the frequencies of certain keywords and any references to the research. These moderators made sure that questions from participants were answered and followed up.

Low Carb Intervention

The standard DCUK Low Carb Program is ten weeks long. The adapted Low Carb Program was increased to 12 weeks to fall in line with current research interventions (Mcswiney et al., 2017). Information around managing T2D and terminology of the illness such as 'HBA1C' or 'Ketoacidosis' were removed from the current program so the focus remained on the diet change itself. This change was necessary to not confuse participants with information that was not directly relevant to them and the study. The program educated participants on how to eat protein and fat rich foods and how to reduce their carbohydrate intake to the levels recommended for each dietary intervention. This was carried out using weekly educational videos and pop-up interactions through the participants program profile.

Ketogenic Intervention

Like the adapted LCD, the KD was created to be 12 weeks long. All information surrounding the management of T2D, as well as popular terminology of the illness were removed from the program. The main difference between the two programs, LCD and KD, were that the KD included videos on reducing total daily carbohydrates further than the LCD to initiate a state of ketosis. These videos were filmed by DCUK with direction from the researcher. The KD was later made available to the public in late 2019 via their 'Gro' app.

Diet Composition

The diet compositions in this study were as follows. Neither diets were calorie restricted, nor were they isocaloric or calorie matched. Participants were asked to eat ad libitum or until fully satiated, regardless of which program they followed, the KD or the LCD. This is standard for the DCUK programs. This reduced the possibility of participants consciously maintaining a calorie deficit which would result in weight loss. If participants had consciously lost weight, it may have biased the results of the study by increasing the chances of improving mood. It is also important to note that there is the possibility that participants with low daily carbohydrate intake, in a state of ketosis, may have experienced reduced appetite from the presence of ketones. Therefore, they may have eaten less overall as a result. This is normal, and to be expected. This may have caused weight loss unintentionally, most notably in the KD. This was considered when designing the study and weight measurements were collected at time point T0, T1, T2 and T3.

Psychological Measures

The eight dependent variables measured through valid psychometric scales repeatedly over this study were, stress (PSS), generalised anxiety (GAD), depressive symptoms (CESD), mental well-being (WEMWBS), positive and negative affect (PANAS) and self-compassion (SCS). Self-compassion is analysed and discussed in more detail in Chapter 3.

Social support (BSSS), and body appreciation (BAS) were measured at time point 1 (T1) only and discussed in more detail in Chapter 3. Depression (PHQ-9) was measured at baseline (T0) only and used as a screening test.

Variables and Measures

Table 2.6: Variables and Measures for Study 1

Variable	*Measure*
Depression Scores at screening (T0) only	Patient Health Questionnaire (PHQ-9)(Kroenke et al., 2001)
Affect	Positive and Negative Affect Scale (PANAS)(Watson et al., 1988)
Mental Well-being	Warwick Edinburgh Mental Well-Being Scale (WEMWBS)(Tennant et al., 2007)
Generalised Anxiety	Generalised Anxiety Disorder – 7 (GAD-7)(Spitzer et al., 2006)
Depressive Symptoms	Centre for Epidemiological Studies Depression Scale (CES-D)(Radloff, 1977)
Stress	Perceived Stress Scale (PSS)(Cohen et al., 1983)

Demographic Questions

Questions included in the baseline questionnaire were age, gender, waist (cm), weight (kg), height (cm), Body Mass Index (BMI), highest level of education, and ethnicity.

Waist (cm) and weight (kg) were measured again at time points T1-T3. This involved the participants measuring their weight at the same time each week and tracking it in their personal profiles online. Participants then submitted their current weight when completing the questionnaires at each time point.

Depression – Patient Health Questionnaire (PHQ-9)

The Patient Health Questionnaire (PHQ9) has been used across fields of research from coronary heart disease (Haddad et al., 2013) to post stroke depression (de Man-van Ginkel et al., 2012). This scale was chosen as it measures depressive symptoms, the severity of current depression and it can be used as a provisional diagnosis tool to be followed up by a formal process (Wittkampf, 2010).

A short, self-administered, nine item scale, the Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001), taken from the full PHQ was designed to screen patients with possible major depressive episodes (Wittkampf et al., 2007). In this study it was used to determine which psych health condition participants were allocated to. This measure was used in the baseline screening questionnaire at T0 only.

Each item of the PHQ-9 is scored on a Likert scale of 0-3 (0=not at all; 1=several days; 2=more than a week; 3=nearly every day). The scale looks at each of the nine criteria measured by the DSM-IV for depressive disorders. It asks

participants, how often they have been bothered by certain things over the past two weeks. Example items are 'Feeling down, depressed, or hopeless', and 'Little interest or pleasure in doing things'.

Scores of less than five are indicative of few, mild or no depressive symptoms. Scores from five to 19 represent moderate and moderately severe depression. Scores of 20 and above represent severe depression. For this study, those who scored less than five were allocated to the 'healthy adults' psych health condition and those with a score of five to 19 were allocated to the 'depressive symptoms' psych health condition. Those who scored 20 or above were excluded from taking part in the study due to their higher risk of depressive episodes (see section 2.2.2 for screening and inclusion criteria).

PHQ-9 reliability and consistency are good, Cronbach's α = .892 (Sun et al., 2020), and its validity has been proven in many studies (Martin et al., 2006; Wittkampf et al., 2007). The internal reliability and consistency of the 9-item PHQ-9 in the present study was good, Cronbach's α = .844.

This scale was included to be used as a screening tool for depressive symptoms in this study. The grouping and cut off feature of the outcomes of this scale was better suited for participants compared to using a measure that produces a scale outcome with varying depression scores. By grouping participants in this way and following the cut off marks, it was easier to allocate participants to interventions.

Affect – Positive and Negative Affect Schedule (PANAS)

This scale was chosen as it is the most widely used scale to measure changes in mood and emotion (Tran, 2013). This scale is a 20-item, self-administered report of positive and negative affect which was developed by Watson et al. (1988). The measure was used across all time point questionnaires (T1-T4) apart from baseline (T0).

Each item is scored on a 5-point Likert scale from very slightly or not at all to extremely (1=very slightly or not at all; 2=a little; 3=moderately; 4=quite a bit; 5=extremely). Participants are asked to choose how often they have felt in such a way over the past week. Example items are 'Irritable' and 'Attentive' (Watson et al., 1988). To calculate the positive affect score, responses on positive items were summed. Scores ranged from 10-50 with higher scores indicating higher levels of positive affect. To calculate the negative affect score, responses on negative items were summed. Scores ranged from 10-50 with lower scores indicating lower levels of negative affect.

Reliability, consistency, and validity have been demonstrated to be of good level Cronbach's α = >.860 for PANAS-POS and Cronbach's α = >.870 for PANAS-NEG (Watson et al., 1988). The internal reliability and consistency of the 20-item PANAS in the present study was acceptable, Cronbach's α = .715.

Separate indices of reliability were obtained for positive and negative subscales with values higher for each, positive affect = .928, and negative affect = .875.

Mental Well-being – Warwick Edinburgh Mental Well-being Scale – Short (WEMWBS-S)

This scale was chosen as it measures positive thoughts and feelings as well as functioning aspects of mental well-being. This short scale 7-item, self-administered report of Mental Well-being was developed by Tennant et al. (2007). The measure was used across all time point questionnaires (T1-T4) apart from baseline (T0).

Each item is scored on a 5-point Likert scale from none of the time to all of the time (1=none of the time; 2=rarely; 3=some of the time; 4=often; 5=all of the time). Participants are asked to choose the response to statements about feelings and thoughts that best describes their experience over the previous two weeks. Example items are 'I've been feeling close to other people' and 'I've been feeling optimistic about the future' (Tennant et al., 2007). Response scores were summed to create a total score. These total raw scores were then transformed using a conversion table into metric scores. Cut off scores for higher positive mental well-being were 27.5 and lower mental well-being were 19.5.

Reliability, consistency, and validity have been demonstrated to be of an excellent level, Cronbach's α = .910 (Tennant et al., 2007). The internal reliability and consistency of the 7-item WEMWBS in the present study was good, Cronbach's α = .887.

Generalised Anxiety – Generalised Anxiety Disorder (GAD-7)

This scale was chosen as it is quick to administer to individuals. It assesses the severity of generalised anxiety and is also used as a screening tool for the

disorder. The GAD-7 has assessed the severity of anxiety symptoms in research on the ketogenic diet for the treatment of post-concussion syndrome (Rippee et al., 2020) and in research on a low carbohydrate, ketogenic diet (50g daily carbohydrates confirmed urinary ketones) in overweight young women (Hu et al., 2022). The GAD-7 has also been used to measure anxiety in areas such as primary care (Ruiz et al., 2011) as well as the general population (Löwe et al., 2008). This 7-item, self-administered report of Generalised Anxiety Disorder was developed by Spitzer et al. (2006). The measure was used across all time point questionnaires (T1-T4) apart from baseline (T0). Each item is scored on a 4-point Likert scale from not at all to nearly every day (0=not at all; 1=several days; 2=more than half the days; 3=nearly every day).

The questions ask participants how often they have been bothered by the following problems in the past two weeks. Example items are 'feeling nervous, anxious or on edge?' and 'not being able to stop or control worrying?' (Spitzer et al., 2006). Response scores were summed to give a total score out of 21. Cut off scores of 5 indicated mild anxiety, 10 indicated moderate anxiety and 15 indicated severe anxiety.

Reliability, consistency, and validity have been demonstrated to be of a good level, Cronbach's α = >.800 (Spitzer et al., 2006). The internal reliability and consistency of the 7-item GAD in the present study was good, Cronbach's α = .888.

Depressive Symptoms – Centre for Epidemiological Studies (CES-D)

This scale was chosen as it is used frequently in research and is one of the only self-reporting depression scales. This scale is a 20-item, self-administered report of depressive symptoms which was developed by Radloff (1977). The measure was used across all time point questionnaires (T1-T4) apart from baseline (T0). Each item is scored on a 4-point Likert scale from rarely or none of the time to most or almost all of the time (0=rarely or none of the time; 1=some or little of the time; 2=moderately or much of the time; 3=most or almost all of the time).

Participants are asked to choose how often they have experienced characteristics of depression, such as poor appetite, over the past week. Example items are 'I was bothered by things that usually don't bother me' and 'I thought my life had been a failure' (Radloff, 1977). Positive response items were reversed, and responses were summed to create a total score. Scores range from 0-60. Cut of scores of 16 or higher indicate those at risk for clinical depression. Higher scores indicate higher levels of depressive symptoms. Reliability, consistency, and validity have been demonstrated to be of a good level Cronbach's α = >.800 (Radloff, 1977). The internal reliability and consistency of the 20-item CES-D in the present study was excellent, Cronbach's α = .922.

The researcher was unable to use the more popular and widely used depression severity scale "Beck's Depression inventory (BDI)" (Beck, 1961). This is because a fee must be paid for each copy used as it is a copyrighted measure.

Stress – Perceived Stress Scale (PSS)

This scale was chosen as it is the most widely used scale to measure perceived stress amongst adults. Perceived Stress using the PSS has been measured across many fields in research from graduate nursing students (Stillwell et al., 2017) to dementia patients and their caregivers (Deeken et al., 2018). This 10-item, self-administered report of Perceived Stress was developed by Cohen et al. (1983a). This measure was used across all time point questionnaires (T1-T4) apart from baseline (T0).

This scale measures how stressful participants find different aspects of their life. It measures feelings and thoughts over the past month. Each item is scored on a 5-point Likert scale from never to very often (0=never; 1=almost never; 2=sometimes; 3=fairly often; 4=very often). The questions ask participants about their feelings and thoughts during the last month. It asks them to indicate how often they felt or thought a certain way using the 5-point scale. Example items are 'how often have you felt nervous and stressed?' and 'how often have you found that you could not cope with all the things that you had to do?' (Cohen et al., 1983).

Scores were reversed for four items, questions 4, 5, 7, and 8. Then all responses were summed to give a total score. Total scores on the PSS can range from 0-40. Higher stress total scores indicate higher perceived stress levels in participants. Reliability, consistency, and validity have been demonstrated to be of good level, Cronbach's α = >.800 (Cohen et al., 1983). The internal reliability and consistency of the 10-item PSS in the present study was good, Cronbach's α = .882.

Other Measures

At the end of each questionnaire at each time point there were six to fifteen additional questions covering the participants experience of the study and intervention so far. These were a mix of quantitative and qualitative questions. For the quantitative questions, all were answered with a Likert scale (see Appendices K to O). For example, 'In general, how would you say your health has been in the past month?' on a scale from fair to excellent (1-5) and 'Following this way of eating for me has been:' on a scale from not difficult at all to extremely difficult (1-5). For the qualitative questions, participants were asked to add further comments at each time point. They were also asked about possible improvements (T1-T3), their likes and dislikes of the diets (T2-T3), to expand on responses if they wished (T2-T4) and if they would be interested in discussing their experience of the dietary intervention with the researcher (T3).

Data Protection

The online survey software Qualtrics was used to present all questionnaires for both the screening at baseline (T0) and at each time point (T1-T4). Each set of questionnaires for each time point were integrated with the DCUK online programs. A private Excel spreadsheet was shared from DCUK with the researcher. This included a unique numerical ID for each participant, their total score from the PHQ-9, and the diet and psych health groups in which they would be allocated to.

Completed questionnaires were downloaded securely and directly from Qualtrics intermittently over the course of the program. The Qualtrics software is GDPR compliant. The following information about online data protection and security

was provided to all participants in the information sheet prior to initiating the study.

"The online version of these questionnaires have been constructed as anonymous surveys using Qualtrics, meaning no emails, IP addresses and/or geolocation data will be identified in the responses. HTTPS survey links (also known as secure survey links) have been used, giving Secure Sockets Layer (SSL) Encryption while a questionnaire is being completed. During the study data collected online will be stored on an EU-based server and will be subject to EU Data Protection acts. All online data will be destroyed following completion of data collection".

2.2.4 Procedure

Baseline Questionnaire (T0)

Once participants had been recruited, they were sent the information sheet and consent form to complete. After agreeing to take part, all participants (N=2491) were asked to fill out their first online questionnaire (T0). The questionnaire was accessed through the URL: www.DCUK/CARBS. The first questionnaire collected baseline information such as demographics, assessed eligibility for the study and determined which psych health condition the participant would be allocated to (see Appendix K). The DCUK team allocated participants who completed T0 and were eligible to take part into their respective groups based on their responses (N=1074). Participants were then emailed by the DCUK team with a unique code that granted them access to their allocated online intervention.

Beginning of the Intervention (T1)

Day 1 (T1) of the study began once eligible participants logged into their online profile and accessed their program. They were then emailed their first time point questionnaire (T1) which was accessed in the same way as the baseline questionnaire (see Appendix K). Once this questionnaire was complete (N=370 completed), the participants journey through the study was either on the KD, the LCD or as a wait list control. During the study, all intervention participants (KD and LCD) watched the educational videos and learnt how to apply the dietary interventions to their lifestyle. They purchased their own food and prepared meals and snacks in line with the recommendations of their intervention.

End of Wait List Control (T2), Intervention (T3), and Study (T4)

Participants were then emailed a questionnaire at six weeks (T2) (see Appendix M). This marked the end of the wait list control groups participation in the research, as well as the halfway mark of the dietary interventions (N=118 completed). A questionnaire was sent out to all intervention participants at the end of the online intervention at 12 weeks (T3) (N=29 completed), and again at the end of the study at 24 weeks (T4) (N=22 completed) (see Appendices N and O). Email and profile prompts were intermittently sent throughout the study by the DCUK team to participants who had clicked on a questionnaire but not completed it. This kept the study blind to the researcher.

Ethical Considerations

Ethical approval was granted from DCUK for all studies in this program of research. Ethical approval from the University of East London was granted. As issues arose, ethical amendments were submitted and approved throughout the duration of the research (see Appendices A to E).

Participant Information, Consent and Debrief

Contact details for DCUK were provided on the information sheet (see Appendix I) at the start of the study for all participants. All participants were given a letter that they were advised to take to their consulting doctor prior to signing up for the study (see Appendix H). Evidence of this was not collected but was the participants own responsibility to notify their doctor. Participants were encouraged to discuss the study with their doctor, contact DCUK or the researcher with any questions about the study prior to taking part. Information on the study was provided. Participants were informed that they may experience mild short term side effects during the first few weeks of the intervention. For example, side effects may include:

- Flu like symptoms (Headache, Lethargy)
- Changes in bowel habits
- Leg cramps
- Bad breath
- Loss of energy

It was explained to all participants that they could withdraw their personal data from the research at any time up to two weeks after the completion of the study without needing an explanation. A consent form was then attached to the

information sheet (see Appendix J). Participants stated that they agreed with the terms of the research before they gave their consent to taking part in the study. A debrief sheet was sent to all participants at the end of the study (see Appendix P). It stated what the study comprised of, and the reasons behind the research. Further reading was also provided.

2.2.5 Analysis

The study looked to see if outcomes differed depending on which group the participants were in. The study looked for differences rather than associations. This study tested the differences in eventual outcomes using a combination of Analysis of Variances (ANOVAs). The alpha was set at 0.05 but in cases that were nearing significance, trends were identified, and main effects were dismantled looking at the linear and quadratic components of the ANOVA. The ANOVA was used when data conformed to parametric requirements as well as when it did not conform as it can tolerate violations of normality relatively well (Blanca et al., 2017).

Data Cleaning

A total of five datasets were cleaned before being merged (T0, T1, T2, T3 and T4). Data was scored and coded, and duplicates were identified and removed. New variables were created where necessary to best answer the research questions. Reliability tests, descriptive statistics, and tests for normality, skewness and kurtosis were run on all measures across all timeframes. Participants were then matched across the datasets using a unique ID. Pivot tables were created to understand how many participants completed each questionnaire of the study and their percentage completion.

Based on the questionnaire structure, it was decided that all participants who had completed 17% or less of any questionnaires, would be excluded as part of that time point dataset. This is because they had not provided enough data for analysis. 17% completion allowed for at least one full psychological measure to be analysed. A full list of duplicate numbers, exclusion numbers and reasons were produced. Once the data was cleaned and scored, it was inputted to SPSS ready for statistical analysis. To answer the research questions of this study, a series of statistical tests were carried out.

Missing Values

The data was scrutinised, and missing variables were identified. The data was analysed and any data that looked incorrect was removed and replaced with a missing value ('999'). For example, some weight measurements appeared incorrect and inconsistent with previous measurements and were therefore removed. People had entered their height instead of their weight and their weight instead of their waist. Where it was clear that this had occurred, the data was switched to the correct variable. In other cases, if not obvious, the data was removed and replaced with a missing value.

The data for each psychological measure was analysed. Missing responses were dealt with by calculating the mean of the rest of the measure. The missing value was then replaced with this. These missing value calculations were carried out across the datasets (see section 2.3). Once the full dataset was scored and totals calculated and all that remained was numerical data, the data was imported into SPSS V27 for analysis.

SPSS

Once the full dataset was imported to SPSS, variables were renamed, labels were given, and missing values identified as '999'. Values were added for each variable and identified as ordinal, scale or nominal data. Reliability tests were run on each of the psychological measures to confirm levels of reliability. Quantitative data analysis using parametric and non-parametric tests were carried out as appropriate, including mixed ANOVAs. In some cases, homogeneity was not met, and the data was not normally distributed. ANOVAs were still carried out on the data. In this study there were issues with drop out. To fully understand the data, there is a breakdown within the analysis of the variables. Some analysis shows all four time points, with other subsequent analysis showing subsets of time points. The researcher has referred to this statement in the results section where relevant.

2.3 Results

2.3.1 Overview and rationale for proposed analysis

Table 2.5 Repeated: Breakdown of number of participants in each diet type and psych health condition who completed a questionnaire at each time point through until the end of the study at T4

Diet Type Group	*Psych Health Condition*	*Completed T1*	*Completed T2*	*Completed T3*	*Completed T4*
Keto	Healthy	177	39	12	9
	Depressive Symptoms	76	14	6	6
Low Carb	Healthy	57	15	10	5
	Depressive Symptoms	29	3	1	2
Control	Healthy	18	11	-	-
	Depressive Symptoms	13	6	-	-
Total		370	88	29	22

Due to high attrition rates in study 1, participants dropped out at different time points across the study making it challenging to analyse the data as one dataset from T1-T4. A total of 370 participants completed T1, with 384 completing a questionnaire at a time point, and in the end 22 participants remained (see Table 2.5). This is much lower than those who completed fewer time points or who completed time points earlier in the study. Therefore, it is justified to take a closer look at other time points in more detail.

Combinations of time points were analysed separately to identify if any were significant. In the following results section, each psychological well-being dependent variable will be presented with six versions of each analysis.

1. Time points 1 → Time point 2 (KD, LCD and Controls)
2. Time points 1 → Time point 2 (KD and LCD only)
3. Time points 2 → Time point 3 (KD and LCD only)
4. Time points 3 → Time point 4 (KD and LCD only)
5. Time points 1 → Time point 2 → Time point 3 (KD and LCD only)
6. All time points: Time point 1 → Time point 2 → Time point 3 → Time point 4 (KD and LCD only)

Scores from psychological measures were subjected to a three-way mixed analysis of variance (ANOVA), with one within measure (time) and two between participants variables (diet type and psych health). Levene's test confirmed that the assumption of homogeneity of variance was met for all time points (all $p>.05$) except where indicated in the following individual sections.

For each psychological well-being dependent variable, the means, standard deviations, and number of participants are presented in an initial overview table which includes healthy and depressive symptom participants (and totals for the cohort), in both the ketogenic and low carbohydrate conditions across all time points, T1, T2, T3 and T4 (e.g., see Table 2.8).

The control conditions are not included in this overview table, but details of this condition can be found in the first version of the analysis of each variable (e.g., see Table 2.9).

2.3.2 Demographics and characteristics

Table 2.7: Demographic and characteristics table of all participants, KD, LCD, and controls at baseline (T0)

Variable	*Items*	*Total (%)*
		(*n* = 384)
Gender	Male	56 (14.6%)
	Female	324 (84.4%)
	Non-binary, Transgender, No gender, Other	0 (0%)
Age (years)		M = 48.5 (SD = 9.01)
Waist (cm)		M = 92.85cm (SD = 13.36)
Weight (kg)		M = 83.59kg (SD = 16.17)
Height (cm)		M = 166.23cm (SD = 8.07)
BMI		M = 30.44 (SD = 5.50)
Highest Level of Education (or equivalent)	No formal education	4 (1%)
	GCSE	71(18.5%)
	A Levels	63 (16.4%)
	Undergraduate Degree	160 (41.7%)
	Master's degree	73 (19%)
	PhD	9 (2.3%)
Ethnicity	White English	329 (85.7%)
	White Irish	3 (.8%)
	Asian British Bangladeshi	2 (.5%)
	Asian British Chinese	2 (.5%)
	Asian British Indian	9 (2.3%)
	Other Asian	1 (.3%)
	Any other white background	17 (4.4%)
	Black African Caribbean	4 (1%)
	Black African	4 (1%)

Table 2.7: (Continued)

Variable	*Items*	*Total (%)*
	Mixed - White and Asian	3 (.8%)
	Mixed - White and Black African	1 (.3%)
	Any other mixed / Multiple ethnic background	4 (1%)
	Mixed - White and Black Caribbean	1 (.3%)
Received a diagnosis of depression or anxiety?	No	330 (85.9%)
	Yes	50 (13%)
Currently taking antidepressant medication?	No	12 (3.1%)
	Yes	38 (9.9%)

Demographical data was collected and reports the distribution of characteristics found in this sample population (see Table 2.7).

2.3.3 Perceived Stress Scale (PSS)

PSS Overview of Means, Standard Deviations and Number of Participants

Table 2.8: Perceived stress in healthy and depressive participants (and total sample) across all diet groups at baseline (PSS1), 6 weeks follow up (PSS2), intervention end (PSS3) and end of study (PSS4). Numbers (italics), Means (bold) and SDs (brackets)

	PSS 1			PSS 2			PSS 3			PSS 4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **7.17** (4.12)	*2* **15.00** (4.24)	*8* **9.13** (5.28)	*6* **7.67** (4.46)	*2* **17.00** (8.49)	*8* **10.00** (6.57)	*6* **7.00** (3.35)	*2* **12.50** (.707)	*8* **8.38** (3.82)	*6* **8.50** (5.28)	*2* **7.50** (6.36)	*8* **8.25** (5.09)
Low Carb	*5* **13.80** (9.07)	*1* **25.00** (.)	*6* **15.67** (9.31)	*5* **8.40** (8.50)	*1* **13.00** (.)	*6* **9.17** (7.83)	*5* **13.40** (8.39)	*1* **7.00** (.)	*6* **12.33** (7.94)	*5* **14.00** (9.70)	*1* **12.00** (.)	*6* **13.67** (8.71)
Total	*11* **10.18** (7.31)	*3* **18.33** (6.51)	*14* **11.93** (7.72)	*11* **8.00** (6.25)	*3* **15.67** (6.43)	*14* **9.64** (6.86)	*11* **9.91** (6.70)	*3* **10.67** (3.22)	*14* **10.07** (6.02)	*11* **11.00** (7.73)	*3* **9.00** (5.20)	*14* **10.57** (7.13)

PSS Time points 1 and 2, With Controls

Table 2.9: Perceived stress in healthy and depressive participants (and total sample) across all diet groups and controls at baseline (PSS1) and 6 weeks follow up (PSS2). Numbers (italics), Means (bold) and SDs (brackets)

	PSS 1			PSS 2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	37 **10** (5.43)	13 **22.08** (6.41)	50 **13.14** (7.77)	37 **10.19** (5.53)	13 **20.62** (5.69)	50 **12.90** (7.20)
Low Carb	13 **12.54** (7.86)	3 **21.00** (4.00)	16 **14.13** (7.95)	13 **9.46** (6.63)	3 **16.00** (6.08)	16 **10.69** (6.86)
Control	5 **12.40** (8.44)	4 **19.50** (6.81)	9 **15.56** (8.19)	5 **14.20** (4.76)	4 **14.50** (7.33)	9 **14.33** (5.61)
Total	55 **10.82** (6.33)	20 **21.40** (6.00)	75 **13.64** (7.79)	55 **10.38** (5.78)	20 **18.70** (6.34)	75 **12.60** (6.96)

This subsection includes participants (controls) added to the waiting list at the beginning of the study and only assessed at the first two time points.

A 2x3x4 mixed ANOVA was carried out and there was a significant main effect of time ($F(1, 69) = 4.13$, $p = .046$) with the levels of perceived stress reported at time point 2 lower than the levels at time point 1 across groups.

There was also a highly significant main effect of psych health ($F(1, 69) = 19.34$, $p<0.001$), due to the depressive symptoms group reporting more perceived stress overall than the healthy group, regardless of time or diet-type. The main effect of diet-type was not significant ($p>.05$).

For the time*psych-health interaction there is a weak, non-significant trend *(F*(1, 69) = 2.82, *p* = .097), suggesting that the main effect of time was in part moderated by psych health group (see Figure 2.2).

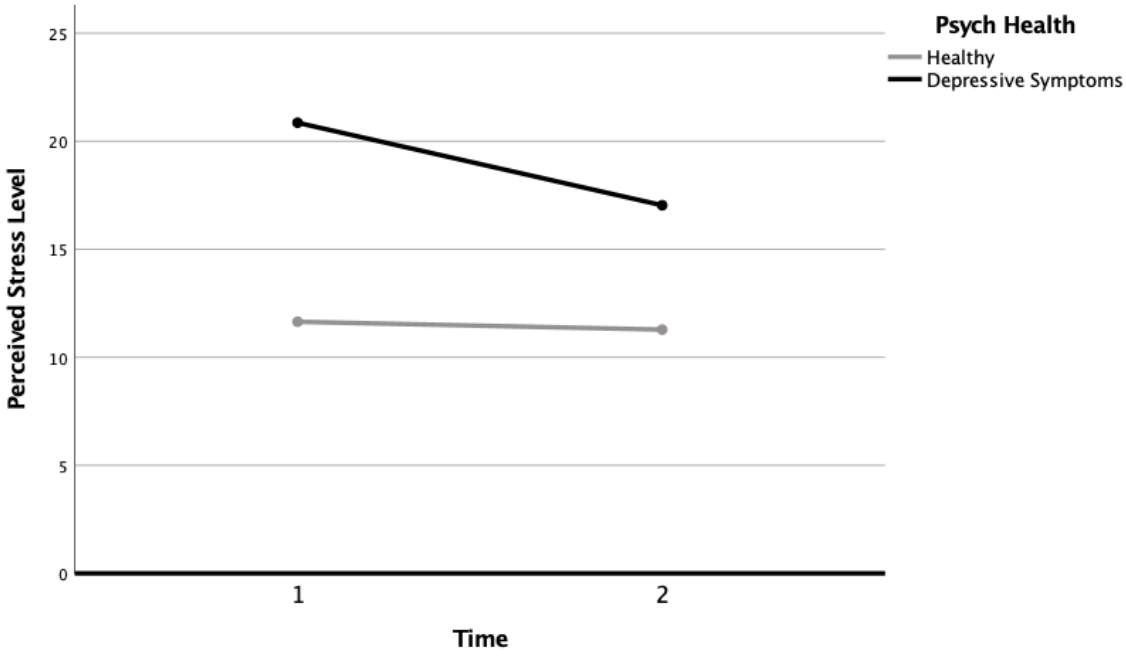

Figure 2.2: Perceived stress scores in healthy and depressive symptom conditions (collapsed across diet types) at time point 1 (baseline) and time point 2 (6 week follow up)

This trend indicated that there was a reduction in perceived stress levels across time in the depressive symptoms group, but no substantive change in the healthy group. This suggests a slight improvement in perceived stress levels over time, moderated by participant mental health.

There was no significant three-way time*diet-type*psych-health interaction (*p*>.05), so no conclusions can be drawn here about diet type and the effect on these trends.

Finally, neither of the sets of interactions of diet-type*psych-health or time*diet-type were significant (for all standard and linear interactions $p>.05$).

PSS Time points 1 and 2, No Controls

Table 2.10: Perceived stress in healthy and depressive participants (and total sample) across all diet groups at baseline (PSS1) and 6 weeks follow up (PSS2). Numbers (italics), Means (bold) and SDs (brackets)

	PSS 1			PSS 2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*37* **10** (5.43)	*13* **22.08** (6.41)	*50* **13.14** (7.77)	*37* **10.19** (5.53)	*13* **20.62** (5.69)	*50* **12.90** (7.20)
Low Carb	*13* **12.54** (7.86)	*3* **21.00** (4.00)	*16* **14.13** (7.95)	*13* **9.46** (6.63)	*3* **16.00** (6.08)	*16* **10.69** (6.86)
Total	*50* **10.66** (6.17)	*16* **21.88** (5.93)	*66* **13.38** (7.76)	*50* **10.00** (5.78)	*16* **19.75** (5.86)	*66* **12.36** (7.13)

There was a significant main effect of time ($F(1, 62) = 4.37$, $p = .041$) with the levels of perceived stress reported at time point 2 lower than the levels at time point 1 across groups.

There was also an expected significant main effect of psych health ($F(1, 62) = 26.41$, $p < 0.001$), due to the depressive symptoms group reporting more perceived stress than the healthy group, regardless of time or diet type.

The main effect of diet type was not significant ($p>.05$).

Finally, none of the sets of interactions of time*diet-type, time*psych-health, diet-type*psych-health and time*diet-type*psych-health were significant (for all standard and linear interactions $p>.05$).

PSS Time points 2 and 3, No Controls

Table 2.11: Perceived stress in healthy and depressive participants (and total sample) across all diet groups at 6 weeks follow up (PSS2) and intervention end (PSS3). Numbers (italics), Means (bold) and SDs (brackets)

	PSS 2			PSS 3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	12 **7.58** (4.96)	6 **19.33** (7.74)	18 **11.50** (8.13)	12 **7.92** (5.92)	6 **18.00** (11.45)	18 **11.28** (9.23)
Low Carb	10 **7.70** (5.89)	1 **13.00** (.)	11 **8.18** (5.81)	10 **8.20** (7.98)	1 **7.00** (.)	11 **8.09** (7.58)
Total	22 **7.64** (5.27)	7 **18.43** (7.46)	29 **10.24** (7.41)	22 **8.05** (6.76)	7 **16.43** (11.25)	29 **10.07** (8.64)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 3 ($p<.05$), however, ANOVA was carried out on the data.

There was a borderline significant main effect of psych health ($F(1, 25) = 3.09$, $p = .091$) with the levels of perceived stress decreasing over time across groups.

There were no significant main effects of time or diet type and no significant interactions between time*diet-type, time*psych-health, or time*diet-type*psych-health (all $p>.05$).

PSS Time points 3 and 4, No Controls

Table 2.12: Perceived stress in healthy and depressive participants (and total sample) across all diet groups at intervention end (PSS3) and end of study (PSS4). Numbers (italics), Means (bold) and SDs (brackets)

	PSS 3			PSS 4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **7.00** (3.35)	*3* **10.67** (3.22)	*9* **8.22** (3.60)	*6* **8.50** (5.28)	*3* **9.33** (5.51)	*9* **8.78** (5.02)
Low Carb	*5* **13.40** (8.39)	*1* **7.00** (.)	*6* **12.33** (7.94)	*5* **14.00** (9.70)	*1* **12.00** (.)	*6* **13.67** (8.71)
Total	*11* **9.91** (6.70)	*4* **9.75** (3.20)	*15* **9.87** (5.85)	*11* **11.00** (7.73)	*4* **10.00** (4.70)	*15* **10.73** (6.90)

There were no significant main effects of time, diet type or psych health between time points 3 and 4 for perceived stress. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

PSS Time points 1, 2 and 3, No Controls

Table 2.13: Perceived stress in healthy and depressive participants (and total sample) across all diet groups at baseline (PSS1), 6 weeks follow up (PSS2) and intervention end (PSS3). Numbers (italics), Means (bold) and SDs (brackets)

	PSS 1			PSS 2			PSS 3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	12 **8.92** (6.54)	5 **18.00** (8.40)	17 **11.59** (8.08)	12 **7.58** (4.96)	5 **20.80** (7.67)	17 **11.47** (8.38)	12 **7.92** (5.92)	5 **20.20** (11.30)	17 **11.53** (9.45)
Low Carb	9 **10.89** (8.61)	1 **25.00** (.)	10 **12.30** (9.26)	9 **7.89** (6.21)	1 **13.00** (.)	10 **8.40** (6.08)	9 **8.33** (8.46)	1 **7.00** (.)	10 **8.20** (7.98)
Total	21 **9.76** (7.36)	6 **19.17** (8.04)	27 **11.85** (8.37)	21 **7.71** (5.39)	6 **19.50** (7.56)	27 **10.33** (7.63)	21 **8.10** (6.92)	6 **18.00** (11.45)	27 **10.30** (8.93)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 3 ($p<.05$), however, ANOVA was carried out on the data.

There was a significant main effect of psych health ($F(1, 23) = 6.51$, $p = .018$), due to participants with depressive symptoms generally reporting higher perceived stress scores than the healthy participants, regardless of time or diet type.

There was no overall main effect of time, but there was a borderline significant linear trend ($F_{lin}(1, 23) = 3.85$, $p = .062$) in reported levels of perceived stress.

The main effect of diet type was not significant ($p>.05$).

The time*diet-type linear interaction was significant ($F_{lin}(1, 23) = 4.86$, $p = .038$). This suggests that the main effect of time was impacted by diet type (see Figure 2.3). Scores remained stable in the keto diet group whilst those in the low carb group showed a linear like decline in stress scores.

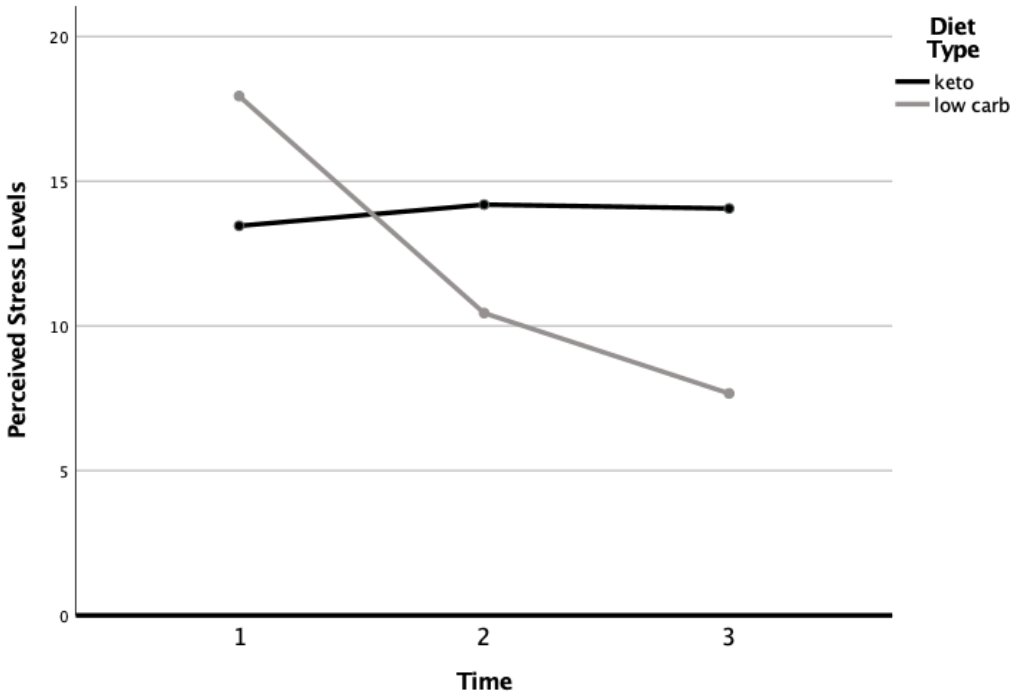

Figure 2.3: Perceived stress scores in keto and low carb diet types at time points 1, 2 and 3

The three way linear time*diet-type*psych-health interaction was nearing significance *(F_{lin}*(1, 23) = 3.57, p = .072), suggesting that the main effect of time was partially impacted by both diet type and psych health (see Figure 2.4).

All groups remained reasonably stable across all three time points except for the depressive low carb group, who showed a marked decline in reported stress across the three time points. This suggests that diet type has no impact on stress levels in healthy participants and that the ketogenic diet specifically has minimal effects in those with depressive symptoms. However, the low carb diet appears to be positively impacting the stress levels of participants with depressive symptoms.

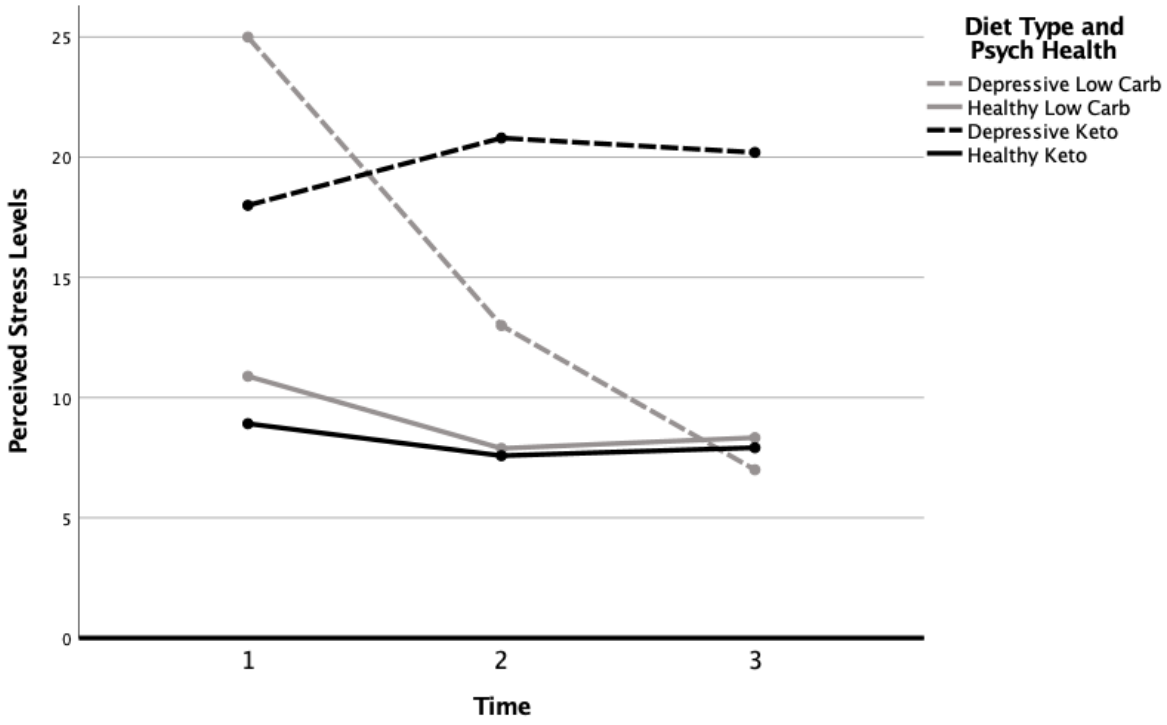

Figure 2.4: Perceived stress scores for each diet type in both healthy and depressive symptom conditions across time points 1, 2 and 3

Finally, neither of the sets of interactions of diet-type*psych-health or time*psych-health were significant (for all standard, linear, and quadratic interactions $p>.05$).

PSS All Time points, No Controls

There were no significant main effects of time, diet type or psych health (for all analyses $p>.05$).

For the time*psych-health linear interaction there was a weak, non-significant trend ($F_{lin}(1, 10) = 4.26$, $p = .066$), likely due to a reduction in perceived stress levels across time in the depressive symptoms group, but no substantive change in the healthy group (see Figure 2.5).

There was no significant three-way time*diet-type*psych-health interaction (p>.05), so no conclusions can be drawn here about diet type and the effect on this weak trend.

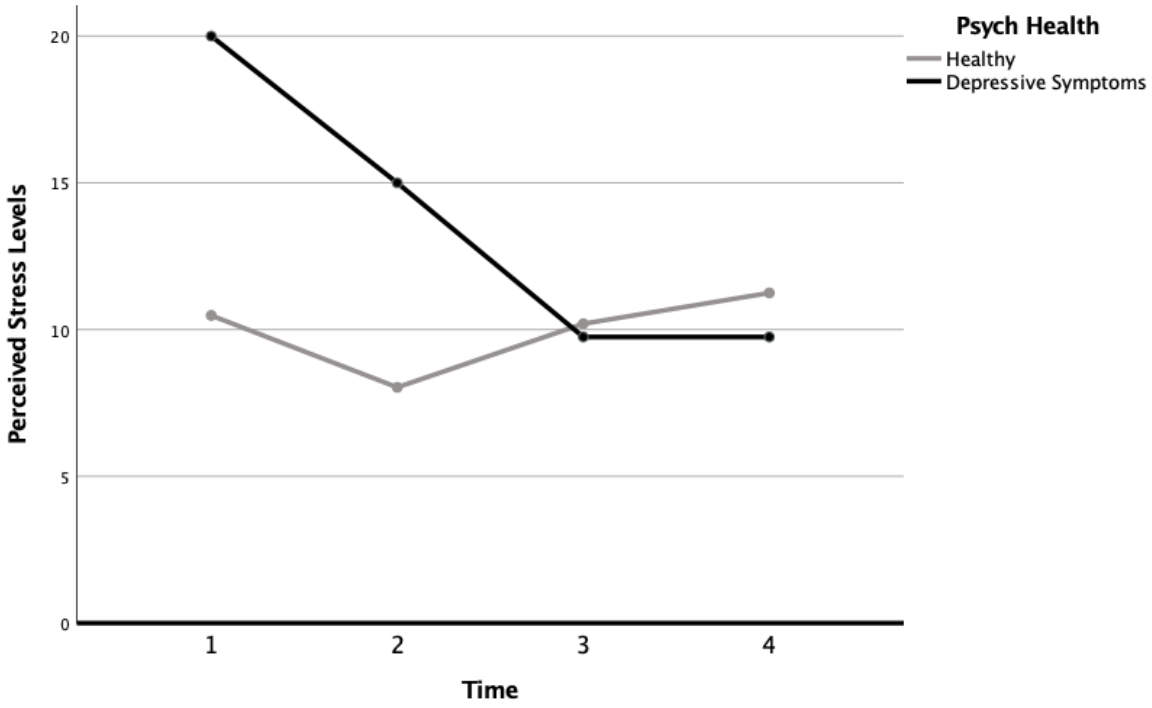

Figure 2.5: Perceived stress scores in healthy and depressive symptom conditions at time point 1, 2, 3 and 4

Finally, neither of the interactions diet-type*psych-health or time*diet-type were significant (for both interactions p>.05).

2.3.4 Generalised Anxiety Disorder (GAD)

GAD Overview of Means, Standard Deviations and Number of Participants

Table 2.14: Generalised anxiety disorder in healthy and depressive participants (and total sample) across all diet groups at baseline (GAD1), 6 weeks follow up (GAD2), intervention end (GAD3) and end of study (GAD4). Numbers (italics), Means (bold) and SDs (brackets)

	GAD 1			GAD 2			GAD 3			GAD 4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **.67** (1.03)	*2* **3.50** (2.12)	*8* **1.38** (1.77)	*6* **.33** (.52)	*2* **6.50** (7.78)	*8* **1.88** (4.12)	*6* **1.50** (2.51)	*2* **4.00** (4.24)	*8* **2.13** (2.90)	*6* **1.83** (1.84)	*2* **2.00** (1.41)	*8* **1.88** (1.64)
Low Carb	*5* **.60** (1.34)	*1* **12.00** (.)	*6* **2.50** (4.81)	*5* **1.80** (3.49)	*1* **1.00** (.)	*6* **1.67** (3.14)	*5* **1.80** (3.49)	*1* **2.00** (.)	*6* **1.83** (3.13)	*5* **1.60** (2.30)	*1* **3.00** (.)	*6* **1.83** (2.14)
Total	*11* **.64** (1.12)	*3* **6.33** (5.13)	*14* **1.86** (3.30)	*11* **1.00** (2.37)	*3* **4.67** (6.35)	*14* **1.79** (3.60)	*11* **1.64** (2.84)	*3* **3.33** (3.22)	*14* **2.00** (2.88)	*11* **1.73** (1.95)	*3* **2.33** (1.16)	*14* **1.86** (1.79)

GAD Time points 1 and 2, With Controls

Table 2.15: Generalised anxiety disorder in healthy and depressive participants (and total sample) across all diet groups and controls at baseline (GAD1) and 6 weeks follow up (GAD2). Numbers (italics), Means (bold) and SDs (brackets)

	GAD 1			GAD 2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*36* **2.31** (2.47)	*11* **8.00** (4.05)	*47* **3.64** (3.76)	*36* **1.94** (2.47)	*11* **7.73** (4.43)	*47* **3.30** (3.88)
Low Carb	*13* **1.69** (1.89)	*3* **10.33** (2.89)	*16* **3.31** (4.01)	*13* **1.69** (2.46)	*3* **5.33** (8.39)	*16* **2.38** (4.05)
Control	*5* **3.20** (5.63)	*4* **10.00** (5.35)	*9* **6.22** (6.28)	*5* **2.20** (2.95)	*4* **7.50** (3.11)	*9* **4.56** (3.97)
Total	*54* **2.24** (2.72)	*18* **8.83** (4.11)	*72* **3.89** (4.22)	*54* **1.91** (2.47)	*18* **7.28** (4.73)	*72* **3.25** (3.92)

There was a significant main effect of time ($F(1, 66) = 5.85$, $p = .018$). The reported levels of generalised anxiety disorder at time point 2 were significantly lower than the levels at time point 1. This shows that on average, all scores were decreasing.

There was also a highly significant main effect of psych health ($F(1, 66) = 50.61$, $p<0.001$) due to the depressive symptoms group reporting more perceived stress overall than the healthy group, regardless of time or diet-type.

The main effect of diet-type was not significant ($p>.05$), so there was no difference in the scoring across participants in these groups.

For the time*psych-health interaction there is a weak, non-significant trend *(F*(1, 66) = 2.88, *p* = .094), suggesting that the main effect of time was in part moderated by psych health group (see Figure 2.6).

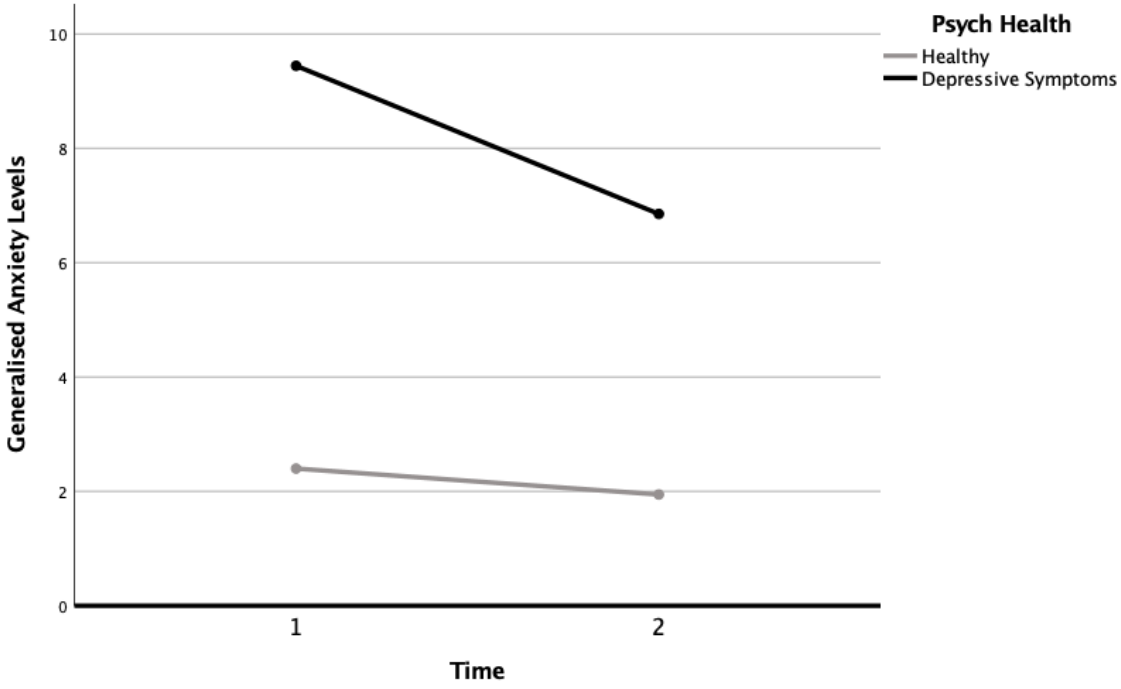

Figure 2.6: Generalised anxiety scores in healthy and depressive symptom conditions (collapsed across diet types) at time point 1 (baseline) and time point 2 (6 week follow up)

This trend indicates that there is a reduction in generalised anxiety levels across time in the depressive symptoms group. Whereas there is only a slight change in the healthy group. This suggests a slight improvement in generalised anxiety levels over time, moderated by the state of the participants mental health.

Finally, none of the sets of interactions of diet-type*psych-health, time*diet-type*psych-health or time*diet-type were significant (for all standard and linear interactions *p*>.05).

GAD Time points 1 and 2, No Controls

Table 2.16: Generalised anxiety disorder in healthy and depressive participants (and total sample) across all diet groups at baseline (GAD1) and 6 weeks follow up (GAD2). Numbers (italics), Means (bold) and SDs (brackets)

	GAD 1			GAD 2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	36 **2.31** (2.47)	11 **8.00** (4.05)	47 **3.64** (3.76)	36 **1.94** (2.47)	11 **7.73** (4.43)	47 **3.30** (3.88)
Low Carb	13 **1.69** (1.89)	3 **10.33** (2.89)	16 **3.31** (4.01)	13 **1.69** (2.46)	3 **5.33** (8.39)	16 **2.38** (4.05)
Total	49 **2.14** (2.33)	14 **8.50** (3.86)	63 **3.56** (3.80)	49 **1.88** (2.45)	14 **7.21** (5.19)	63 **3.06** (3.91)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 ($p<.05$), however, ANOVA was carried out on the data.

There was a significant main effect of time ($F(1, 59) = 4.68$, $p = .035$) with the levels of generalised anxiety reported at time point 2 lower than the levels at time point 1 across groups.

There was also an expected significant main effect of psych health ($F(1, 59) = 46.14$, $p<0.001$) due to the depressive symptoms group reporting more generalised anxiety than the healthy group, regardless of time or diet type.

The main effect of diet type was not significant ($p>.05$).

The time*psych-health interaction was nearing significance ($F(1, 59) = 3.56$, $p = .064$) but the time*diet-type interaction was not significant ($p>.05$).

The three way time*diet-type*psych-health interaction was bordering on significance *(F*(1, 59) = 3.82, *p* = .055), suggesting that the main effect of time was partially impacted by both diet type and psych health (see Figure 2.7).

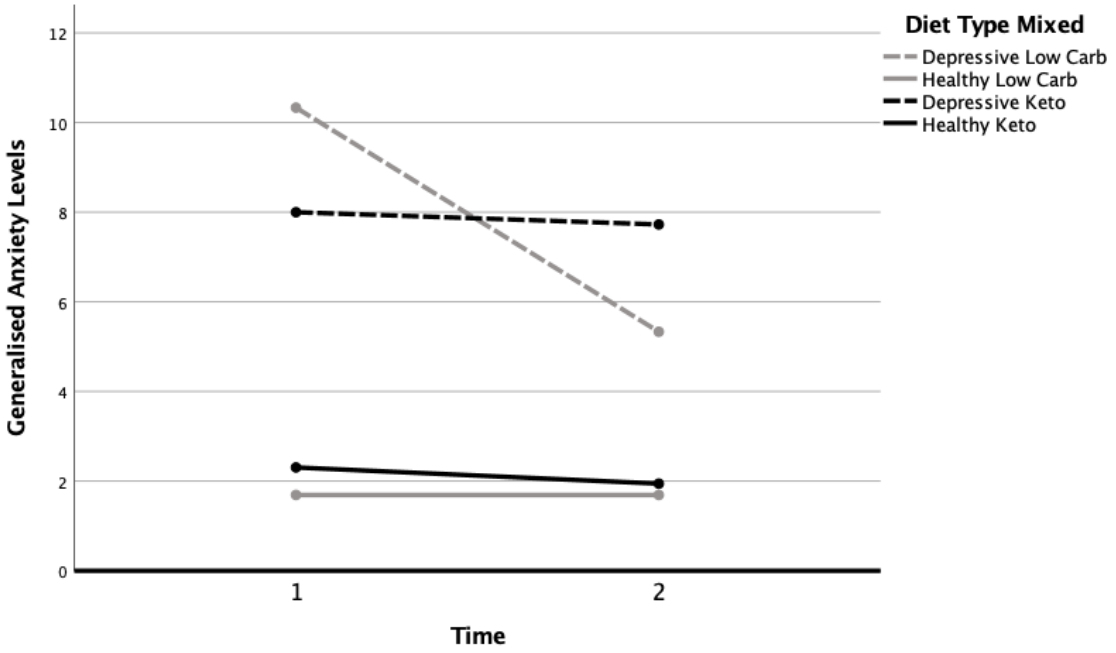

Figure 2.7: Generalised anxiety scores for each diet type in both healthy and depressive symptom conditions across time points 1 and 2

Finally, the diet-type*psych-health interaction was not significant (for all standard and linear interactions *p*>.05).

GAD Time points 2 and 3, No Controls

Table 2.17: Generalised anxiety disorder in healthy and depressive participants (and total sample) across all diet groups at 6 weeks follow up (GAD2) and intervention end (GAD3). Numbers (italics), Means (bold) and SDs (brackets)

	GAD 2			GAD 3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	11 **1.36** (2.06)	6 **7.50** (4.51)	17 **3.53** (4.26)	11 **1.73** (2.80)	6 **7.00** (5.69)	17 **3.59** (4.66)
Low Carb	10 **1.40** (2.50)	1 **1.00** (.)	11 **1.36** (2.38)	10 **1.00** (2.49)	1 **2.00** (.)	11 **1.09** (2.39)
Total	21 **1.38** (2.22)	7 **6.57** (4.79)	28 **2.68** (3.74)	21 **1.38** (2.62)	7 **6.29** (5.53)	28 **2.61** (4.07)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 ($p<.05$), however, ANOVA was carried out on the data.

There was a borderline significant main effect of psych health ($F(1, 24) = 3.92$, $p = .059$) due to the depressive symptoms group reporting more generalised anxiety than the healthy group, regardless of time or diet type.

The main effect of diet type was nearing significance ($F(1, 24) = 4.04$, $p = .056$).

There was no significant main effect of time.

The diet-type*psych-health interaction was also nearing significance ($F(1, 24) = 3.17$, $p = .087$).

Finally, none of the sets of interactions of time*diet-type, time*psych-health, and time*diet-type*psych-health were significant (for all standard and linear interactions $p>.05$).

GAD Time points 3 and 4, No Controls

Table 2.18: Generalised anxiety disorder in healthy and depressive participants (and total sample) across all diet groups at intervention end (GAD3) and end of study (GAD4). Numbers (italics), Means (bold) and SDs (brackets)

	GAD 3			GAD 4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	6 **1.50** (2.51)	3 **3.33** (3.22)	9 **2.11** (2.71)	6 **1.83** (1.84)	3 **2.33** (1.16)	9 **2.00** (1.58)
Low Carb	5 **1.80** (3.49)	1 **2.00** (.)	6 **1.83** (3.13)	5 **1.60** (2.30)	1 **3.00** (.)	6 **1.83** (2.14)
Total	11 **1.64** (2.84)	4 **3.00** (2.71)	15 **2.00** (2.78)	11 **1.73** (1.95)	4 **2.50** (1.00)	15 **1.93** (1.75)

There were no significant main effects of time, diet type or psych health between time points 3 and 4 for generalised anxiety disorder. There were also no significant interactions between time*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

GAD Time point 1, 2 and 3, No Controls

Table 2.19: Generalised anxiety disorder in healthy and depressive participants (and total sample) across all diet groups at baseline (GAD1), 6 weeks follow up (GAD2) and intervention end (GAD3). Numbers (italics), Means (bold) and SDs (brackets)

	GAD 1			GAD 2			GAD 3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	11 **2.36** (2.94)	5 **8.00** (5.79)	16 **4.12** (4.69)	11 **1.36** (2.06)	5 **8.20** (4.66)	16 **3.50** (4.40)	11 **1.73** (2.80)	5 **8.00** (5.75)	16 **3.69** (4.80)
Low Carb	9 **1.11** (1.69)	1 **12.00** (.)	10 **2.20** (3.80)	9 **1.44** (2.65)	1 **1.00** (.)	10 **1.40** (2.50)	9 **1.00** (2.65)	1 **2.00** (.)	10 **1.10** (2.51)
Total	20 **1.80** (2.48)	6 **8.67** (5.43)	26 **3.38** (4.39)	20 **1.40** (2.28)	6 **7.00** (5.10)	26 **2.69** (3.87)	20 **1.40** (2.68)	6 **7.00** (5.69)	26 **2.69** (4.21)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 1 ($p<.05$), however, ANOVA was carried out on the data.

There was an overall significant main effect of time *(*$F(2, 44) = 4.72$, $p = .014$) as well as a significant linear trend *(*$F_{lin}(1, 22) = 9.27$, $p = .006$) in reported levels of generalised anxiety.

There was also a significant linear main effect of psych health *(*$F(1, 22) = 11.34$, $p = .003$) due to participants with depressive symptoms generally reporting higher generalised anxiety scores than the healthy participants, regardless of time or diet type.

The main effect of diet type was not significant ($p>.05$).

For the time*psych-health linear interaction there was a significant trend *(*$F_{lin}(1, 22) = 6.87$, $p = .016$)

The overall time*diet-type interaction was significant *(*$F(2, 44) = 3.57$, $p = .037$) and there was also a significant linear trend *(*$F_{lin}(1, 22) = 7.21$, $p = .014$). This suggests that the main effect of time was impacted by diet type (see Figure 2.8). Scores remained stable in the keto diet group whilst those in the low carb group showed a linear like decline in generalised anxiety scores.

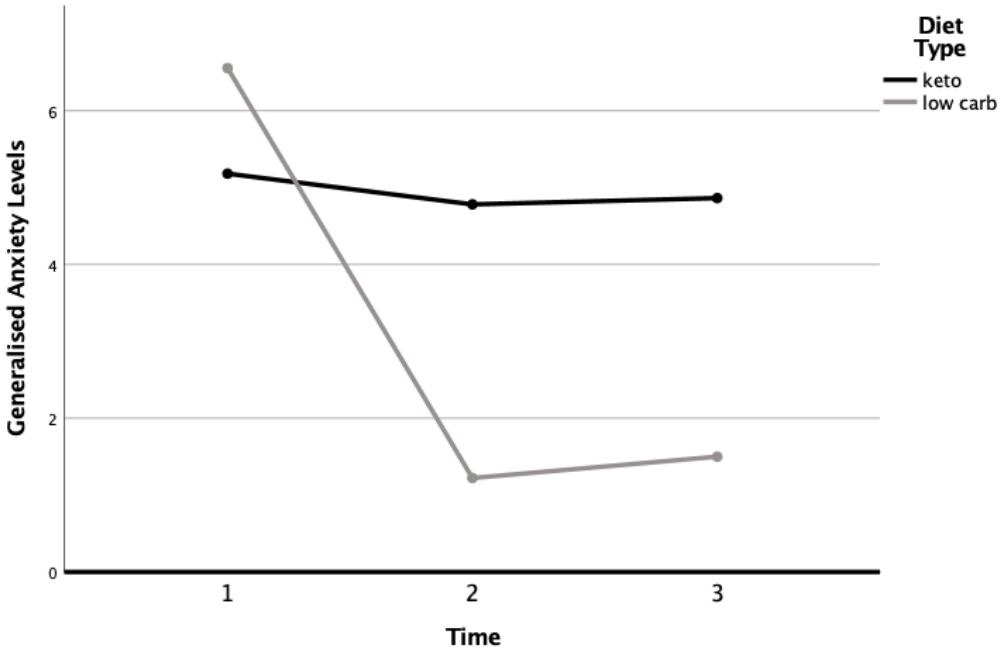

Figure 2.8: Generalised anxiety scores in keto and low carb diet types at time points 1, 2 and 3

The overall time*diet-type*psych-health interaction showed a significant trend *(*$F(2, 44) = 5.18$, $p = .010$) and the linear interaction was also significant *(*$F_{lin}(1, 22) = 8.90$, $p = .007$). This suggests that the main effect of time was partially impacted by both diet type and psych health (see Figure 2.9).

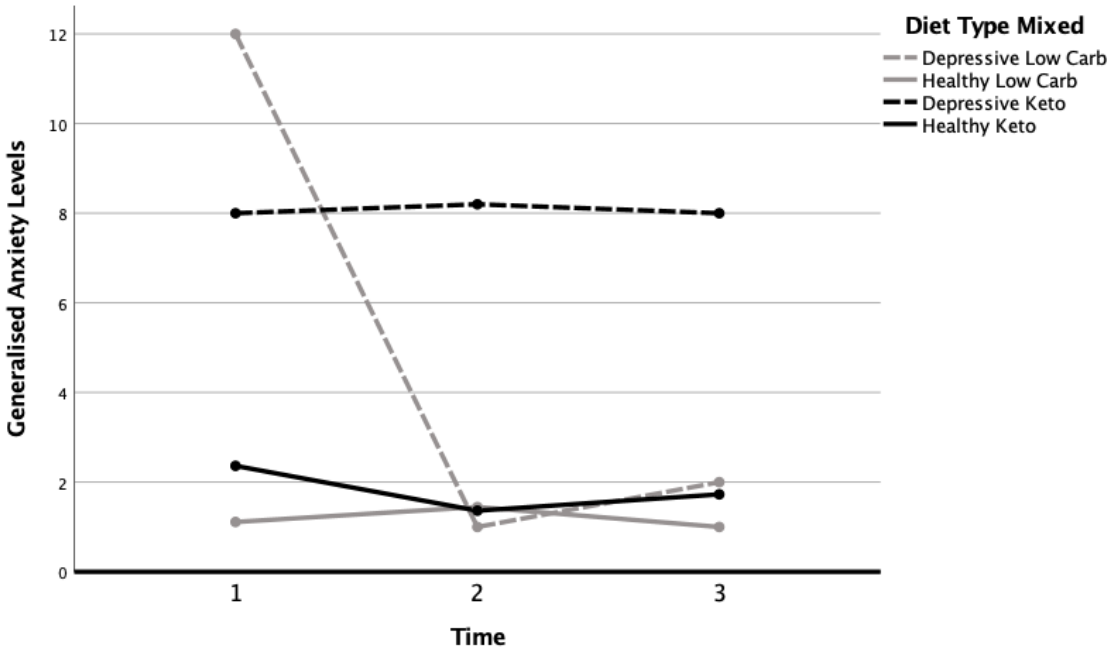

Figure 2.9: Generalised anxiety scores for each diet type in both healthy and depressive symptom conditions across time points 1, 2 and 3

Finally, the diet-type*psych-health set of interactions were not significant (for all standard, linear, and quadratic interactions p>.05).

GAD All Time points, No Controls

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 (p<.05), however, ANOVA was carried out on the data.

Though the overall main effect of time was not significant, there was a significant linear trend *(F_{lin}*(1, 10) = 8.44, p = .016) showing that the levels of generalised anxiety reported decreased over time.

There was also a significant main effect of psych health *(F*(1, 10) = 7.33, p = .022) due to participants with depressive symptoms reporting higher generalised anxiety scores than the healthy participants regardless of time or diet type.

There was no significant main effect of diet type (p>.05).

The overall time*psych-health interaction was significant (F(3, 30) = 3.27, p = .035), as was the linear interaction (F_{lin}(1, 10) = 21.75, p = .001). This may be due to a reduction in generalised anxiety scores across time in the depressive symptoms group, and a slight increase in the healthy group (see Figure 2.10).

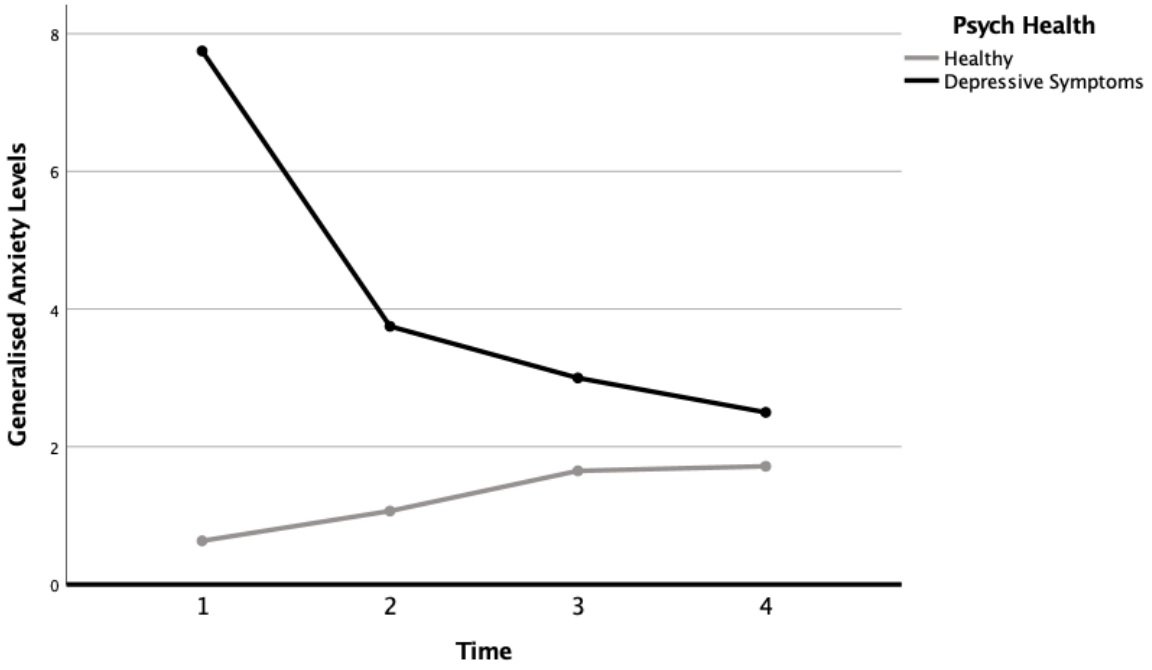

Figure 2.10: Generalised anxiety scores in healthy and depressive symptom conditions at time point 1, 2, 3 and 4

The time*diet-type interaction was borderline significant (F(3, 30) = 2.91, p = .051) with the linear interaction showing a significant trend (F_{lin}(1, 10) = 5.62, p = .039) and the quadratic interaction showing a weak non-significant trend (F_{quad}(1, 10) = 4.69, p = .056). This significant linear interaction is due to a large reduction in generalised anxiety scores in the low carb group and a slight increase in the keto diet group (see Figure 2.11).

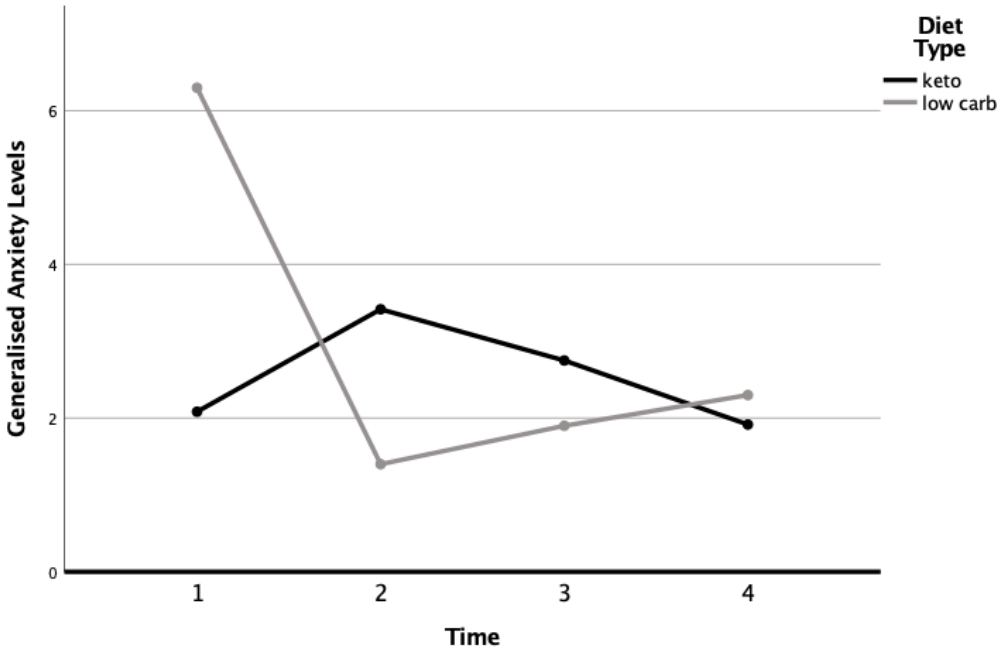

Figure 2.11: Generalised anxiety scores in keto and low carb diet types at time points 1, 2, 3 and 4

There was an overall significant three-way time*diet-type*psych-health interaction *(*$F(3, 30) = 4.26$, $p = .013$). There was also a weak non-significant linear interaction *(*$F_{lin}(1, 10) = 3.95$, $p = .075$) followed by a significant quadratic interaction *(*$F_{quad}(1, 10) = 7.65$, $p = .020$). This suggests that the main effect of time was impacted by both diet type and psych health (see Figure 2.12).

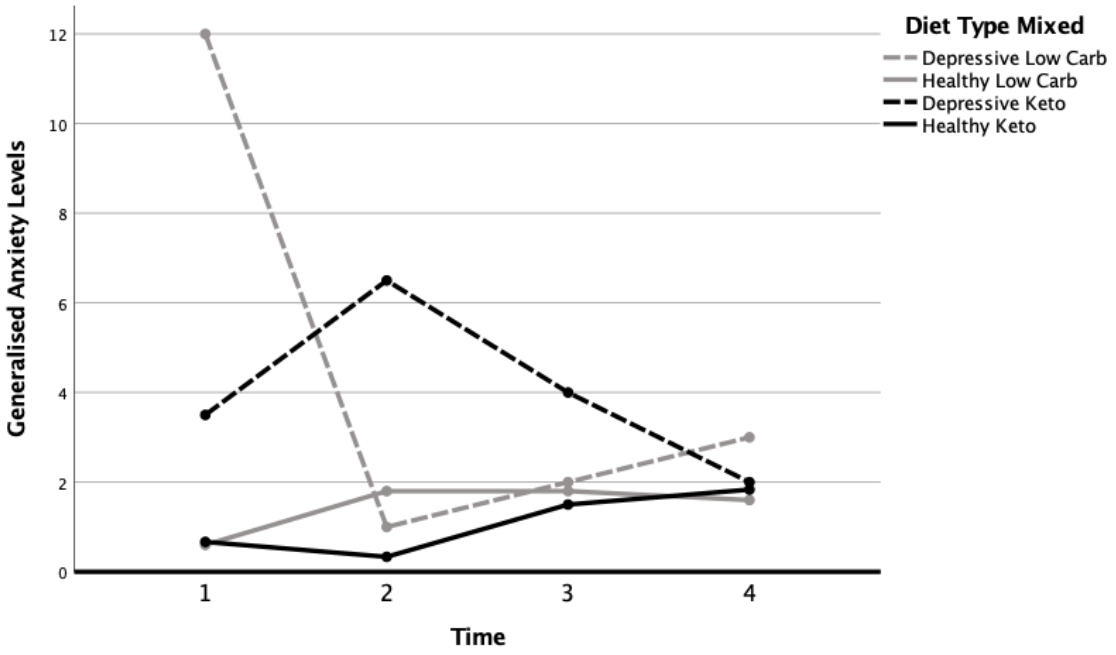

Figure 2.12: Generalised anxiety scores for each diet type in both healthy and depressive symptom conditions across time points 1, 2, 3 and 4

Finally, the diet-type*psych-health set of interactions were not significant (for all standard, linear, quadratic, and cubic interactions $p>.05$).

2.3.5 Center for Epidemiological Studies-Depression (CES-D)

CESD Overview of Means, Standard Deviations and Number of Participants

Table 2.19: Depressive symptoms in healthy and depressive participants (and total sample) across all diet groups at baseline (CESD1), 6 weeks follow up (CESD2), intervention end (CESD3) and end of study (CESD4). Numbers (italics), Means (bold) and SDs (brackets)

	CESD 1			CESD 2			CESD 3			CESD 4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **4.67** (2.25)	*2* **12.50** (13.44)	*8* **6.63** (6.52)	*6* **4.33** (4.76)	*2* **14.50** (17.68)	*8* **6.88** (9.11)	*6* **3.17** (3.97)	*2* **7.50** (6.36)	*8* **4.25** (4.59)	*6* **5.33** (2.73)	*2* **5.00** (5.66)	*8* **5.25** (3.15)
Low Carb	*5* **5.20** (5.22)	*1* **35.00** (.)	*6* **10.17** (13.03)	*5* **10.60** (12.08)	*1* **9.00** (.)	*6* **10.33** (10.82)	*5* **12.20** (7.40)	*1* **2.00** (.)	*6* **10.50** (7.82)	*5* **6.60** (5.27)	*1* **14.00** (.)	*6* **7.83** (5.60)
Total	*11* **4.91** (3.67)	*3* **20.00** (16.09)	*14* **8.14** (9.57)	*11* **7.18** (8.97)	*3* **12.67** (12.90)	*14* **8.36** (9.64)	*11* **7.27** (7.21)	*3* **5.67** (5.51)	*14* **6.93** (6.72)	*11* **5.91** (3.91)	*3* **8.00** (6.56)	*14* **6.36** (4.38)

CESD Time points 1 and 2, With Controls

Table 2.20: Depressive symptoms in healthy and depressive participants (and total sample) across all diet groups and controls at baseline (CESD1) and 6 weeks follow up (CESD2). Numbers (italics), Means (bold) and SDs (brackets)

	CESD 1			CESD 2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*36* **7.97** (7.38)	*11* **20.82** (12.35)	*47* **10.98** (10.24)	*36* **6.08** (5.21)	*11* **7.36** (9.34)	*47* **8.72** (7.93)
Low Carb	*13* **7.00** (6.12)	*3* **24.67** (11.68)	*16* **10.31** (9.95)	*13* **9.77** (9.81)	*3* **22.00** (17.58)	*16* **12.06** (11.94)
Control	*5* **15.00** (19.18)	*4* **18.50** (9.00)	*9* **16.56** (14.76)	*5* **12.80** (10.55)	*4* **18.25** (6.95)	*9* **15.22** (9.05)
Total	*54* **8.39** (8.77)	*18* **20.94** (11.13)	*72* **11.53** (10.82)	*54* **7.59** (7.31)	*18* **18.33** (9.96)	*72* **10.28** (9.25)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 1 or 2 ($p<.05$), however, ANOVA was carried out on the data.

There were no significant main effects of time or diet type between time points 1 and 2 for depressive symptoms.

There was a significant main effect of psych health ($F(1, 66) = 19.49$ $p < 0.001$), to be expected. This may be due to participants with depressive symptoms generally reporting higher depressive symptoms scores than the healthy participants, regardless of time or diet type.

Finally, there were no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, p>.05).

CESD Time points 1 and 2, No Controls

Table 2.21: Depressive symptoms in healthy and depressive participants (and total sample) across all diet groups at baseline (CESD1) and 6 weeks follow up (CESD2). Numbers (italics), Means (bold) and SDs (brackets)

	CESD 1			CESD 2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*36* **7.97** (7.38)	*11* **20.82** (12.35)	*47* **10.98** (10.24)	*36* **6.08** (5.21)	*11* **17.36** (9.34)	*47* **8.72** (7.93)
Low Carb	*13* **7.00** (6.12)	*3* **24.67** (11.68)	*16* **10.31** (9.95)	*13* **9.77** (9.81)	*3* **22.00** (17.58)	*16* **12.06** (11.94)
Total	*49* **7.71** (7.02)	*14* **21.64** (11.88)	*63* **10.81** (10.09)	*49* **7.06** (6.82)	*14* **18.36** (10.89)	*63* **9.57** (9.13)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 (p<.05), however, ANOVA was carried out on the data.

There were no significant main effects of time or diet type between time points 1 and 2 for depressive symptoms.

There was a significant main effect of psych health (F(1, 59) = 33.62, p <0.001), to be expected. This may be due to participants with depressive symptoms generally reporting higher depressive symptoms scores than the healthy participants, regardless of time or diet type.

Finally, there were no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

CESD Time points 2 and 3, No Controls

Table 2.22: Depressive symptoms in healthy and depressive participants (and total sample) across all diet groups at 6 weeks follow up (CESD2) and intervention end (CESD3). Numbers (italics), Means (bold) and SDs (brackets)

	CESD 2			CESD 3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*11* **5.36** (6.01)	*6* **17.00** (9.70)	*17* **9.47** (9.21)	*11* **5.09** (6.76)	*6* **14.67** (13.91)	*17* **8.47** (10.55)
Low Carb	*10* **7.90** (8.84)	*1* **9.00** (.)	*11* **8.00** (8.39)	*10* **7.40** (7.28)	*1* **2.00** (.)	*11* **6.91** (7.09)
Total	*21* **6.57** (7.41)	*7* **15.86** (9.35)	*28* **8.89** (8.77)	*21* **6.19** (6.93)	*7* **12.86** (13.57)	*28* **7.86** (9.23)

There were no significant main effects of time, diet type or psych health between time points 2 and 3 for depressive symptoms. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

CESD Time points 3 and 4, No Controls

Table 2.23: Depressive symptoms in healthy and depressive participants (and total sample) across all diet groups at intervention end (CESD3) and end of study (CESD4). Numbers (italics), Means (bold) and SDs (brackets)

	CESD 3			CESD 4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **3.17** (3.97)	*3* **9.67** (5.86)	*9* **5.33** (5.39)	*6* **5.33** (2.73)	*3* **7.67** (6.11)	*9* **6.11** (3.92)
Low Carb	*5* **12.20** (7.40)	*1* **2.00** (.)	*6* **10.50** (7.82)	*5* **6.60** (5.27)	*1* **14.00** (.)	*6* **7.83** (5.60)
Total	*11* **7.27** (7.21)	*4* **7.75** (6.13)	*15* **7.40** (6.73)	*11* **5.91** (3.91)	*4* **9.25** (5.91)	*15* **6.80** (4.55)

There were no significant main effects of time, diet type or psych health between time points 3 and 4 for depressive symptoms.

The time*psych-health interaction was significant *($F(1, 11) = 4.95$, $p = .048$)* suggesting that the main effect of time was in part moderated by psych health group (see Figure 2.13).

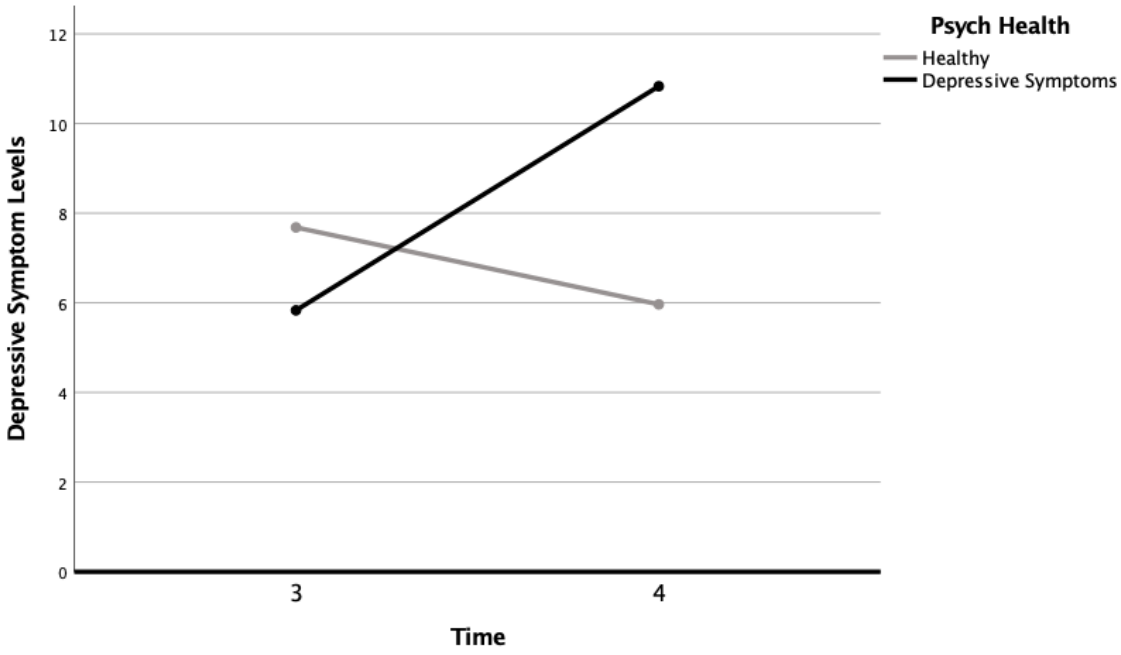

Figure 2.13: Depressive symptoms scores in healthy and depressive symptom conditions (collapsed across diet types) at time point 3 (intervention end) and time point 4 (end of study)

The three-way time*diet-type*psych-health interaction was also significant *(F*(1, 11) = 12.99, *p* = .004) suggesting that the main effect of time was partially impacted by both diet type and psych health (see Figure 2.14).

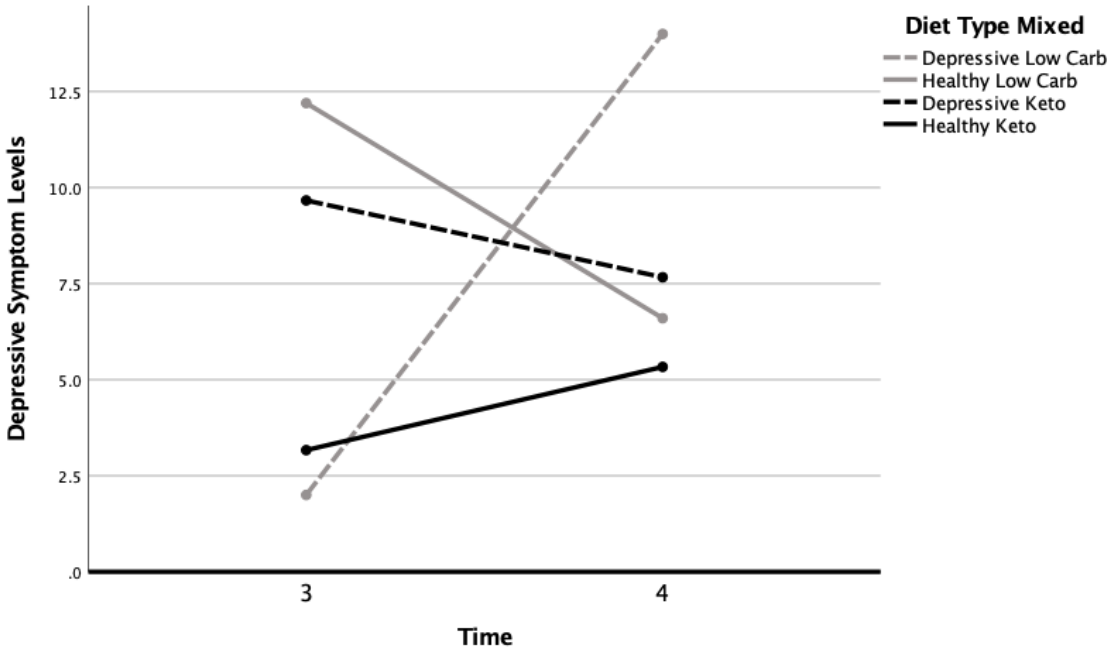

Figure 2.14: Depressive symptoms scores for each diet type in both healthy and depressive symptom conditions across time points 3 and 4

Finally, there were no significant interactions between time*diet-type or diet-type*psych-health (for all effects and interactions, $p>.05$).

CESD Time points 1, 2 and 3, No Controls

Table 2.24: Depressive symptoms in healthy and depressive participants (and total sample) across all diet groups at baseline (CESD1), 6 weeks follow up (CESD2) and intervention end (CESD3). Numbers (italics), Means (bold) and SDs (brackets)

	CESD 1			CESD 2			CESD 3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*11* **7.73** (8.98)	*5* **21.20** (17.85)	*16* **11.94** (13.43)	*11* **5.36** (6.01)	*5* **16.80** (10.83)	*16* **8.94** (9.23)	*11* **5.09** (6.76)	*5* **14.80** (15.55)	*16* **8.13** (10.79)
Low Carb	*9* **5.78** (5.45)	*1* **35.00** (.)	*10* **8.70** (10.57)	*9* **8.67** (9.01)	*1* **9.00** (.)	*10* **8.70** (8.50)	*9* **7.89** (7.54)	*1* **2.00** (.)	*10* **7.30** (7.35)
Total	*20* **6.85** (7.48)	*6* **23.50** (16.93)	*26* **10.69** (12.29)	*20* **6.85** (7.48)	*6* **15.50** (10.19)	*26* **8.85** (8.79)	*20* **6.35** (7.07)	*6* **12.67** (14.86)	*26* **7.81** (9.46)

There was an overall highly significant main effect of time *(F*(1.52, 33.52) = 8.36, *p* = .003) and a significant linear trend *(F_{lin}*(1, 22) = 23.81, *p* <0.001) with the levels of depressive symptoms reported at time points 2 and 3, lower than the levels at time point 1 across groups.

There was also an overall significant main effect of psych health *(F*(1, 22) = 4.38, *p* = .048) due to participants with depressive symptoms generally reporting higher depressive symptoms scores than the healthy participants, regardless of time or diet type.

The main effect of diet type was not significant (*p*>.05).

The overall time*psych-health interaction was highly significant *(F*(1.52, 33.52) = 8.17, *p* = .003) as was the time*psych-health linear interaction *(F_{lin}*(1, 22) = 22.57, *p* <0.001), (see Figure 2.15).

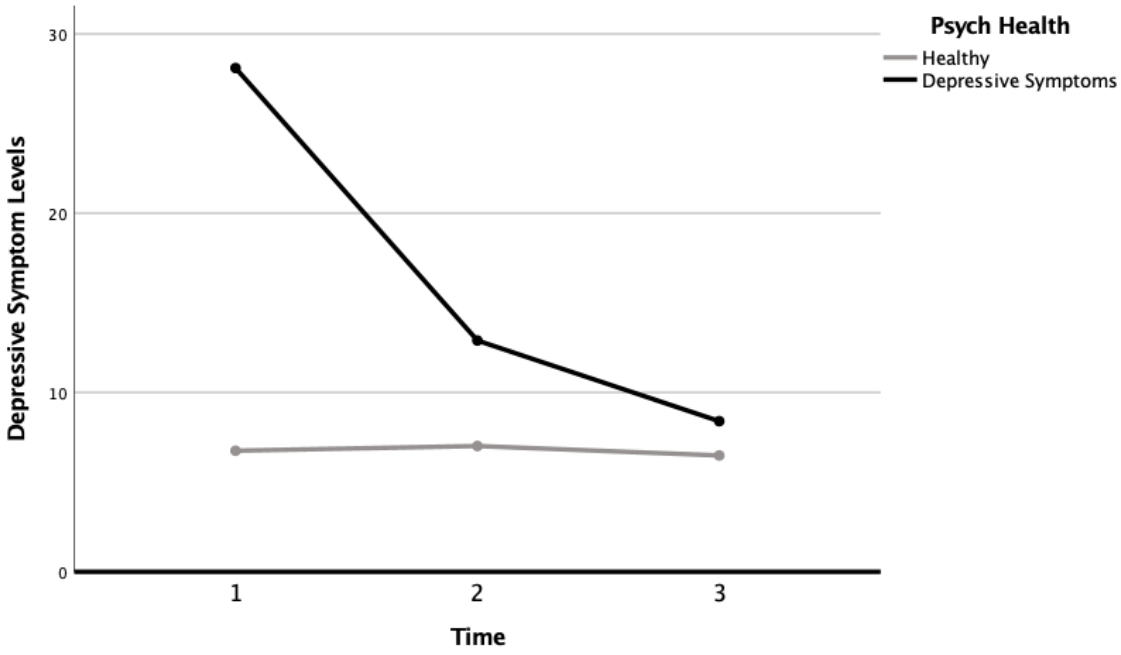

Figure 2.15: Depressive symptoms scores in healthy and depressive symptom conditions (collapsed across diet types) at time point 1 (baseline), time point 2 (6 week follow up) and time point 3 (intervention end)

For the time*diet-type overall interaction there was no significance (p>.05) but for the time*diet-type linear interaction there was a significant trend *(F_{lin}*(1, 22) = 7.13, p = .014). This suggests that the main effect of time was impacted by diet type (see Figure 2.16). Scores remained stable in the keto diet group whilst those in the low carb group showed a linear like decline in depressive symptoms scores.

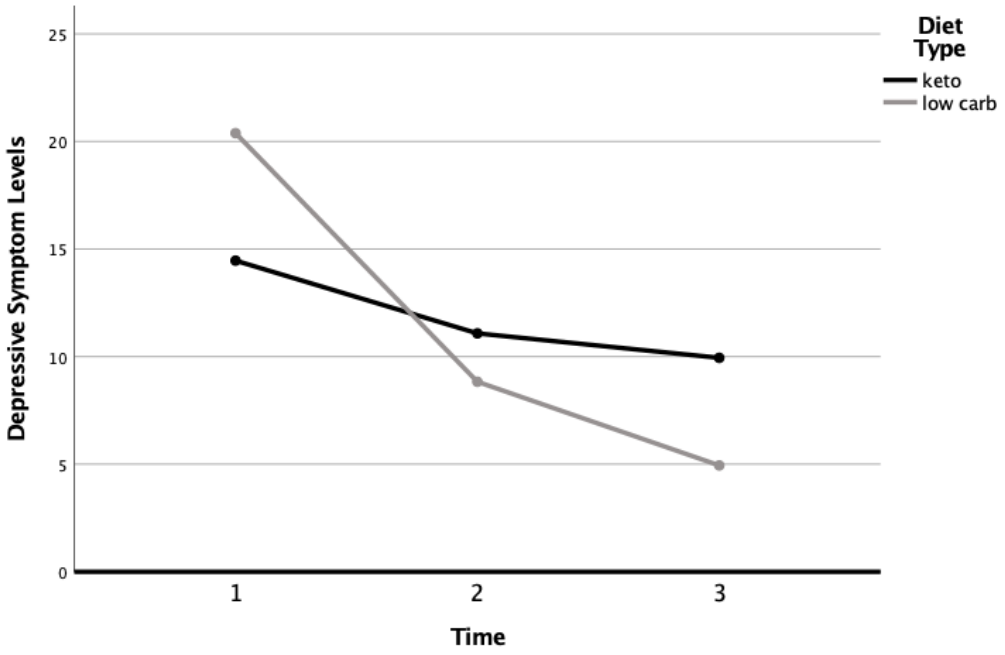

Figure 2.16: Depressive symptoms scores in keto and low carb diet types at time points 1, 2 and 3

The overall three-way time*diet-type*psych-health interaction was also significant *(*$F(1.52, 33.52) = 5.57$, $p = .013$) as was the linear interaction *(*$F_{lin}(1, 22) = 14.68$, $p = .001$). This suggests that the main effect of time was partially impacted by both diet type and psych health (see Figure 2.17).

Finally, the diet-type*psych-health interaction was not significant ($p>.05$).

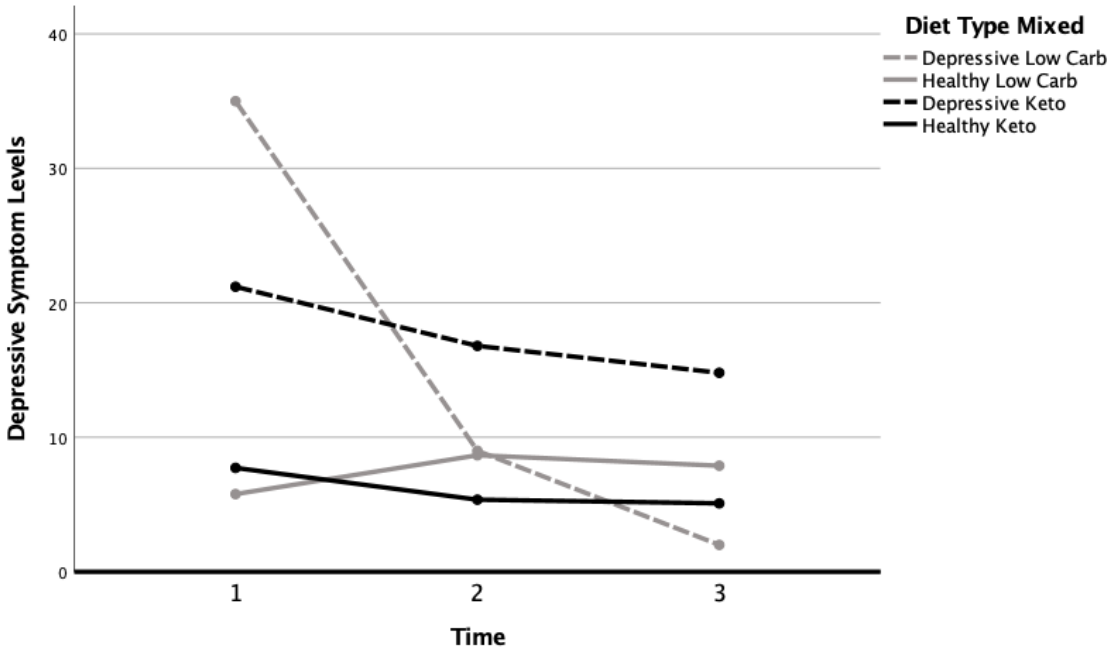

Figure 2.17: Depressive symptoms scores for each diet type in both healthy and depressive symptom conditions across time points 1, 2 and 3

CESD All Time points, No Controls

Levene's test confirmed that the assumption of homogeneity of variance was not met for time points 2 or 3 ($p<.05$), however, ANOVA was carried out on the data.

There was an overall significant main effect of time *(*$F(3, 30) = 4.37$, $p = .011$) showing that the levels of depressive symptoms reported at time point 2 were lower than the levels at time point 1 across groups. There was also a significant linear like decline in depressive symptom scores *(*$F_{lin}(1, 10) = 15.30$, $p = .003$).

There was no significant main effect of diet type or psych health (for all analysis $p>.05$).

The overall time*psych-health interaction was highly significant *(F*(3, 30) = 7.41, *p* = .001), as was the linear interaction *(F_{lin}*(1, 10) = 19.98, *p* = .001). This is due to a reduction in depressive symptom scores across time in the depressive symptoms group, and a slight increase in the healthy group (see Figure 2.18).

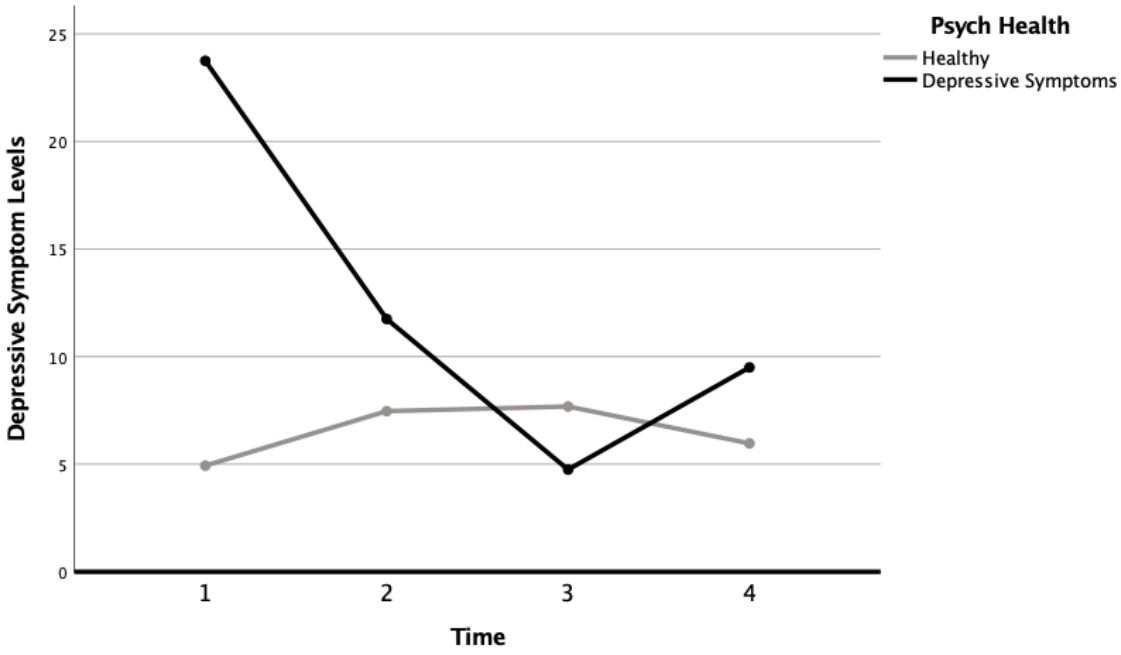

Figure 2.18: Depressive symptoms scores in healthy and depressive symptom conditions at time point 1, 2, 3 and 4

There was a highly significant three-way time*diet-type*psych-health interaction *(F*(3, 30) = 6.51, *p* = .002) and a nearing significance linear interaction *(F_{lin}*(1, 10) = 3.67, *p* = .085) followed by another highly significant quadratic interaction *(F_{quad}*(1, 10) = 10.87, *p* = .008), (see Figure 2.19).

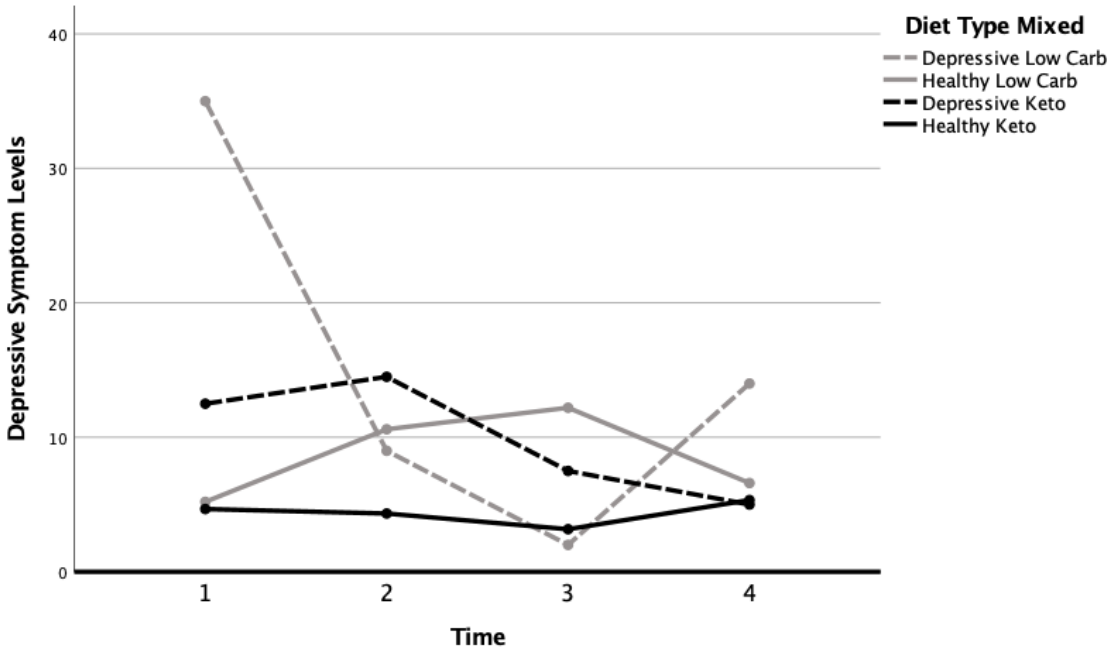

Figure 2.19: Depressive symptoms scores for each diet type in both healthy and depressive symptom conditions across time points 1, 2, 3 and 4

Finally, the time*diet-type and diet-type*psych-health set of interactions were not significant (for all interactions $p>.05$).

2.3.6 Warwick-Edinburgh Mental Well-being Scale (WEMWBS)

WEMWBS Overview of Means, Standard Deviations and Number of Participants

Table 2.25: Mental well-being in healthy and depressive participants (and total sample) across all diet groups at baseline (WEMWBS1), 6 weeks follow up (WEMWBS2), intervention end (WEMWBS3) and end of study (WEMWBS4). Numbers (italics), Means (bold) and SDs (brackets)

	WEMWBS 1			WEMWBS 2			WEMWBS 3			WEMWBS 4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **24.33** (3.01)	*2* **20.00** (7.07)	*8* **23.25** (4.20)	*6* **27.67** (5.85)	*2* **22.00** (8.49)	*8* **26.25** (6.45)	*6* **27.67** (4.50)	*2* **24.00** (4.24)	*8* **26.75** (4.46)	*6* **26.00** (5.80)	*2* **31.00** (5.66)	*8* **27.25** (5.83)
Low Carb	*5* **27.60** (6.99)	*1* **17.00** (.)	*6* **25.83** (7.60)	*5* **27.20** (8.32)	*1* **24.00** (.)	*6* **26.67** (7.55)	*5* **21.20** (10.31)	*1* **25.00** (.)	*6* **21.83** (9.35)	*5* **22.20** (10.47)	*1* **23.00** (.)	*6* **22.33** (9.37)
Total	*11* **25.82** (5.19)	*3* **19.00** (5.29)	*14* **24.36** (5.79)	*11* **27.45** (6.70)	*3* **22.67** (6.11)	*14* **26.43** (6.67)	*11* **24.73** (8.00)	*3* **24.33** (3.06)	*14* **24.64** (7.12)	*11* **24.27** (8.04)	*3* **28.33** (6.11)	*14* **25.14** (7.65)

WEMWBS Time points 1 and 2, With Controls

Table 2.26: Mental well-being in healthy and depressive participants (and total sample) across all diet groups and controls at baseline (WEMWBS1) and 6 weeks follow up (WEMWBS2). Numbers (italics), Means (bold) and SDs (brackets)

	WEMWBS 1			WEMWBS 2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*35* **24.40** (3.97)	*11* **18.82** (3.34)	*46* **23.07** (4.49)	*35* **25.86** (4.72)	*11* **18.82** (3.55)	*46* **24.17** (5.37)
Low Carb	*10* **25.00** (5.98)	*3* **19.00** (3.46)	*13* **23.62** (5.98)	*10* **24.90** (6.56)	*3* **20.33** (4.73)	*13* **23.85** (6.32)
Control	*5* **24.20** (7.43)	*4* **19.00** (3.46)	*9* **21.89** (6.29)	*5* **24.20** (6.76)	*4* **20.50** (4.12)	*9* **22.56** (5.75)
Total	*50* **24.50** (4.70)	*18* **18.89** (3.18)	*68* **23.01** (4.99)	*50* **25.50** (5.24)	*18* **19.44** (3.70)	*68* **23.90** (5.55)

There were no significant main effects of time or diet type across time points 1 and 2 with controls for mental well-being (for all effects $p>.05$).

There was a highly significant main effect of psych-health ($F(1, 62) = 13.38$, $p < 0.001$), which is to be expected due to participants with depressive symptoms generally reporting lower mental well-being scores than the healthy participants, regardless of time or diet type.

There were no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all standard and linear interactions $p>.05$).

WEMWBS Time points 1 and 2, No Controls

Table 2.27: Mental well-being in healthy and depressive participants (and total sample) across all diet groups at baseline (WEMWBS1) and 6 weeks follow up (WEMWBS2). Numbers (italics), Means (bold) and SDs (brackets)

	WEMWBS 1			WEMWBS 2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*35* **24.40** (3.97)	*11* **18.82** (3.34)	*46* **23.07** (4.49)	*35* **25.86** (4.72)	*11* **18.82** (3.55)	*46* **24.17** (5.37)
Low Carb	*10* **25.00** (5.98)	*3* **19.00** (3.46)	*13* **23.62** (5.98)	*10* **24.90** (6.56)	*3* **20.33** (4.73)	*13* **23.85** (6.32)
Total	*45* **24.53** (4.42)	*14* **18.86** (3.23)	*59* **23.19** (4.81)	*45* **25.64** (5.12)	*14* **19.14** (3.68)	*59* **24.10** (5.54)

There were no significant main effects of time or diet type across time points 1 and 2 for mental well-being (for all effects $p>.05$).

There was a highly significant main effect of psych-health ($F(1, 55) = 13.91$, $p < 0.001$), which is to be expected due to participants with depressive symptoms generally reporting lower mental well-being scores than the healthy participants, regardless of time or diet type.

There were no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all standard and linear interactions $p>.05$).

WEMWBS Time points 2 and 3, No Controls

Table 2.28: Mental well-being in healthy and depressive participants (and total sample) across all diet groups at 6 weeks follow up (WEMWBS2) and intervention end (WEMWBS3). Numbers (italics), Means (bold) and SDs (brackets)

	WEMWBS 2			WEMWBS 3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*12* **27.25** (6.02)	*6* **20.00** (4.90)	*18* **24.83** (6.55)	*12* **26.50** (5.47)	*6* **21.67** (5.13)	*18* **24.89** (5.71)
Low Carb	*9* **26.11** (6.17)	*1* **24.00** (.)	*10* **25.90** (5.86)	*9* **24.44** (8.50)	*1* **25.00** (.)	*10* **24.50** (8.02)
Total	*21* **26.76** (5.96)	*7* **20.57** (4.72)	*28* **25.21** (6.22)	*21* **25.62** (6.82)	*7* **22.14** (4.85)	*28* **24.75** (6.48)

There were no significant main effects of time, diet type or psych health between time points 2 and 3 for mental well-being. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

WEMWBS Time points 3 and 4, No Controls

Table 2.29: Mental well-being in healthy and depressive participants (and total sample) across all diet groups at intervention end (WEMWBS3) and end of study (WEMWBS4). Numbers (italics), Means (bold) and SDs (brackets)

	WEMWBS 3			WEMWBS 4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **27.67** (4.50)	*3* **24.00** (3.00)	*9* **26.44** (4.28)	*6* **26.00** (5.80)	*3* **28.67** (5.69)	*9* **26.89** (5.56)
Low Carb	*5* **21.20** (10.31)	*1* **25.00** (.)	*6* **21.83** (9.35)	*5* **22.20** (10.47)	*1* **23.00** (.)	*6* **22.33** (9.37)
Total	*11* **24.73** (8.00)	*4* **24.25** (2.50)	*15* **24.60** (6.86)	*11* **24.27** (8.04)	*4* **27.25** (5.44)	*15* **25.07** (7.37)

There were no significant main effects of time, diet type or psych health between time points 3 and 4 for mental well-being. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

WEMWBS Time points 1, 2 and 3, No Controls

Table 2.30: Mental well-being in healthy and depressive participants (and total sample) across all diet groups at baseline (WEMWBS1), 6 weeks follow up (WEMWBS2) and intervention end (WEMWBS3). Numbers (italics), Means (bold) and SDs (brackets)

	WEMWBS 1			WEMWBS 2			WEMWBS 3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*12* **24.58** (4.54)	*5* **19.00** (5.15)	*17* **22.94** (5.26)	*12* **27.25** (6.02)	*5* **19.60** (5.37)	*17* **25.00** (6.71)	*12* **26.50** (5.47)	*5* **21.20** (5.59)	*17* **24.94** (5.88)
Low Carb	*8* **26.50** (5.66)	*1* **17.00** (.)	*9* **25.44** (6.17)	*8* **26.38** (6.55)	*1* **24.00** (.)	*9* **26.11** (6.17)	*8* **24.13** (9.03)	*1* **25.00** (.)	*9* **24.22** (8.45)
Total	*20* **25.35** (4.97)	*6* **18.67** (4.68)	*26* **23.81** (5.60)	*20* **26.90** (6.08)	*6* **20.33** (5.13)	*26* **25.38** (6.43)	*20* **25.55** (6.99)	*6* **21.83** (5.23)	*26* **24.69** (6.72)

There were no significant main effects of time or diet across time points 1, 2 and 3 for mental well-being (for all effects $p>.05$).

There was a weak non-significant main effect of psych-health ($F(1, 22) = 2.96$, $p = .099$), which is to be expected due to participants with depressive symptoms generally reporting lower mental well-being scores than the healthy participants, regardless of time or diet type.

There were no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all standard, linear, and quadratic interactions $p>.05$).

WEMWBS All Time points, No Controls

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 1 ($p<.05$), however, ANOVA was carried out on the data.

There were no significant main effects of time, diet type or psych health across all time points for mental well-being (for all effects $p>.05$).

Overall, the three-way time*diet-type*psych-health interaction was not significant. However there was a weak non-significant quadratic interaction ($F_{quad}(1, 10) = 4.34$, $p = .064$).

Finally, there were no significant interactions between time*psych-health, diet-type*psych-health or time*diet-type (for all standard, linear, quadratic, and cubic interactions $p>.05$).

2.3.7 Positive and Negative Affect Scale - Positive Affect (PANAS POS)

PANAS POS Overview of Means, Standard Deviations and Number of Participants

Table 2.31: Positive affect in healthy and depressive participants (and total sample) across all diet groups at baseline (PANASPOS1), 6 weeks follow up (PANASPOS2), intervention end (PANASPOS3) and end of study (PANASPOS4). Numbers (italics), Means (bold) and SDs (brackets)

	PANASPOS1			PANASPOS2			PANASPOS3			PANASPOS4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **35.83** (3.43)	*2* **26.50** (3.54)	*8* **33.50** (5.37)	*6* **37.83** (4.92)	*2* **28.50** (17.68)	*8* **35.50** (8.98)	*6* **36.33** (8.60)	*2* **36.00** (5.66)	*8* **36.25** (7.57)	*6* **38.33** (10.25)	*2* **45.50** (4.95)	*8* **40.13** (9.46)
Low Carb	*5* **31.40** (14.93)	*1* **19.00** (.)	*6* **29.33** (14.28)	*5* **30.60** (17.27)	*1* **33.00** (.)	*6* **31.00** (15.48)	*5* **31.20** (16.12)	*1* **37.00** (.)	*6* **32.17** (14.61)	*5* **35.40** (15.42)	*1* **34.00** (.)	*6* **35.17** (13.81)
Total	*11* **33.82** (10.02)	*3* **24.00** (5.00)	*14* **31.71** (9.93)	*11* **34.55** (12.07)	*3* **30.00** (12.77)	*14* **33.57** (11.87)	*11* **34.00** (12.17)	*3* **36.33** (4.04)	*14* **34.50** (10.83)	*11* **37.00** (12.25)	*3* **41.67** (7.51)	*14* **38.00** (11.31)

PANAS POS Time points 1 and 2, With Controls

Table 2.32: Positive affect in healthy and depressive participants (and total sample) across all diet groups and controls at baseline (PANASPOS1) and 6 weeks follow up (PANASPOS2). Numbers (italics), Means (bold) and SDs (brackets)

	PANASPOS1			PANASPOS2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*37* **35.22** (6.38)	*12* **24.17** (7.08)	*49* **32.51** (8.07)	*37* **36.65** (5.52)	*12* **26.92** (8.36)	*49* **34.27** (7.53)
Low Carb	*13* **31.38** (11.03)	*3* **28.00** (7.81)	*16* **30.75** (10.36)	*13* **33.62** (12.31)	*3* **29.00** (7.81)	*16* **32.75** (11.52)
Control	*5* **35.00** (10.20)	*4* **25.00** (7.96)	*9* **30.56** (10.18)	*5* **31.40** (7.80)	*4* **28.25** (12.84)	*9* **30.00** (9.75)
Total	*55* **34.29** (8.03)	*19* **24.95** (7.07)	*74* **31.89** (8.77)	*55* **35.45** (7.86)	*19* **27.53** (8.82)	*74* **33.42** (8.78)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 (p<.05), however, ANOVA was carried out on the data.

There was a highly significant main effect of psych health (F(1, 68) = 9.57, p = .003). This is an expected effect which indicates that those with depressive symptoms reported less positive affect than those who are healthy, regardless of time or diet-type. There were no significant main effects of time or diet type (all p>.05). Finally, none of the sets of interactions of diet-type*psych-health, time*diet-type, time*psych-health or time*diet-type*psych-health were significant (for all standard and linear interactions p>.05).

PANAS POS Time points 1 and 2, No Controls

Table 2.33: Positive affect in healthy and depressive participants (and total sample) across all diet groups at baseline (PANASPOS1) and 6 weeks follow up (PANASPOS2). Numbers (italics), Means (bold) and SDs (brackets)

	PANASPOS1			PANASPOS2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*37* **35.22** (6.38)	*12* **24.17** (7.08)	*49* **32.51** (8.07)	*37* **36.65** (5.52)	*12* **26.92** (8.36)	*49* **34.27** (7.53)
Low Carb	*13* **31.38** (11.03)	*3* **28.00** 7.81)	*16* **30.75** (10.36)	*13* **33.62** (12.31)	*3* **29.00** (7.81)	*16* **32.75** (11.52)
Total	*50* **34.22** (7.91)	*15* **24.93** (7.12)	*65* **32.08** (8.63)	*50* **35.86** (7.83)	*15* **27.33** (8.02)	*65* **33.89** (8.61)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 ($p<.05$), however, ANOVA was carried out on the data.

There was a highly significant main effect of psych health ($F(1, 61) = 9.12$, $p = .004$). This is an expected effect which indicates that those with depressive symptoms reported less positive affect than those who are healthy, regardless of time or diet-type. There were no significant main effects of time or diet type (all $p>.05$).

Finally, none of the sets of interactions of diet-type*psych-health, time*diet-type, time*psych-health or time*diet-type*psych-health were significant (for all standard and linear interactions $p>.05$).

PANAS POS Time points 2 and 3, No Controls

Table 2.34: Positive affect in healthy and depressive participants (and total sample) across all diet groups at 6 weeks follow up (PANASPOS2) and intervention end (PANASPOS3). Numbers (italics), Means (bold) and SDs (brackets)

	PANASPOS2			PANASPOS3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*12* **38.50** (4.21)	*6* **29.00** (10.55)	*18* **35.33** (8.09)	*12* **36.52** (8.44)	*6* **33.33** (9.99)	*18* **35.39** (8.81)
Low Carb	*10* **35.40** (12.77)	*1* **33.00** (.)	*11* **35.18** (12.14)	*10* **36.00** (12.30)	*1* **37.00** (.)	*11* **36.09** (11.67)
Total	*22* **37.09** (9.04)	*7* **29.57** (9.74)	*29* **35.28** (9.61)	*22* **36.23** (10.11)	*7* **33.86** (9.23)	*29* **35.66** (9.80)

There were no significant main effects of time, diet type or psych health between time points 2 and 3 for positive affect. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

PANAS POS Time points 3 and 4, No Controls

Table 2.35: Positive affect in healthy and depressive participants (and total sample) across all diet groups at intervention end (PANASPOS3) and end of study (PANASPOS4). Numbers (italics), Means (bold) and SDs (brackets)

	PANASPOS3			PANASPOS4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **36.33** (8.60)	*3* **36.33** (4.04)	*9* **36.33** (7.09)	*6* **38.33** (10.25)	*3* **40.67** (9.07)	*9* **39.11** (9.36)
Low Carb	*5* **31.20** (16.12)	*1* **37.00** (.)	*6* **32.17** (14.61)	*5* **35.40** (15.42)	*1* **34.00** (.)	*6* **35.17** (13.81)
Total	*11* **34.00** (12.17)	*4* **36.50** (3.32)	*15* **34.67** (10.46)	*11* **37.00** (12.25)	*4* **39.00** (8.12)	*15* **37.53** (11.05)

There were no significant main effects of time, diet type or psych health between time points 3 and 4 for positive affect. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

PANAS POS Time points 1, 2 and 3, No Controls

Table 2.36: Positive affect in healthy and depressive participants (and total sample) across all diet groups at baseline (PANASPOS1), 6 weeks follow up (PANASPOS2) and intervention end (PANASPOS3). Numbers (italics), Means (bold) and SDs (brackets)

	PANASPOS1			PANASPOS2			PANASPOS3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*12* **36.17** (6.46)	*5* **26.20** (6.30)	*17* **33.24** (7.78)	*12* **38.50** (4.21)	*5* **27.60** (11.15)	*17* **35.29** (8.34)	*12* **36.42** (8.44)	*5* **32.60** (10.99)	*17* **35.29** (9.07)
Low Carb	*9* **32.33** (10.77)	*1* **19.00** (.)	*10* **31.00** (11.00)	*9* **34.89** (13.44)	*1* **33.00** (.)	*10* **34.70** (12.69)	*9* **35.67** (13.00)	*1* **37.00** (.)	*10* **35.80** (12.26)
Total	*21* **34.52** (8.55)	*6* **25.00** (6.36)	*27* **32.41** (8.96)	*21* **36.95** (9.24)	*6* **28.50** (10.21)	*27* **35.07** (9.93)	*21* **36.10** (10.34)	*6* **33.33** (9.99)	*27* **35.48** (10.14)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 ($p<.05$), however, ANOVA was carried out on the data.

There was an overall significant main effect of time *(*$F(2, 46) = 4.03$, $p = .024$) and a significant linear trend *(*$F_{lin}(1, 23) = 8.29$, $p = .008$) with the levels of positive affect reported at time point 2, higher than the levels at time point 1 across groups. The main effects of psych health and diet type were not significant (for both $p>.05$).

The overall time*psych-health interaction showed a non-significant trend *(*$F(2, 46) = 2.09$, $p = .135$) but the linear interaction was significant *(*$F_{lin}(1, 23) = 4.59$, $p = .043$) due to an increase in positive affect across time in the depressive symptoms group, and no change in the healthy group. This suggests that the main effect of time was in part moderated by psych health group (see Figure 2.20).

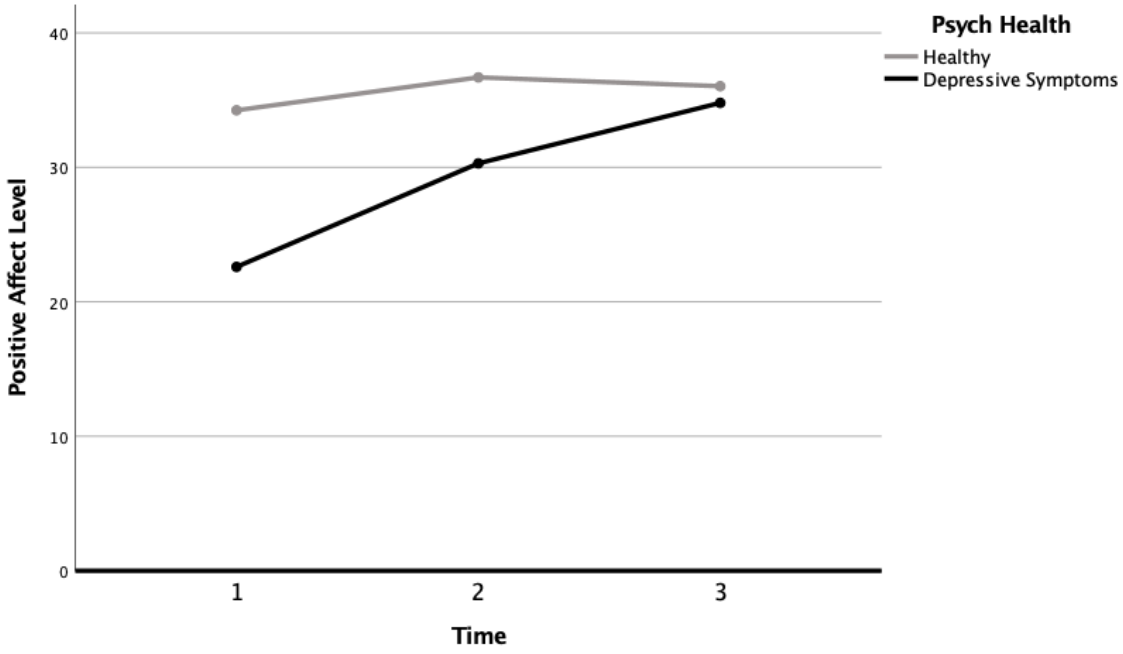

Figure 2.20: Positive affect scores in healthy and depressive symptom conditions (collapsed across diet types) at time point 1 (baseline) time point 2 (6 week follow up) and time point 3 (intervention end)

Finally, none of the sets of interactions of diet-type*psych-health, time*diet-type or time*diet-type*psych-health were significant (for all standard, linear, and quadratic interactions $p>.05$).

PANAS POS All Time points, No Controls

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 ($p<.05$), however, ANOVA was carried out on the data.

There was a significant main effect of time *($F(3, 30) = 4.37$, $p = .011$) and a significant linear effect ($F_{lin}(1, 10) = 16.58$, $p = .002$). This shows that the levels of positive affect reported at time point 2 were higher than the levels at time point 1 across groups.

There was no significant main effect of psych health or diet type ($p>.05$).

For the time*psych-health interaction there was a borderline significant trend ($F(3, 30) = 2.52$, $p = .077$) and a significant linear interaction ($F_{lin}(1, 10) = 8.56$, $p = .015$) due to an increase in positive affect across time in the depressive symptoms group (see Figure 2.21).

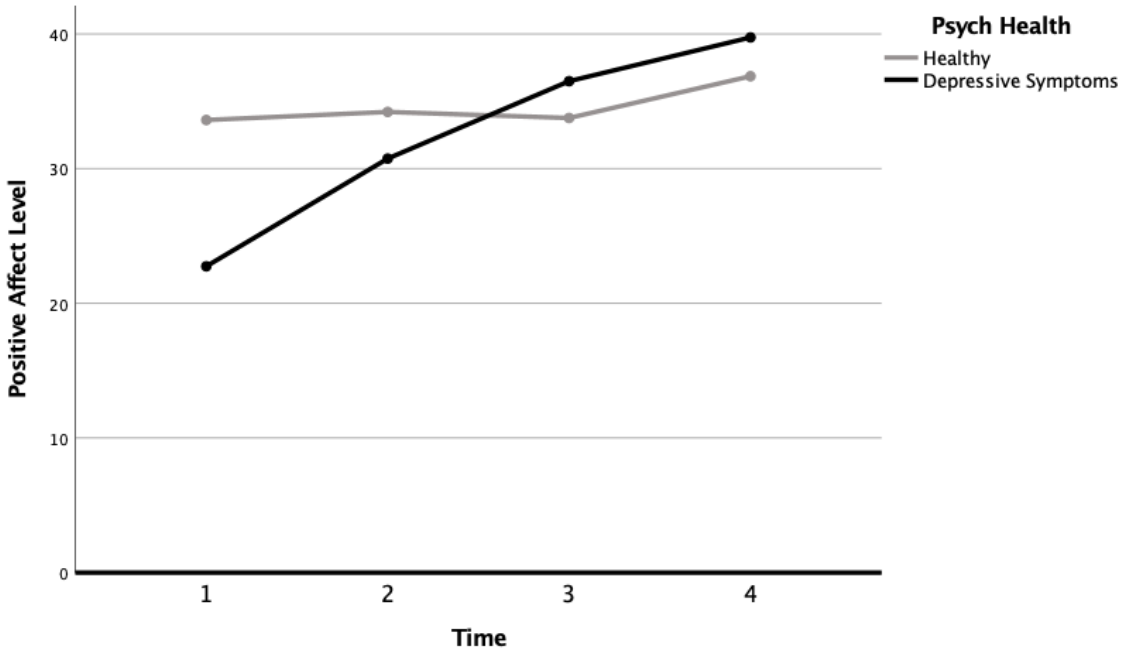

Figure 2.21: Positive affect scores in healthy and depressive symptom conditions (collapsed across diet types) at time point 1 (baseline), time point 2 (6 week follow up), time point 3 (intervention end) and time point 4 (end of study)

Finally, none of the sets of interactions of diet-type*psych-health, time*diet-type or time*diet-type*psych-health were significant (for all standard, linear, quadratic, and cubic interactions $p>.05$).

2.3.8 Positive and Negative Affect Scale - Negative Affect (PANAS NEG)

PANAS NEG Overview of Means, Standard Deviations and Number of Participants

Table 2.37: Negative affect in healthy and depressive participants (and total sample) across all diet groups at baseline (PANASNEG1), 6 weeks follow up (PANASNEG2), intervention end (PANASNEG3) and end of study (PANASNEG4). Numbers (italics), Means (bold) and SDs (brackets)

	PANASNEG1			PANASNEG2			PANASNEG3			PANASNEG4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **11.83** (1.33)	*2* **23.50** (12.02)	*8* **14.75** (7.15)	*6* **11.67** (1.75)	*2* **21.00** (11.31)	*8* **14.00** (6.26)	*6* **12.50** (3.51)	*2* **15.50** (.71)	*8* **13.25** (3.28)	*6* **13.33** (4.27)	*2* **13.50** (.707)	*8* **13.38** (3.62)
Low Carb	*5* **12.00** (2.35)	*1* **27.00** (.)	*6* **14.50** (6.47)	*5* **14.00** (6.29)	*1* **12.00** (.)	*6* **13.67** (5.68)	*5* **13.80** (2.86)	*1* **12.00** (.)	*6* **13.50** (2.67)	*5* **11.40** (1.67)	*1* **15.00** (.)	*6* **12.00** (2.10)
Total	*11* **11.91** (1.76)	*3* **24.67** (8.74)	*14* **14.64** (6.61)	*11* **12.73** (4.34)	*3* **18.00** (9.54)	*14* **13.86** (5.79)	*11* **13.09** (3.15)	*3* **14.33** (2.08)	*14* **13.36** (2.93)	*11* **12.45** (3.36)	*3* **14.00** (1.00)	*14* **12.79** (3.04)

PANAS NEG Time points 1 and 2, With Controls

Table 2.38: Negative affect in healthy and depressive participants (and total sample) across all diet groups and controls at baseline (PANASNEG1) and 6 weeks follow up (PANASNEG2). Numbers (italics), Means (bold) and SDs (brackets)

	PANASNEG1			PANASNEG2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*37* **14.49** (4.48)	*12* **23.33** (6.47)	*49* **16.65** (6.28)	*37* **14.30** (4.73)	*12* **21.83** (7.74)	*49* **16.14** (6.42)
Low Carb	*13* **13.46** (4.48)	*3* **23.00** (4.58)	*16* **15.25** (5.80)	*13* **13.46** (5.19)	*3* **19.67** (11.60)	*16* **14.63** (6.76)
Control	*5* **19.40** (9.81)	*4* **20.75** (8.66)	*9* **20.00** (8.76)	*5* **16.00** (5.48)	*4* **17.50** (1.92)	*9* **16.67** (4.12)
Total	*55* **14.69** (5.24)	*19* **22.74** (6.45)	*74* **16.76** (6.56)	*55* **14.25** (4.85)	*19* **20.58** (7.45)	*74* **15.88** (6.23)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 ($p<.05$), however, ANOVA was carried out on the data.

There was a significant main effect of time ($F(1, 68) = 3.94$, $p = .051$). The reported levels of negative affect at time point 2 were significantly lower than the levels at time point 1. This shows that on average, all scores were decreasing.

There was a highly significant main effect of psych health ($F(1, 68) = 14.04$, $p < 0.001$) with the levels of negative affect decreasing over time across groups. This is an expected effect which indicates that those with depressive symptoms

reported more negative affect than those who are healthy, regardless of time or diet-type.

There was no significant main effect of diet type between time points 1 and 2 for negative affect. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

PANAS NEG Time points 1 and 2, No Controls

Table 2.39: Negative affect in healthy and depressive participants (and total sample) across all diet groups at baseline (PANASNEG1) and 6 weeks follow up (PANASNEG2). Numbers (italics), Means (bold) and SDs (brackets)

	PANASNEG1			PANASNEG2		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*37* **14.49** (4.48)	*12* **23.33** (6.47)	*49* **16.65** (6.28)	*37* **14.30** (4.73)	*12* **21.83** (7.74)	*49* **16.14** (6.42)
Low Carb	*13* **13.46** (4.48)	*3* **23.00** (4.58)	*16* **15.25** (5.80)	*13* **13.46** (5.19)	*3* **19.67** (11.59)	*16* **14.63** (6.76)
Total	*50* **14.22** (4.46)	*15* **23.27** (5.99)	*65* **16.31** (6.15)	*50* **14.08** (4.81)	*15* **21.40** (8.19)	*65* **15.77** (6.49)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 ($p<.05$), however, ANOVA was carried out on the data.

There was a highly significant main effect of psych health ($F(1, 61) = 22.76$, $p <0.001$). This is an expected effect which indicates that those with depressive

symptoms reported more negative affect than those who are healthy, regardless of time or diet-type.

There were no significant main effects of time or diet type between time points 1 and 2 for negative affect. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, $p>.05$).

PANAS NEG Time points 2 and 3, No Controls

Table 2.40: Negative affect in healthy and depressive participants (and total sample) across all diet groups at 6 weeks follow up (PANASNEG2) and intervention end (PANASNEG3). Numbers (italics), Means (bold) and SDs (brackets)

	PANASNEG2			PANASNEG3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*12* **12.92** (2.84)	*6* **21.17** (7.68)	*18* **15.67** (6.21)	*12* **13.83** (5.36)	*6* **18.83** (5.71)	*18* **15.50** (5.83)
Low Carb	*10* **12.50** (4.53)	*1* **12.00** (.)	*11* **12.45** (4.30)	*10* **12.30** (2.58)	*1* **12.00** (.)	*11* **12.27** (2.45)
Total	*22* **12.73** (3.62)	*7* **19.86** (7.82)	*29* **14.45** (5.71)	*22* **13.14** (4.30)	*7* **17.86** (5.82)	*29* **14.28** (5.04)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 ($p<.05$), however, ANOVA was carried out on the data.

The main effect of diet type was nearing significance ($F(1, 25) = 3.81$, $p = .062$).

There were no significant main effects of time or psych health between time points 2 and 3 for negative affect. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, *p*>.05).

PANAS NEG Time points 3 and 4, No Controls

Table 2.41: Negative affect in healthy and depressive participants (and total sample) across all diet groups at intervention end (PANASNEG3) and end of study (PANASNEG4). Numbers (italics), Means (bold) and SDs (brackets)

	PANASNEG3			PANASNEG4		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*6* **12.50** (3.51)	*3* **15.00** (1.00)	*9* **13.33** (3.08)	*6* **13.33** (4.27)	*3* **14.00** (1.00)	*9* **13.56** (3.43)
Low Carb	*5* **13.80** (2.86)	*1* **12.00** (.)	*6* **13.50** (2.67)	*5* **11.40** (1.67)	*1* **15.00** (.)	*6* **12.00** (2.10)
Total	*11* **13.09** (3.15)	*4* **14.25** (1.71)	*15* **13.40** (2.82)	*11* **12.45** (3.35)	*4* **14.25** (.96)	*15* **12.93** (2.99)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 4 (p<.05), however, ANOVA was carried out on the data.

There were no significant main effects of time, diet type or psych health between time points 3 and 4 for positive affect. There were also no significant interactions between time*psych-health, diet-type*psych-health, time*diet-type or time*diet-type*psych-health (for all effects and interactions, *p*>.05).

PANAS NEG Time points 1, 2 and 3, No Controls

Table 2.42: Negative affect in healthy and depressive participants (and total sample) across all diet groups at baseline (PANASNEG1), 6 weeks follow up (PANASNEG2) and intervention end (PANASNEG3). Numbers (italics), Means (bold) and SDs (brackets)

	PANASNEG1			PANASNEG2			PANASNEG3		
Group	Healthy	Depressive	Total	Healthy	Depressive	Total	Healthy	Depressive	Total
Ketogenic	*12* **13.00** (4.45)	*5* **22.60** (7.13)	*17* **15.82** (6.83)	*12* **12.92** (2.84)	*5* **22.40** (7.89)	*17* **15.71** (6.40)	*12* **13.83** (5.36)	*5* **19.80** (5.81)	*17* **15.59** (6.00)
Low Carb	*9* **11.89** (2.71)	*1* **27.00** (.)	*10* **13.40** (5.42)	*9* **12.56** (4.80)	*1* **12.00** (.)	*10* **12.50** (4.53)	*9* **12.33** (2.74)	*1* **12.00** (.)	*10* **12.30** (2.58)
Total	*21* **12.52** (3.76)	*6* **23.33** (6.62)	*27* **14.93** (6.35)	*21* **12.76** (3.70)	*6* **20.67** (8.24)	*27* **14.52** (5.90)	*21* **13.19** (4.40)	*6* **18.50** (6.09)	*27* **14.37** (5.21)

Levene's test confirmed that the assumption of homogeneity of variance was not met for time point 2 ($p<.05$), however, ANOVA was carried out on the data.

There was an overall significant effect of time *(*$F(2, 46) = 4.46$, $p = .017$) and a highly significant linear trend *(*$F_{lin}(1, 23) = 8.27$, $p = .009$) with the levels of negative affect reported at time point 2, lower than the levels at time point 1 across groups.

There was also an expected significant main effect of psych health *(*$F(1, 23) = 9.34$, $p = .006$) due to participants with depressive symptoms generally reporting higher negative affect scores than the healthy participants, regardless of time or diet type.

The main effect of diet type was not significant ($p>.05$).

The time*psych-health interaction was significant overall *(*$F(2, 46) = 5.67$, $p = .006$) and at the linear interaction level *(*$F_{lin}(1, 23) = 11.02$, $p = .003$).

The time*diet-type overall interaction was significant *(*$F(2, 46) = 3.26$, $p = .048$) and there was also a significant linear trend *(*$F_{lin}1, 23) = 4.80$, $p = .039$). This suggests that the main effect of time was impacted by diet type (see Figure 2.22). Scores remained stable in the keto diet group whilst those in the low carb group showed a linear like decline in negative affect scores.

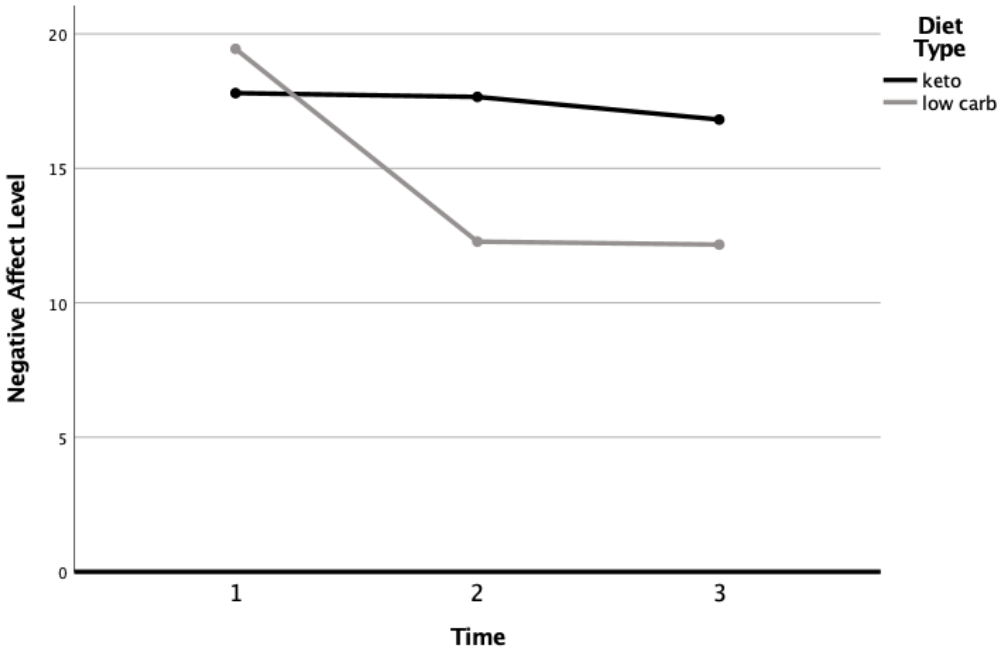

Figure 2.22: Negative affect scores in keto and low carb diet types at time points 1, 2 and 3

The overall three-way time*diet-type*psych-health interaction was significant *(F*(2, 46) = 3.59, *p* = .035). This suggests that the main effect of time was partially impacted by both diet type and psych health (see Figure 2.23). Finally, the diet-type*psych-health interaction was not significant (*p*>.05).

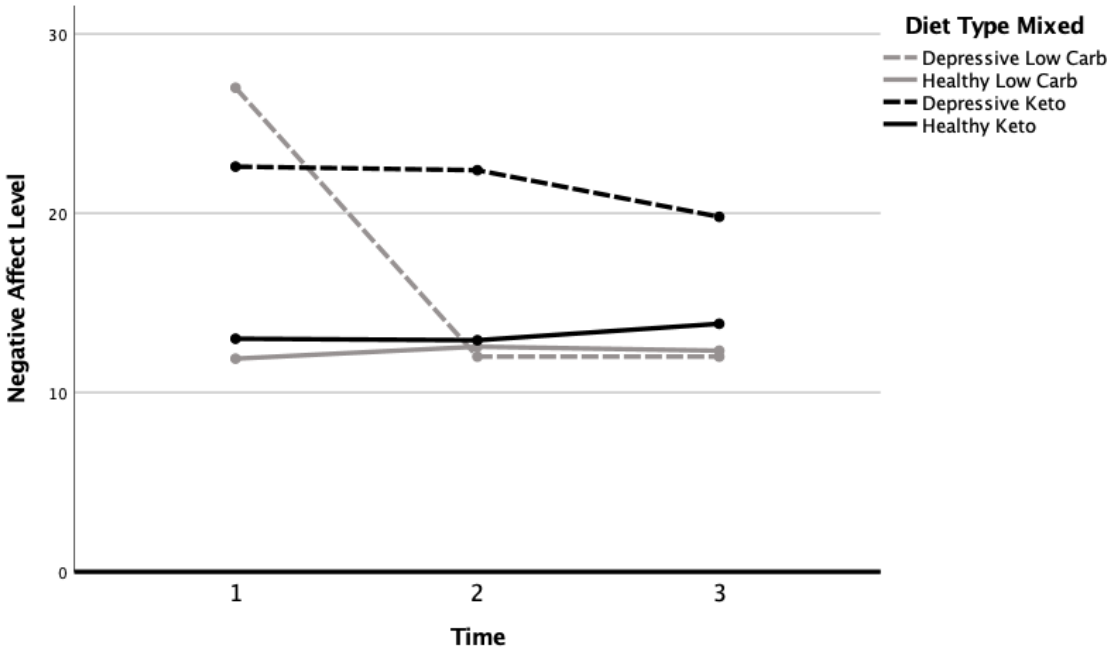

Figure 2.23: Negative affect scores for each diet type in both healthy and depressive symptom conditions across time points 1, 2 and 3

PANAS NEG All Time points, No Controls

Levene's test confirmed that the assumption of homogeneity of variance was not met for time points 1, 2 or 4 (p<.05), however, ANOVA was carried out on the data.

There was a significant main effect of time *(*$F(3, 30) = 4.04$, $p = .016$) and a significant linear trend *(*$F_{lin}(1, 10) = 6.52$, $p = .029$). This shows that the levels of negative affect reported at time point 2 were lower than the levels at time point 1 across groups.

There was a significant main effect of psych health ($F(1, 10) = 7.06$, $p = .024$). This is an expected effect which indicates that those with depressive symptoms

reported more negative affect than those who are healthy, regardless of time or diet-type.

There was no significant main effect of diet type (p>.05).

There was a highly significant time*psych-health interaction *(F*(3, 30) = 5.56, p = .004) and a significant linear trend *(F_{lin}*(1, 10) = 7.85, p = .019). There was also a significant quadratic trend *(F_{quad}*(1, 10) = 7.48, p = .021). This is most likely due to a reduction in negative affect levels across time in the depressive symptoms group, and no change in the healthy group (see Figure 2.24).

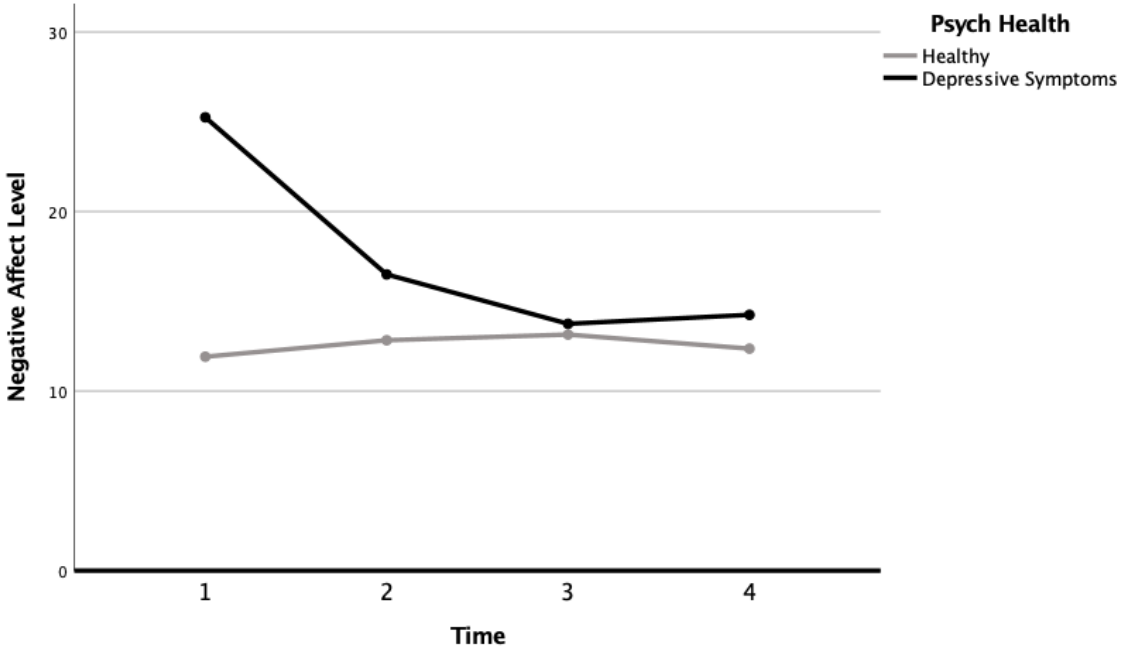

Figure 2.24: Negative affect scores in healthy and depressive symptom conditions (collapsed across diet types) at time point 1 (baseline), time point 2 (6 week follow up), time point 3 (intervention end) and time point 4 (end of study)

The overall three-way time*diet-type*psych-health interaction was not significant (p>.05) but there was a significant quadratic interaction *(F_{quad}*(1, 10) = 8.17, p = .017) suggesting that the main effect of time was partially impacted by both diet type and psych health (see Figure 2.25).

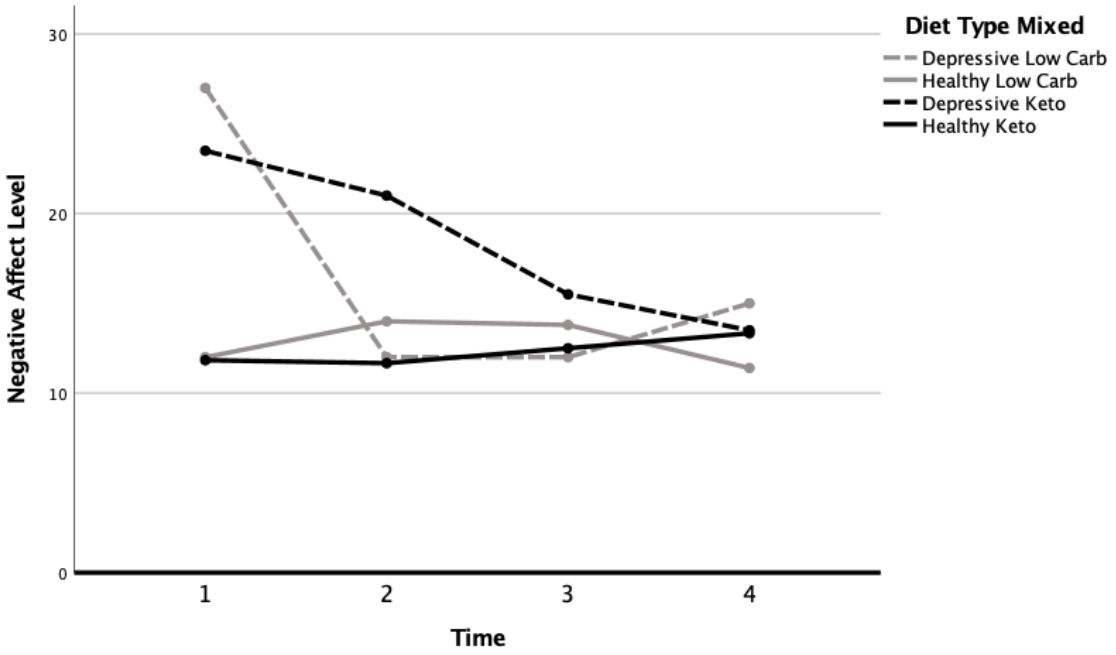

Figure 2.25: Negative affect scores for each diet type in both healthy and depressive symptom conditions across time points 1, 2, 3 and 4

Finally, both the time*diet-type interaction and the diet-type*psych-health interaction were not significant (for all standard, linear, quadratic, and cubic interactions p>.05).

All findings across all time points can be seen in table 2.43 below, along with the main effects and interaction values.

Table 2.43: Summary of findings across each time point, main effects (ME), Borderline Main Effects (BME), and interaction with their values

Time point	PSS	GAD	CESD	WEMWBS	PANAS POS	PANAS NEG
T1-T2 Controls	ME of Time .046	ME of Time .018 ME of Psych Health .000	ME of Psych Health .000	ME of Psych Health .001	ME of Psych Health .003	BME of Time .051 ME of Psych Health .000
T1-T2 No Controls	ME of Time .041 ME of Psych Health .000	ME of Time .035 ME of Psych Health .000 Interaction Time*Diet*Psych Health .055	ME of Psych Health .000	ME of Psych Health .000	ME of Psych Health .004	ME of Psych Health .000
T2-T3	None	BME of Diet .056, ME of Psych Health .059	None	None	None	None
T3-T4	None	None	Interaction Time*Psych Health .048 Time*Diet*Psych Health .004	None	None	None

Table 2.43: (Continued)

Time point	PSS	GAD	CESD	WEMWBS	PANAS POS	PANAS NEG
T1-T2 -T3	BME of Time .062 ME Psych Health .018 Interaction Time*Diet .038	ME of Time .006 ME of Psych Health .003 Interaction Time*Diet .014 Time*Psych Health .016 Time*Diet*Psych Health .007	ME of Time .000 ME of Psych Health .048 Interaction Time*Diet .014 Time*Psych Health .000 Time*Diet*Psych Health .001	None	ME of Time .008 Interaction Time*Psych Health .043	ME of Time .009 ME of Psych Health .006 Interaction Time*Diet .039 Time*Psych Health .003 Time*Diet*Psych Health .051
T1-T2-T3-T4	None	ME of Time .016 ME of Psych Health .022 Interaction Time*Diet .039 Time*Psych Health .001	ME of Time .003 Interaction Time*Psych Health .001	None	ME of Time .002 Interaction Time*Psych Health .015	ME of Time .029 ME of Psych Health .024 Interaction Time*Psych Health .019 Time*Diet*Psych Health Quadratic .017

2.4 Discussion

The present study sought to investigate whether reducing carbohydrate intake would improve aspects of psychological well-being in those with depressive symptoms. Using a ketogenic diet, and a low carbohydrate diet as interventions and a diet as usual wait list group as a control, the online intervention was run for 12 weeks in a mixed sample of healthy adults and those with depressive symptoms. This was followed by 12 weeks of no online intervention before the study end at 24 weeks.

2.4.1 Hypothesis 1: Ketogenic diet

The first hypothesis for this study was that 'Lowering carbohydrate intake to initiate ketosis will improve psychological well-being in people with mild to moderate symptoms of depression'. The question of whether the ketogenic dietary intervention improved psychological well-being in those with depressive symptoms compared to those in the wait list control group (with depressive symptoms) was investigated.

The results of this study found that over six weeks, from time point 1 to time point 2, the KD intervention did not improve the five aspects of psychological well-being (stress, anxiety, depression, positive and negative affect, and mental well-being) more than the wait list control group who followed diet as usual.

The results found were not in line with the hypothesis, that lowering carbohydrate intake, whilst initiating ketosis, in other words, following the KD intervention, would improve aspects of psychological well-being in those with

mild to moderate symptoms of depression. However, it could be argued that the KD had not been initiated for long enough to see a difference.

No significant improvements were found in other measures of psychological well-being across all time points (T1, T2, T3 and T4), such as stress, anxiety, depressive symptoms, mental well-being, positive affect, or negative affect in those following the KD intervention within the depressive symptoms group.

This is not in keeping with the improvements found in a recent study by Danan et al. (2022). Their participants experienced a clinically significant reduction in depression symptoms from 25.4 points on the Hamilton Depression Rating Scale down to 7.7. These findings are also not in keeping with rodent studies which show a decrease in anxiety levels (Ari et al., 2016; Hollis et al., 2018) and reduced susceptibility to anxiety (Murphy et al., 2004), anxiety like symptoms (Kashiwaya et al., 2013), stress (Brownlow et al., 2017), depressive like behaviours (Guan et al., 2020), and depression (Gumus et al., 2022; Sussman et al., 2015), which suggested that the ketogenic diet may have antidepressant properties. Once again, it is difficult to extrapolate these findings to humans as there are only a few case studies and no large, well-controlled trials to compare to.

As this study focused on reducing the carbohydrates in the diet in order to reach ketosis it did not encourage the increase of fats in the diet. This dietary intervention composition is still characteristic of a ketogenic diet however, some variations of the ketogenic diet, including the medical ketogenic diet that is used to treat treatment resistant epilepsy, uses a higher fat approach with a ratio of

3:1 fat: protein + carbohydrate ratio, therefore keeping carbohydrates low and fat high. Perhaps as suggested by Murphy et al. (2013) in their findings in rodents, that it is the high fat that is anxiolytic and reduces anxiety. Perhaps the reduction in carbohydrates alone is not enough to reduce anxiety levels within the time frame of this study. If participants reduced their carbohydrates low enough to induce ketosis, as they enter ketosis, they produce ketones which will be utilised by the brain once created. But maybe this mechanism takes time to work or is impaired in some way in those with higher levels of anxiety and depressive symptoms and overall poorer psychological well-being. It could be that they need the additional fat to compensate during this time. One case study of a lady with MDD saw her depression scores reduce from moderately severe, to no symptoms reported over 12 weeks at 65% fat, 25% protein and 10% carbohydrates (Tillery et al., 2021).

It could also be that the KD dietary intervention did not reduce carbohydrates low enough to initiate ketosis as the guidelines were set to <50g per day. This may be low enough for some but not all. Recent research by Tidman et al. (2022) in participants with Parkinson's disease found improvements in anxiety after 12 weeks of following a KD with <16g carbohydrates per day but not in depressive symptoms. This possibly higher level of dietary carbohydrates alongside the absent focus on increasing fat levels could have left participants without the anxiolytic mechanism.

2.4.2 Hypothesis 2: Low carbohydrate diet

The second hypothesis for the study was that 'Lowering carbohydrate intake without initiating ketosis will improve psychological well-being in people with

mild to moderate symptoms of depression'. The question whether the LCD intervention improves psychological well-being in those with depressive symptoms compared to those following diet as usual in the control group (with depressive symptoms) was explored.

It was expected that there would be some improvements in aspects of psychological well-being over six weeks in the LCD intervention group compared to the control group but that the improvements may not be as significant as the KD intervention group.

Over six weeks from time point 1 to time point 2, the LCD intervention did not significantly improve psychological well-being more than the control group. Therefore, for this hypothesis, there were no improvements to report based on the LCD. However, it could be argued that the diet had not been initiated for long enough for improvements to be observed.

When looking at the data over a longer period of time, in this case the 12 week intervention (T1, T2, T3), the LCD did show a significant reduction in anxiety (p = .037), stress (p = .038) and negative affect (p = .048) scores. This was across T1 at baseline, T2 at 6 weeks follow up and T3 at 12 weeks intervention end. These improvements were observed specifically in participants within the depressive symptoms groups, for anxiety (p = .010) nearing significance for stress (p = .072), and negative affect (p = .035).

When looking at the LCD depressive symptoms group across the entire study, all four time points, T1, T2, T3 including T4 at 24 weeks, a significant decrease in depressive symptoms scores was also found (p = .002).

Although looking at the differences from time point 1 to time point 4 (without T2 and T3) would have been ideal, the sample size at T4 was too small to achieve meaningful results.

The results showed that lowering carbohydrate intake, without knowingly initiating ketosis, in other words, following the LCD intervention, improved some aspects of psychological well-being in those with mild to moderate symptoms of depression over the duration of the intervention. Specifically, a decrease in anxiety, stress, and negative affect were found although the LCD intervention did not improve all measures of psychological well-being. Improvements in the remaining aspects of psychological well-being, mental well-being, depressive symptoms, and positive affect were not significant in those following the LCD intervention within the depressive symptoms group.

This is in keeping with recent research using a low carbohydrate approach, in those with food addiction, who also had education and psychosocial support. They experienced an increase in mental well-being from low to population norms over 10-14 weeks (Unwin et al., 2022). Although this study didn't see an improvement in the exact WEMWBS measure of mental well-being, aspects of mental and psychological well-being did improve over the duration of the study.

From these findings, perhaps the higher fat levels are not necessary to produce anxiolytic effects as earlier suggested for hypothesis 1. In the research there are now demonstrated mechanisms of the KD that may ameliorate depression and improve psychological well-being such as alterations in inflammation, oxidative stress, neurotransmitter regulation and glucose metabolism (Norwitz et al.,

2020). However, it does not appear to be that reducing carbohydrates further than <50g per day is necessary, at least to see some improvements in aspects of psychological well-being. The caveat here could be that the participants in this study did reach ketosis unknowingly.

2.4.3 Hypothesis 3: Ketogenic diet vs Low carbohydrate diet

The third hypothesis of this study was that 'The ketogenic diet will show greater improvements in psychological well-being in those with mild to moderate depressive symptoms compared with a low carb diet. The ketogenic diet will have a greater impact because of the ketones that are produced which are not present in the low carb diet'. The questions of which dietary intervention (LCD or KD) had the greatest impact on psychological well-being in those with depressive symptoms was explored.

According to the current literature, it was proposed that those with mild to moderate depressive symptoms following a KD would experience a greater improvement in aspects of psychological well-being compared to those following a LCD. The difference expected would be due to the presence of ketone bodies in the KD group which are created when the total amount of carbohydrates per day is kept below 50g per day (Wylie-Rosett et al., 2013). Ketone bodies have been shown to be neuroprotective and anti-inflammatory and they are, for most people not present when following a LCD with total carbohydrates between 90-130g per day.

The results found in this study do not support this hypothesis. As stated under hypothesis 2 above, depressive symptoms, anxiety, stress, and negative affect

scores were found to decrease in participants with mild to moderate depressive symptoms following the LCD intervention. However, those with mild to moderate depressive symptoms following the KD intervention did not experience any significant improvements in measures of psychological well-being. Therefore, participants in the LCD intervention with mild to moderate depressive symptoms, experienced greater improvements in psychological well-being compared to those in the KD intervention.

2.4.4 Further findings

Overall, as expected, those in the depressive symptoms groups of both dietary interventions showed lower levels of psychological well-being generally compared to those in the healthy groups, regardless of diet or time.

In the depressive symptoms groups, the results further showed a borderline increase in positive affect symptoms (main interaction p = .077, linear interaction p = .015), and a significant decrease in negative affect symptoms (p = .004) across all four time points regardless of diet.

2.4.5 Limitations

There were some limitations to this study that are outlined here. There are some methodological features of this study that should be considered. There were challenges with the recruitment stage which meant that it took longer than initially predicted to recruit the starting sample. Though the study was advertised through many forms, the strict inclusion and exclusion criteria may have been a contributing factor. Also, as this study was recruiting for participants with mild to moderate depressive symptoms, it may be that they did not feel as

motivated to continue the intervention, particularly as they were blinded to the potential impact the diet may have. The results showed that of the 22 participants who remained in the study to the end (T4, 24 weeks), less than half (36.4%) were part of the depressive symptoms group, with mild to moderate depressive symptoms. In future, the importance of running a double blind or blind study should be considered and weighed against the possibility of increasing retention or maintaining sample size from study start to finish in these populations.

The inclusion criteria allowed those on antidepressants for three weeks or more into the study. As seen in the table below, there were some participants in the depressive symptoms psych health condition that were taking antidepressants. The effects of these antidepressants may have been working already to keep the participant as symptom free as possible. This means that perhaps these 20 participants would not be expected to improve further. Alongside this, there were 18 participants in the healthy psych health condition that were taking antidepressants. Perhaps the medications here were also keeping participants as well as possible, so no further improvements in aspects of psychological well-being could be expected.

Table 2.44: Number of participants in each diet type group and psych health condition taking antidepressant medication for three weeks or more at baseline (T0)

Diet Type Group	*Psych Health Condition*	*No. on Antidepressants*
Low Carb	Depressive Symptoms	3
	Healthy	6
Keto	Depressive Symptoms	17
	Healthy	12
Total	Total	38

One of the main reasons to explain the lack of statistical significance across this study is sample size. The results must be considered due to the small sample size at the end of the study and the high level of attrition. This will be addressed further in the next chapter. But as this study did not reach a large sample size, it is possible that the sample was not representative of the general population. It also made it difficult to carry out analysis as the sample size reduced as the study progressed. In order to address this limitation, it was warranted to take a closer look at the data. It was decided that subsections with further analyses across each time point would be added for each of the dependent variables. This is seen in the results section above. The high rate of attrition points to the possible difficulty of following either an online dietary intervention, or specifically a low carbohydrate or ketogenic diet. Future studies should involve and recruit larger sample sizes to allow for these expected higher rates of attrition.

There were also some challenges with the design of this study. The limitation here for the first two hypotheses is that the wait list control group remained in

the study only for six weeks. The short duration of the wait list control group therefore limits the interpretation of these findings.

As the study and allocation to the control group remained blind to participants, these participants were told to keep their diet as normal while recruitment for the study continued, but to complete any questionnaires that they were sent along the way. It was agreed that six weeks may be the longest a participant would continue their diet as normal before dropping out of the study.

There may have been improvements in psychological well-being noted between intervention and control group had the control group stayed for the duration of the study and measures taken at T3, 12 weeks and T4, 24 weeks. This is suggested as improvements in aspects of psychological well-being were found across all time points in this study.

Future studies should consider keeping a control group in for the duration of the study, with other strategies to maintain participant blindness, to see the full impact of the interventions across all time points.

Though during the design of the interventions, care was taken to separate and define the daily carbohydrate levels for each dietary intervention, 90-130g per day for the LCD and <50g per day for the KD, there was no way to measure compliance and adherence to these levels. Therefore, it is important to understand that some participants in the LCD intervention may have reached a state of ketosis unknowingly during this time for many reasons, one of which is due to individual carbohydrate tolerance. This means that though <50g of carbohydrates is required per day to enter ketosis, this can vary from person to

person. Some will need less than this to achieve ketosis and others may achieve ketosis with more. The gap between the two recommended carbohydrate target ranges should have allowed for individual variance, however the researcher cannot be sure.

Adding to this, for this study, as it was self-funded by the researcher, the gold standard of measuring ketones, blood ketone meters or breath meters were not sent to participants due to their high cost. All future research studies should monitor ketones for adherence and compliance where possible.

2.4.6 Implications

As neither the KD nor LCD significantly improved psychological well-being within the first six weeks compared to wait list control group, it appears that it may take time for changes to occur as improvements were noted at 12 and 24 weeks in the LCD. This suggests that the diet should be followed for longer to get the full benefits. This could be for two reasons, the first, that it takes time to adapt to a new diet, follow it correctly and become comfortable knowing what to eat, and the second, that it takes time for the mechanisms of the diets to work in each person depending on their physiological and psychological health. And even then, it may not work for everyone, perhaps only a subsample of those with mild to moderate depressive symptoms or poor psychological well-being.

The results from the LCD intervention do bring some hope, in that they suggest over a period of 12-24 weeks, reducing daily carbohydrate intake could improve aspects of psychological well-being in those with mild to moderate depressive symptoms without needing to reach levels of ketosis. Although research shows

that there are significant mechanisms by which ketones may improve psychological well-being, from this study it may be that it is not necessary to still see some improvements.

The outcomes of this research show that in those with mild to moderate depressive symptoms, following a LCD significantly improves aspects of psychological well-being. Therefore, further studies should be carried out on larger samples and other psychiatric conditions to develop this dietary intervention as an adjunctive therapy to current psychiatric treatments such as psychiatric medications which are well known to have severe debilitating side effects (Correll et al., 2015). This dietary approach may then be extended as a preventative measure to other physiological diseases.

This may in turn prove to be a more cost-effective approach to treating psychiatric conditions and their side effects such as T2D, obesity and other symptoms of metabolic syndrome. It may also reduce the amount of psychiatric medication needed. The results of this study provide further support for future research on the impact of a low carbohydrate dietary intervention for the improvement of psychological well-being.

Chapter 3: Study 1 - Additional Measures

3.1 Introduction

3.1.1 Overview

The core variables and measures that make up the term 'psychological well-being' for this study are depression, anxiety, affect, mental well-being and stress. However, engaging in any dietary intervention will have a positive effect on several different areas of psychological well-being and will interact with many other psychological factors. In this chapter, other variables such as self-compassion, body appreciation, and social support will be explored.

To improve and maintain good physical and mental health, a multifactorial approach is required for a diet to be successful (Alonso-Domínguez et al., 2019), particularly in the management of obesity (Bray et al., 2016; Zapico et al., 2012). There are many educational, psychological, physiological, and behavioural factors associated with creating new healthy behavioural habits (Huttunen-Lenz et al., 2022), managing long term chronic diseases (Kelly et al., 2015) and improving and maintaining overall health (Buscemi et al., 2013). Therefore, in addition to the core measures of diet outcome explored in study 1, it is important to allow for the possible influence of a range of other important psychosocial factors known to affect motivation, adherence, compliance, and well-being. As such this additional analysis includes measures for social support, body appreciation, self-compassion, and gender. All measures were taken at baseline or T1 except for self-compassion which was measured at all time points throughout the study (see Table 3.1).

Table 3.1: Additional variables and when they were measured

Variable	*Time point Measured*
Gender	T0
Berlin Social Support Scale (BSSS)	T1
Body Appreciation Scale (BAS-2)	T1
Self-Compassion Scale (SCS-SF)	T1, T2, T3, T4

When reviewing the literature on social support, it has been suggested that that those with higher levels of social support are healthier, both psychologically and physiologically, compared to those with lower levels of social support (Bardach et al., 2011; Van Weel et al., 2005). Higher levels of social support have also been associated with improved clinical outcomes in metabolic diseases such as type 2 diabetes (Strom & Egede, 2012).

Taking a closer look at psychological well-being, less perceived social support has been shown to be a predictor of depression in cancer caregivers (García-Torres et al., 2020), and low levels of emotional social support has been shown to be a main contributor to depression among patients with psoriasis, particularly in females (Wojtyna, 2017). It has been suggested that greater social support is important in increasing the likelihood of recovery in those with depression (Travis et al., 2004).

Social support will be analysed here to investigate whether it had any impact on the outcomes of study 1 overall. Diet groups (KD and LCD) will be collapsed into one group due to low participant numbers at time point 3 and time point 4. The intervention measures in those with low social support will be compared with those who have high social support, in an attempt to look for differences between

groups. The measure for this is the Berlin Social Support scale (Schwarzer, 2003). Social Support using the BSSS has been measured across fields of research from cancer (Luszczynska et al., 2005) and fertility (Kienle et al., 2009), to stress (Testa et al., 2015) and high social support has been shown to be an important coping resource for good health (Link & Phelan, 1995). The Berlin Social Support Scale (BSSS) was chosen as it assesses both the perceived and received levels of social support, which suggests it is a comprehensive measure of social support in individuals (Schwarzer, 2003). Given the role of social support observed in previous research alongside the positive correlations with health (Van Weel et al., 2005), it is expected that higher levels of social support in participants may be associated with more positive psychological well-being outcomes, regardless of dietary intervention in this study.

Body appreciation literature suggests that high body appreciation levels are associated with lower disordered eating in adolescents (Baceviciene & Jankauskiene, 2020) and conversely, low body appreciation and poor body satisfaction increases the risk of disordered eating (Rounsefell et al., 2020). Body appreciation is also positively related to self-perceived physical health in women (Winter et al., 2017). More recent research shows that an increase in body appreciation, and a decrease in body image dissatisfaction was found in those practicing intermittent fasting (Dairi et al., 2023). Furthermore, in a systematic review and meta-analysis, body appreciation was associated with increased well-being, fewer mental health issues and lower eating disorder specific psychopathology, and overall, the literature suggests that body appreciation may increase psychological well-being (Linardon et al., 2022).

Exploring the research further, there are significant associations between body appreciation and mental health (Soulliard & Vander Wal, 2019). Body appreciation has been shown to be inversely related to body dissatisfaction. As body appreciation increases, depression scores decrease (Ramseyer Winter et al., 2019). It is unclear from the literature if there is a causal relationship here.

It is therefore suggested in this thesis that the dietary interventions used in this research (LCD and KD) may alter eating behaviours which in turn increases body appreciation and decreases depression and depressive symptoms. Therefore, if depressive symptoms and depression scores decrease, or psychological well-being improves as a result of these dietary interventions, perhaps an increase in body appreciation levels will be observed. With this in mind, body appreciation was added as a measure for this study. The Body Appreciation Scale (Avalos et al., 2005) has been used widely across multiple studies and is selected for the current work (Baceviciene & Jankauskiene, 2020; Halliwell et al., 2017). The prediction is that those participants with lower levels of body appreciation will see greater improvements in psychological well-being over time, compared to those with higher levels of body appreciation.

Self-compassion is the tendency or ability to treat oneself kindly in times of failure or distress (Brenton-Peters et al., 2021) and has been associated with healthy ways of eating and negatively associated with maladaptive eating behaviours such as emotional eating (Carbonneau et al., 2020, 2021). Investigating the research further, higher levels of self-compassion are associated with lower levels of mental health symptoms such as anxiety, depression, and stress (Macbeth & Gumley, 2012).

In this study self-compassion was measured with the Self Compassion Scale (Neff, 2003; Raes et al., 2011) and collected at all time points. This scale was chosen as it is the most widely used measure of this variable in the literature. This scale measures the compassion an individual shows towards themselves and their situation. Self-compassion has been measured across many fields in research from athletics (Arts-De Jong et al., 2018) to physiological functioning (Breines et al., 2014), including psychological well-being (Arimitsu & Hofmann, 2017; Atkinson et al., 2017; Beshai et al., 2018).

A systematic review and meta-analysis of the current literature states that higher self-compassion is associated with lower anxiety and depression levels in young people (Egan et al., 2022). Körner et al. (2015) reported that self-compassion is related to increased psychological well-being and lower depression in a mixed population of students, internet users and those implementing psychotherapy. Friis et al. (2015) suggested that increasing self-compassion may be used to improve depression and glycemic control in diabetes. Bidirectional links have been suggested between self-compassion, depression, and anxiety levels (Baker et al., 2019; Ferrari et al., 2018).

If this is true, perhaps there could be a bi-directional relationship where improvements in depression via the LCD and KD which also improves glycemic control in diabetes (Alarim et al., 2020), could also increase self-compassion. With this evidence in mind, it is suggested that self-compassion levels may increase over the duration of this study in those with greater depressive symptoms and this may be in line with a reduction in mental ill-health symptoms.

When it comes to gender, differences are found in food choices as well as in energy and nutrient intake, with females more likely to be dieting with an overall greater focus on 'healthy eating' compared to males (Bates et al., 1999; Wardle et al., 2004). In a 12-week Mediterranean dietary intervention, greater improvements in metabolic profiles were found in males than in females (Leblanc et al., 2014). Furthermore, weight loss outcomes were found to be statistically different between males and females when following a low carbohydrate diet with males losing more weight than females (Susanto et al., 2022).

Differences between genders are also found and reported in the outcomes of mental health studies (Matud et al., 2019). Females experience more food related conflict as well as more body weight and shape dissatisfaction compared to males (Rolls et al., 1991). A recent study showed that due to the structural differences of the brain, females are more at risk for poor psychological well-being when their diet lacks key nutrients compared to males (Begdache et al., 2020). This suggests that there are important differences between genders that deserve investigation. Therefore, the variable gender will be explored to see if there are different effects of the KD and/or LCD on aspects of psychological well-being in both males and females.

The research questions related to these measures include:

- If those with better social support will see improvements in psychological well-being
- If those with lower body appreciation levels will see improvements in psychological well-being
- If self-compassion improves in those with depressive symptoms
- If there is a difference in psychological well-being between males and females

3.2 Method

For details of study design, participants, and procedure please see Chapter 2 (section 2.2).

3.2.1 Additional measures used

Table 3.2: Additional Psychological Variables and their Measures for Study 1

Variable	*Measure*
Social Support	Berlin Social Support Scale (BSSS)(Schwarzer, 2003)
Body Appreciation	Body Appreciation Scale (BAS-2)(Tylka & Wood-Barcalow, 2015a)
Self-Compassion	Self-Compassion Scale, Short Form (SCS – SF)(Filip Raes et al., 2011)

Social Support – Berlin Social Support Scale (BSSS)

The BSSS consists of six subscales: Perceived, Actually Provided, and Received Social Support, Need for Support, Support Seeking, Protective Buffering (Schwarzer, 2003).

This study administered three subscales, the Perceived Social Support, Need for Support and Support Seeking. This study did not use the Actually Provided Social Support, Received Social Support, or the Protective Buffering as these are not completed by participants themselves. This scale aims to measure behavioural and cognitive aspects of social support.

Each item is scored on a 4-point Likert scale from strongly disagree (=1) to strongly agree (=4). A total of 21 questions were administered with scores ranging from 21 to 84. The higher the score, the higher the perceived social support. Example items are 'There are some people who truly like me', and 'It is important for me always to have someone who listens to me'. Item responses are added up to give an overall sum score, but the scale mean score can also be calculated.

Reliability, consistency, and validity have been demonstrated to be of an excellent level, Cronbach's α = >.900 (Roomaney et al., 2020). The internal reliability and consistency of the 17-item BSSS in the present study was good, Cronbach's α = .891.

Body Appreciation – Body Appreciation Scale

This 10-item, self-administered scale measures aspects of positive body image (Tylka & Wood-Barcalow, 2015). It focuses on the participants' acceptance, respect, and opinion of their body. These are not subscales, but rather a view of an individual's internal characteristics.

Each item is scored on a 5-point Likert scale from never to always (1=never; 2=seldom; 3=sometimes; 4=often; 5=always). Example items are 'I respect my body' and 'I am comfortable in my body' and responses are summed to give a single score between five and 50. Higher scores represent higher body appreciation.

Reliability, consistency, and validity have been demonstrated to be of an excellent level, Cronbach's α = >.900 (Tylka & Wood-Barcalow, 2015). The

internal reliability and consistency of the 10-item BAS-2 in the present study was excellent, Cronbach's α = .956.

Self-Compassion – Self Compassion Scale – Short Form (SCS-SF)

Most of the current literature on self-compassion uses the Self Compassion Scale Long Form (26 item) and Short Form (12 item) (Filip Raes et al., 2011). The short 12-item form of the scale was used in this study. This measure was used across all time point questionnaires (T1-T4) apart from baseline (T0).

Each item is scored on a 5-point Likert scale from almost never to almost always (1=almost never to 5=almost always) and responses provide a total mean score ranging from one to five with lower scores representing lower levels of self-compassion. It asks participants to indicate how often they behave in the stated manner using this scale. Example items are 'I try to see my failings as part of the human condition' and 'I'm disapproving and judgmental about my own flaws and inadequacies' (reverse scored item).

Reliability, consistency, and validity have been demonstrated to be of good level, Cronbach's α = >.860 (Raes et al., 2011). The internal reliability and consistency of the 12-item SCS in the present study was good, Cronbach's α = .879.

3.2.2 Group formation and analysis

The variables were measured at different time points in this study. Gender was measured at baseline (T0), Body Appreciation and Social Support were measured at time point 1 (day 1) as seen in Table 1, and Self-Compassion was measured at all time points, day 1 (T1), six weeks (T2), 12 weeks (T3) end of intervention, and 24 weeks (T4) end of study.

For this analysis all time points, including at 24 weeks, the end of the study (T4), were analysed. However, this study experienced a high level of attrition, particularly at the end of the study, at time point 4 (see Chapter 2 for full details). Therefore, due to the limited sample size, this study analysed the data up to time point 3 at 12 weeks. This was the end of the online intervention.

To analyse the research questions, groups were formed from the results of the variables measured, as follows:

Social support grouping: As social support was only measured at baseline, the group needed to be split into high and low levels of social support. To determine the cut off, the mean score was calculated from the scores collected. The mean was 51.01. The cut offs for social support were then set by the researcher. Low social support was a score of less than 51 and high social support was a score of 51 and above.

Body appreciation grouping: Regarding the cut off for high and low body appreciation, the author of the BAS2 scale states that higher scores reflect greater body appreciation (Avalos et al., 2005). Therefore, scores of one, two and three were classed as low and scores of four and five were classed as high levels of body appreciation as items are ranked on a five point scale from 1 = never to 5 = always.

Self-compassion grouping: Self-compassion was analysed as one measure across the two psych health groups, those with depressive symptoms and those without (healthy group).

Gender grouping: simple grouping as males and females, as there were no participants in the sample identifying as other (non-binary, trans, no gender or other).

Using SPSS, a combination of mixed ANOVAs were carried out on the data, with control group removed, in order to answer the research questions. The between-subjects factor was group, low vs high baseline scores for both social support and body appreciation, followed by self-compassion, and gender. The within-subjects factor were the time points: day one (time point 1), six weeks (time point 2) and finally at twelve weeks, the end of intervention (time point 3). Baseline (time point 0) and end of study (time point 4) were not included here. The dependent variables were as previously stated – anxiety, depression, perceived stress, positive and negative affect, and mental well-being which were recorded at each time point.

Further analysis beyond time point 3, (e.g., time point 4) was not carried out because with each additional time point, the groups dropped in size, so it was less likely to get a meaningful result. Therefore, more in depth tables and charts are not included. However, these variables may be worth further exploration. This will be referred to in the discussion.

3.3 Results

3.3.1 Social support

Social support as mentioned above was measured once at the start of the study and therefore the group was split into high and low levels of social support. The

diet groups were also collapsed and combined into one for the sake of this analysis due to low sample numbers.

ANOVAs were carried out on the data across all measures of psychological well-being to identify if participants with high levels of social support saw improvements in psychological well-being outside of which diet they were on (LCD or KD) compared to those with lower levels of social support.

There were significant overall main effects for anxiety ($F(1, 24) = 9.135$, $p = .006$), perceived stress ($F(1, 25) = 4.42$, $p = .046$), negative affect ($F(1, 25) = 6.20$, $p = .020$), and depressive symptoms ($F(1, 24) = 13.87$, $p = .001$), with scores lower in the high social support group across all three time points', T1, T2 and T3 at intervention end (see example data for anxiety in Figure 3.1). The same significant main effect was seen for mental well-being ($F(1, 24) = 5.20$, $p = .032$) (see Figure 3.2), with scores higher in the high social support group across all three time points'. For positive affect, there was no significant main effect. For all measures, there were no main effects of time ($p>.05$) and there were no significant interactions (for all analyses $p>.05$).

These findings suggest that there were no significant improvements noted in overall psychological well-being across the three time points in those with higher levels of social support compared to those with lower levels. However, those with higher levels of social support appeared to have better overall psychological well-being compared with those who had less social support.

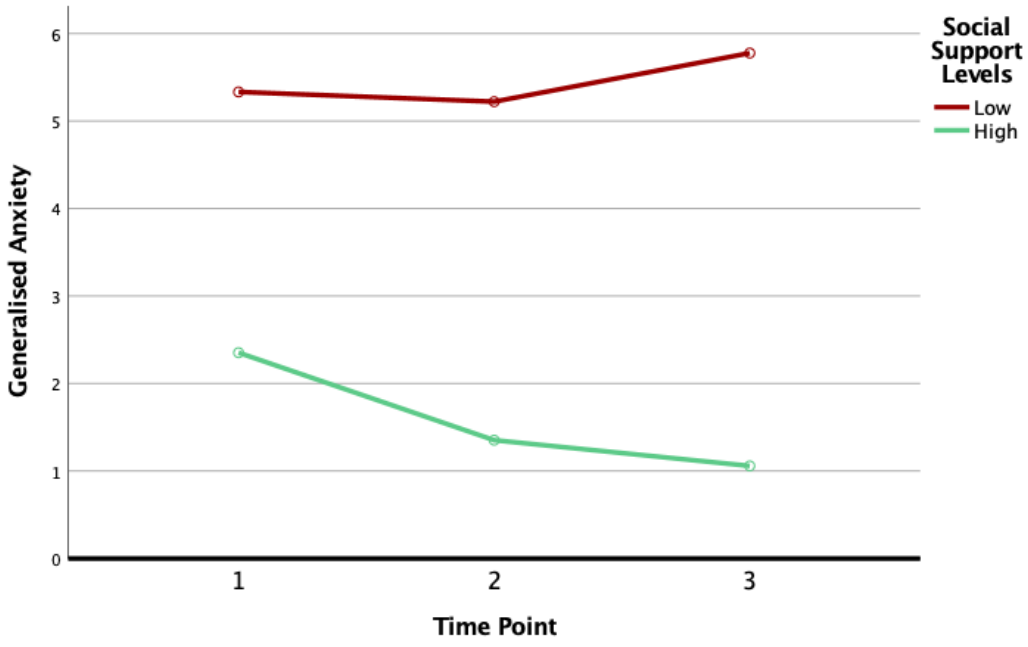

Figure 3.1: Anxiety levels in those with high and low levels of social support (BSS) from time point 1 to 3

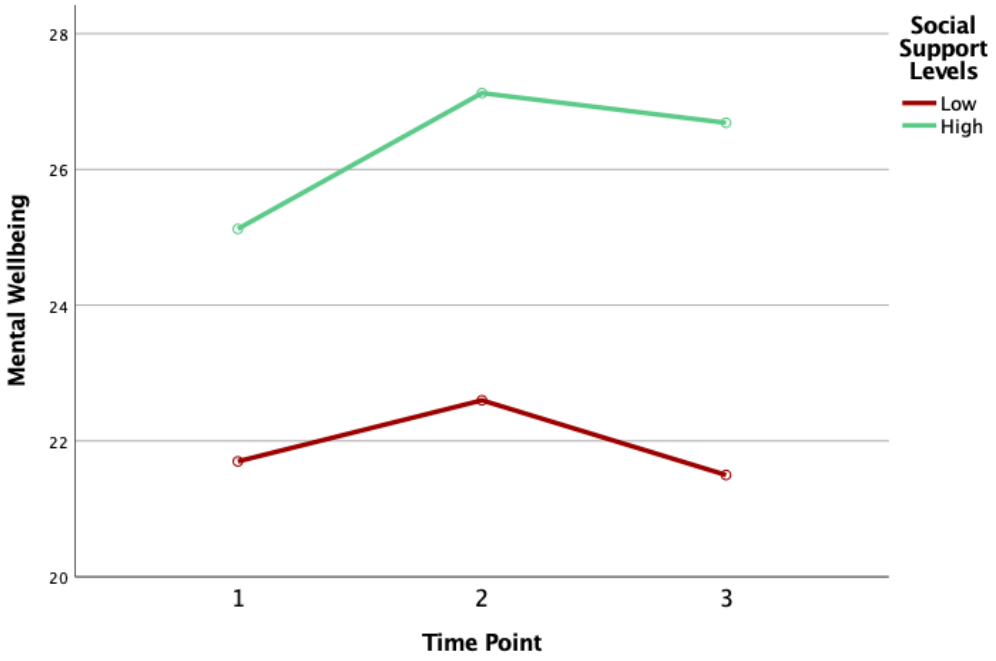

Figure 3.2: Mental well-being levels in those with high and low levels of social support (BSS) from time point 1 to 3

3.3.2 Body appreciation

ANOVAs were carried out on the data across all measures of psychological well-being to identify if those with lower body appreciation levels saw improvements in their psychological well-being compared to those with higher levels of body appreciation.

For positive affect, over three time points, T1, T2 and T3 at intervention end, there were no main effects of time, or body appreciation (p>.05). For the time*body appreciation interaction, the interaction term itself, was not significant (p>.05) but there was a significant linear interaction *(F_{lin}*(1, 25) = 4.46, p = .045). This suggests that positive affect was moderated by body appreciation levels. On closer analysis, those with lower levels of body appreciation at time point 1, saw an increase in positive affect across T2 and T3 (see Figure 3.3). There were no other significant interactions (for all other analyses, e.g., quadratic, p>.05).

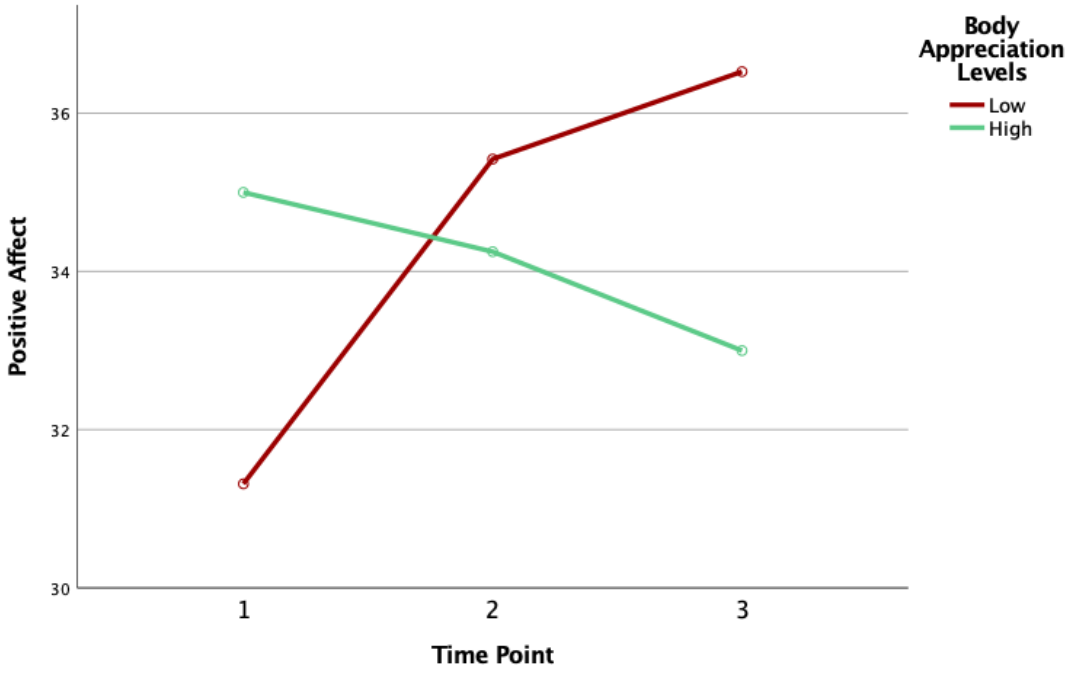

Figure 3.3: Positive affect levels in those with high and low levels of body appreciation (BAS) from time point 1 to 3

For mental well-being, over three time points, T1, T2 and T3 at intervention end, there were no main effects of time, or body appreciation (p>.05). There was however a significant linear time*body appreciation interaction (F_{lin}(1, 24) = 5.32, p = .030). This suggests that mental well-being was in part, moderated by body appreciation levels, and that for those with lower levels of body appreciation at baseline, there was an increase in mental well-being over time, against a drop at T3 in the high group (see Figure 3.4). There were no other significant interactions (for all other analyses p>.05).

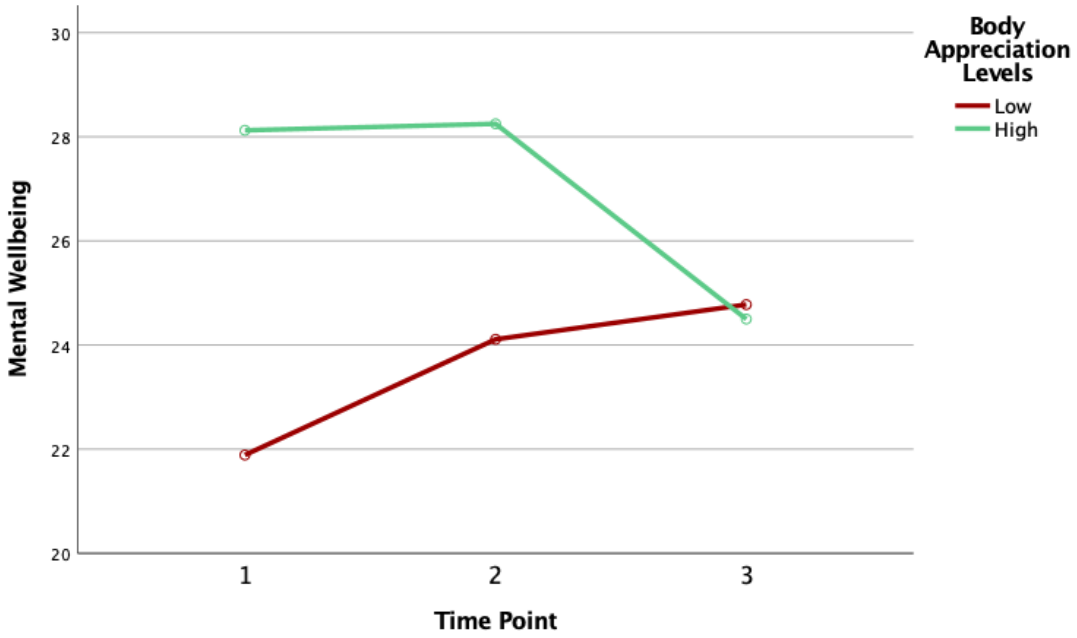

Figure 3.4: Mental well-being levels in those with high and low levels of body appreciation (BAS) from time point 1 to 3

For depressive symptoms, there were no main effects of time, or body appreciation (for all analyses $p>.05$). There was a significant time*body appreciation linear interaction ($F_{lin}(1, 24) = 7.03$, $p = .014$), with the low body appreciation group showing a fall in depressive symptoms after T1, whilst the high group showing mirror image trend to this (see Figure 3.5). There were no other significant interactions (for all other analyses $p>.05$).

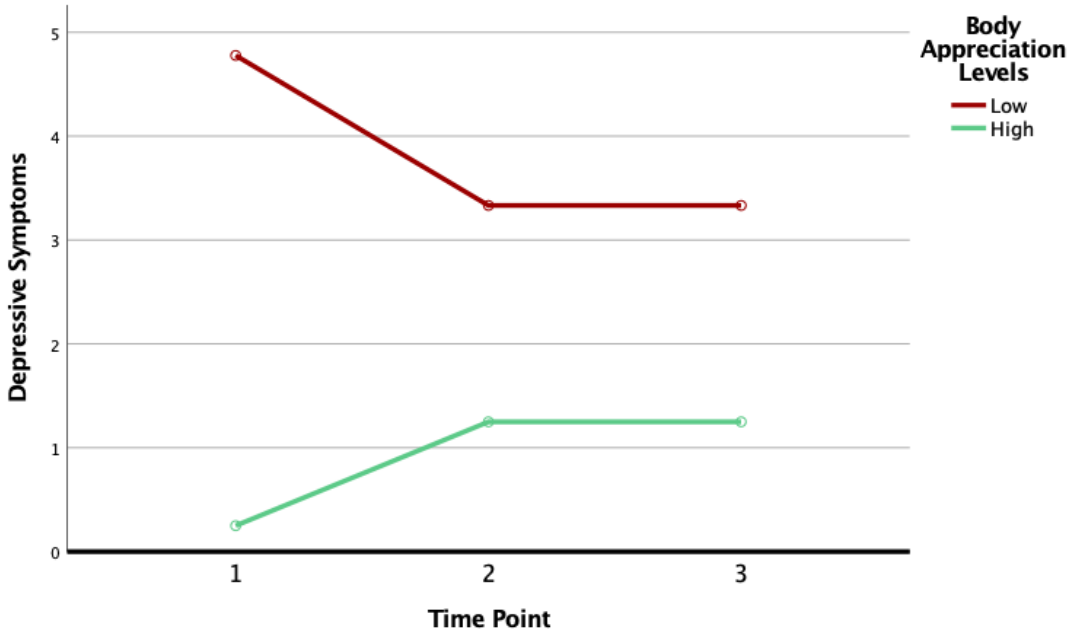

Figure 3.5: Depressive symptoms levels in those with high and low levels of body appreciation (BAS) from time point 1 to 3

For self-compassion, there was no main effect of time (p>.05). There was a highly significant main effect of body appreciation *(*F(1, 24) = 8.67, p = .007). This is due to those with lower body appreciation reporting lower levels of self-compassion regardless of time (see Figure 3.6). There was no significant interaction effect (for all analyses p>.05).

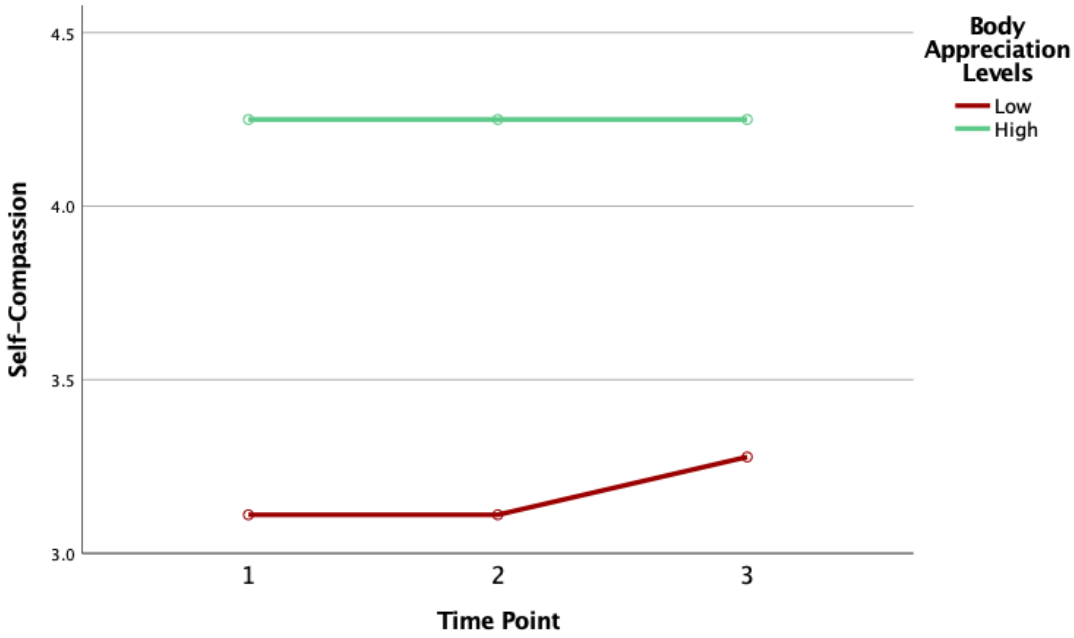

Figure 3.6: Self-compassion levels in those with high and low levels of body appreciation (BAS) from time point 1 to 3

For perceived stress, negative affect, and generalised anxiety, over three time points, T1, T2 and T3 at intervention end, there were no main effects of time, or body appreciation (p>.05) and no significant interactions (for all analyses p>.05).

Overall, these findings suggest that, in those with lower body appreciation levels, significant improvements were seen in positive affect and mental well-being alongside a decrease in depressive symptoms, compared to those with higher levels of body appreciation. Those with lower body appreciation levels reported lower levels of self-compassion regardless of time. Therefore, some aspects of psychological well-being did improve in those with lower levels of body appreciation compared to those with higher levels.

3.3.3 Self-compassion

Self-compassion as described earlier was measured and analysed with the two psych health groups, those with depressive symptoms and those without (healthy group).

Mixed ANOVAs were carried out on the data to explore whether self-compassion improved more in those with depressive symptoms compared to healthy participants.

For self-compassion, there was no main effect of time (p>.05). There was a significant main effect of psych health *(*$F(1, 24) = 4.78$, $p = .039$). This is due to those in the depressive symptoms group reporting lower levels of self-compassion regardless of time (see Figure 3.7).

For the time*psych-health interaction there was a highly significant interaction *(*$F(2, 24) = 6.90$, $p = .002$), and a highly significant quadratic interaction *(*F_{quad} $(1, 24) = 9.59$, $p = .005$). This suggests that self-compassion scores decreased initially from T1 to T2, before increasing again to T3 in the depressive symptoms group. This is seen in the figure below.

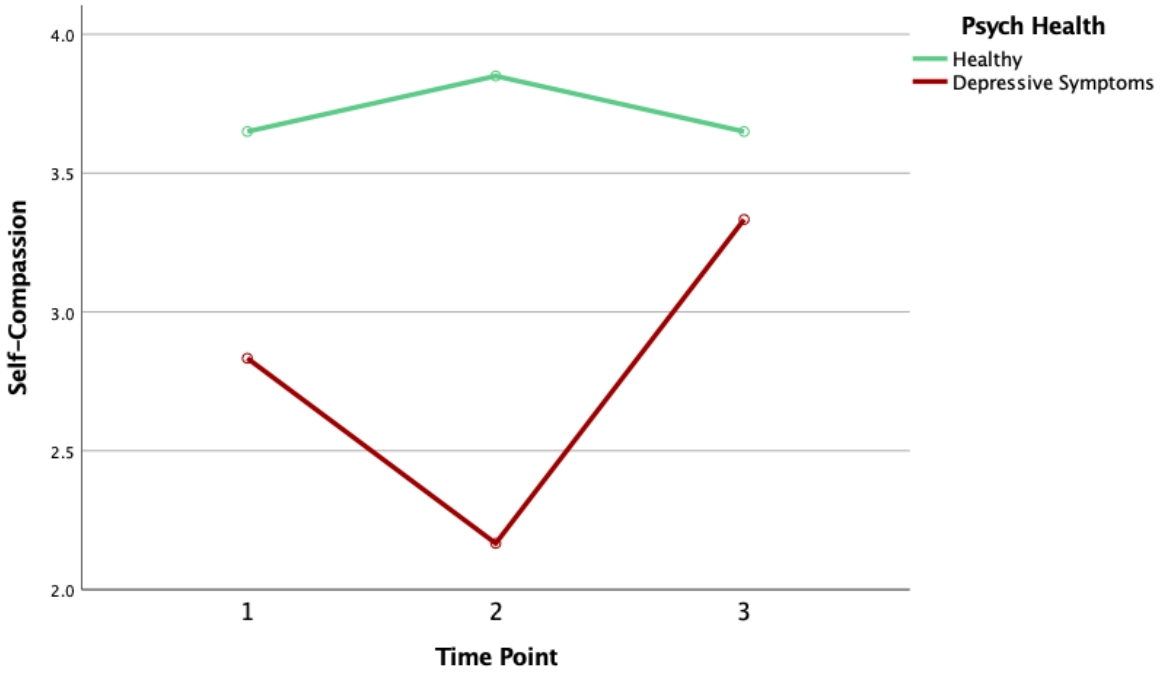

Figure 3.7: Self-compassion levels in participants with depressive symptoms and participants classed as healthy from time point 1 to 3

Overall, these findings suggest that self-compassion didn't improve more in those with depressive symptoms compared to healthy adults. Self-compassion levels fluctuate across the course of the intervention, dropping initially before increasing again after six weeks of intervention. In contrast, the healthy adult groups levels stayed more or less the same.

3.3.4 Gender differences

Analysis in the LCD group could not be completed as there was only one male participant (N=1) to represent the LCD group.

Table 3.3: Number of participants in each diet group by gender

	Males	*Females*
Ketogenic Diet (KD)	5	12
Low Carbohydrate Diet (LCD)	1	9

ANOVAs were then carried out on the data across all measures of psychological well-being to explore whether more improvements were seen in females compared to males in the KD group. For mental well-being, and there was a significant linear main effect of time *(F_{lin}*(1, 15) = 6.22, p = .025). This suggests that mental well-being levels increased over time in both genders (see Figure 3.8). There was no main effect of gender and there were no significant interactions found (for all analyses p>.05).

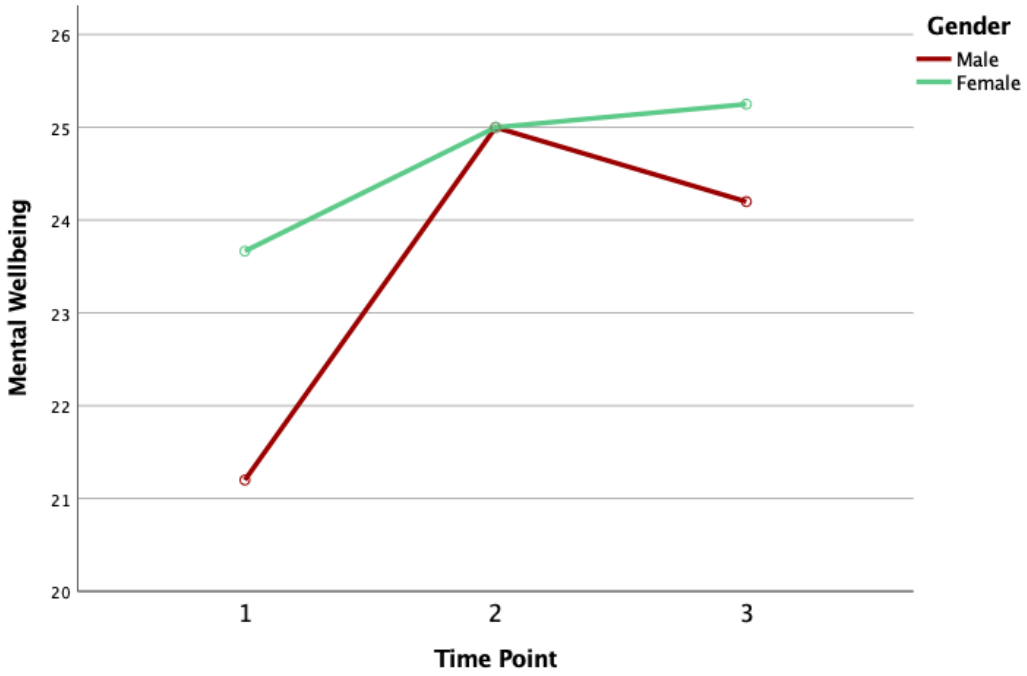

Figure 3.8: Mental well-being levels in males and females from time point 1 to 3

The same was found for depressive symptoms. There was a significant linear main effect of time ($F_{lin}(1, 14) = 7.62$, $p = .015$), suggesting diet linked symptom reduction regardless of gender (see Figure 3.9). There was no main effect of gender and there were no significant interactions found (for all analyses $p > .05$).

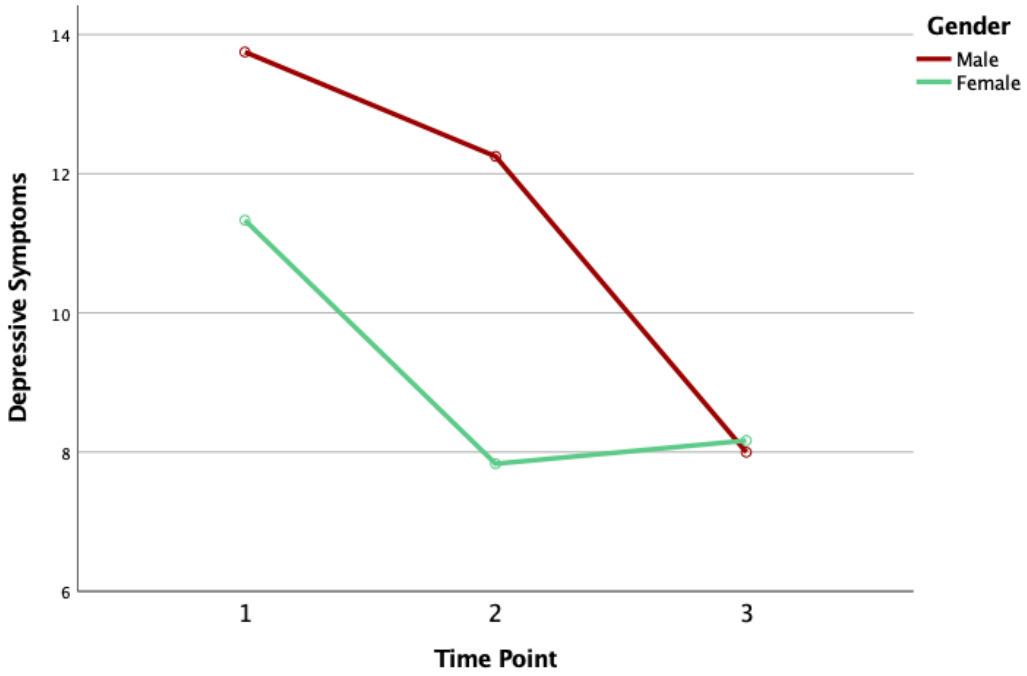

Figure 3.9: Depressive symptoms levels in males and females from time point 1 to 3

For perceived stress, generalized anxiety, self-compassion, positive affect, and negative affect, there was no main effects of time or gender and there were no significant interactions found (for all analyses $p>.05$).

Overall, these findings suggest that psychological well-being did not improve more in females compared to males on the KD. There were no significant findings for perceived stress, generalized anxiety, self-compassion, positive affect, and negative affect. Improvements in mental well-being and depressive symptoms were observed across both gender groups.

3.4 Discussion

The analyses presented in this chapter explored the additional measures captured in Chapter 2. Social support, body appreciation, self-compassion and gender differences were analysed here as possible moderating factors in the data as they may have impacted the outcomes found in the previous chapter.

In Chapter 2, it was hypothesised that the LCD and KD dietary intervention may have an impact on psychological well-being for many reasons stated in the literature. Removing ultra-processed foods, a focus on whole foods, fat loss, the reduction of inflammation and presence of ketones in some cases are a few examples of the mechanisms by which improvements in psychological well-being may occur. Results from the interventions in Chapter 2 found improvements in some aspects of psychological well-being, but not all.

There were four key predictions for this additional analysis, focused on social support, body appreciation, self-compassion, and gender differences.

It was suggested that participants with more social support would experience greater improvements in aspects of psychological well-being compared to those with less social support across the LCD and KD interventions. This is because those with greater social support have been found to be psychologically healthier than those with less according to Bardach et al. (2011) and Van Weel et al. (2005).This may mean that those with more social support are less likely to see improvements in aspects of psychological well-being compared to those with less social support.

Improvements in overall psychological well-being were not found in those with greater social support compared to those with less. However, some improvements were found in specific aspects of psychological well-being. Those who reported less social support had higher perceived levels of stress than those who reported greater levels of social support. These findings are consistent with the work of Ozbay et al. (2007) who stated that low social support is associated with stress promoting physiological changes in the body. In keeping with Bardach et al. (2011) and Van Weel et al. (2005), it was observed that those with greater social support appeared to have higher baseline psychological health compared with those who had less social support.

It was postulated that participants with lower levels of body appreciation would see greater improvements in psychological well-being compared to those with higher levels across the LCD and KD interventions. This second prediction of this study was confirmed as significant improvements in positive affect, mental well-being and depressive symptoms were found in those with lower levels of body appreciation compared to those with higher levels. This is in keeping with the findings of Ramseyer Winter et al. (Winter et al., 2019) mentioned earlier.

It was hypothesized that self-compassion would improve more in participants with higher levels of depressive symptoms (depressive symptoms group) compared to those with lower levels (healthy adults group) across the LCD and KD interventions. This is because high levels of self-compassion are associated with lower levels of depression (Macbeth & Gumley, 2012) and healthy ways of eating (Carbonneau et al., 2020, 2021). By following a dietary intervention and

arguably a healthier way of eating, perhaps self-compassion levels would change, and even improve.

The results from this analysis showed no improvements in self-compassion rates amongst those with more depressive symptoms and levels of self-compassion stayed constant in the healthy adults group. No change in self-compassion rates within this healthy adults group (lower depressive symptoms) is unsurprising as their overall self-compassion levels are already associated with lower levels of depression, which they have (Macbeth & Gumley, 2012). An increase in self compassion rates in those who have few depressive symptoms, is not expected. However, it appears that following the dietary interventions alone is not enough to improve self-compassion rates in those with more depressive symptoms as no improvements were found.

In appears from this analysis, that understanding self-compassion and how it can be improved is more complex in those with more depressive symptoms compared to healthy adults with less. Improving diet quality is likely only one aspect that can contribute to improving self-compassion rates and perhaps it requires and improvement in diet over a longer time scale to see a significant difference. This area warrants future exploration as the participants sample for this analysis is too small for further analysis.

Finally, females are more at risk of poor psychological well-being when they lack essential nutrients compared to males (Begdache et al., 2020). So, by following a dietary intervention that focuses on real whole food and high nutrient density it was predicted that females following the LCD and/or KD intervention would

see greater improvements in their psychological well-being compared to males. However, due to the small sample size, analysis on the LCD could not be completed. Further analysis was carried out to explore the gender differences of those in the KD intervention with the same prediction that females would see greater improvements compared to males. Females have been shown to experience more food related conflict (Rolls et al., 1991), and by following this dietary intervention with a clear plan and guidelines it was suggested that food related conflict could be lower and nutritional quality higher than when following a standard diet. Alongside this, no calorie target was given, meaning participants could eat ad libitum, which should allow them to access all essential nutrients.

However, no further improvements in psychological well-being were found in females in the KD intervention compared to males over and above the general improvements found in both genders. Therefore, similar to self-compassion, understanding how aspects of psychological well-being can be improved across the genders is complex and multifactorial. This area also warrants future investigation with bigger sample sizes to explore possible differences between dietary interventions.

The limitations of this study that apply to this aspect of the data are the same as those mentioned in study 1, see Chapter 2. The sample size in this analysis was a limitation due to the high rate of attrition. This meant that the researcher was unable to carry out the analysis of these variables on all four time points. Analysis was carried out on three time points only. This means that the data for the end of the study was not included and therefore not represented. The data collected at time point four, at the end of the study at 24 week or six months

may have produced different results to what was found here. In future, similar to that stated in Chapter 2, the focus should be on retention and higher recruitment targets in order to reduce the rate of attrition across the lifespan of the study.

As a result of, and secondary to the small sample size, deeper analysis of the data beyond analysis of variance across the three time points was not carried out because with each additional time point, the sample size is reduced. This meant that the findings would be less meaningful and more likely to not be generalizable to the broader population. This is why more in-depth tables and charts are not included in this chapter. However, these variables may be worth further exploration. Future studies should keep attrition as low as possible and analyse these variables for meaningful findings.

Another proposed limitation of some of these variables is that they may not have a single mechanism by which rates can be increased or decreased. In Chapter 2, the variables measured under the 'psychological well-being' umbrella are variables that have been directly influenced by the mechanisms of the LCD and KD dietary interventions, such as anxiety and stress levels. In contrast, the variables analysed here have multiple influencing factors and mechanisms of action. For example, social support is influenced by those outside of the individual themselves as well as internal perceptions of that support. Body appreciation and self-compassion are influenced by a culmination of the thoughts and experiences of an individual.

To conclude, it is clear from this research that psychological well-being is multifactorial, where variables outside of diet can impact the outcome measures. Implementing and following a diet can improve some aspects of psychological well-being, as seen here. However, to see a significant improvement in all aspects of psychological well-being a multifaceted lifestyle change may be necessary. A change that incorporates a biopsychosocial approach. Therefore, further research is necessary in this area.

Chapter 4: Study 2 - Understanding Drop Out and Attrition Rates

4.1 Introduction

4.1.1 Overview

As highlighted in the previous chapters, the power of the previous study (study 1) was impacted by substantive drop out at each time point over the duration of the trial. This is not unusual in longitudinal research generally and has previously been observed in diet-related research, either due to research design, demographics of sample, or the diet itself (Brownell & Kramer, 1989; Dalle Grave et al., 2015; Volkmar et al., 1981). In this current study, the researcher aimed to recruit a minimum of 900 participants. This sample size was chosen as it was much larger than previous studies within the topic scope at the time of design. The largest studies completed at the time were a low carbohydrate versus low fat diet for weight loss and atherosclerosis in 2003 with a sample size of N=132 (Samaha et al., 2003), and a low and high carbohydrates weight loss diet and its effects on mood and cognitive performance with a sample size of N=93 (A. K. Halyburton et al., 2007). Proposing a sample size of 900 participants, with this in mind, should have allowed for attrition rates. However, the researcher did not anticipate how high the attrition rates would be. Therefore, this chapter will investigate reasons for attrition in study 1 to better understand how to reduce attrition rates in future research studies.

4.1.2 Attrition rates in research

In the medical literature, high attrition rates are seen across disciplines, with rates of up to 40-55% seen in cardiac rehabilitation attendance studies (Farley et al., 2003). Attrition rates in oncology clinical trials are common with rates of 26% for the primary endpoint and up to 44% for the end of the study according to a review of 18 clinical trials and 1214 patients (Hui et al., 2013). Even within controlled trials on yoga interventions, attrition rates are expected to be less than 20% but these rates can increase past 40% depending on the participants sampled (Cramer et al., 2016). A review of trials in medical journals showed that 54% of trials reviewed had some level of attrition with a 7% median percentage loss overall (Dumville et al., 2006).

More specifically, the attrition rates in controlled trials of behavioural managements of obesity increased from 11% in 1974, to 21% in 1986 (Brownell & Kramer, 1989). In a study on a commercial weight reduction program, 50% of participants dropped out at six weeks, and 70% at 12 weeks (Volkmar et al., 1981). Recently, in a systematic review of long-term weight loss studies, attrition rates ranged from 30-60% (Douketis et al., 2005).

It is clear that there is a lot of variation with attrition rates in studies and the rates seem to be determined by multiple factors from participant demographics (age) and depression score (Fabricatore et al., 2009), practical difficulties (Crichton et al., 2012), less early success or little progress observed (Hughes & Walker., 2011) to the specific design of the study or intervention. When reviewing attrition guidelines with this in mind, <30% is a minimum requirement for clinical trials to still reach 80% power (Galbraith et al., 2002). What is clear

from the literature is that explanations for high attrition rates in weight loss treatments and dietary interventions are extremely complex. They require an in-depth review to identify important predictors of drop out in any individual study, ideally before the study or intervention is initiated.

4.1.3 Diet trials and intervention design issues

Crichton et al. ran a 12-month study in overweight adults where attrition rates of 49.3% were found (Crichton et al., 2012). Researchers followed up with participants to discuss their reasons for drop out. Many of the factors for this were due to the intervention experimental design. The study was long, at 12 months, 27% of participants were unable to comply with the diet stating that they found it difficult, and 10.8% stated they dropped out due to time commitment. A systematic review of the literature focused on incentives in behavioural change for obesity interventions between 2006 and 2012 found that financial incentives to participants had a positive effect on behaviour change. Unsurprisingly, the larger the incentive, the better the results, although post intervention long term, results were not maintained (Purnell et al., 2014). The work by Burger and Lynham (2009) supports this as they found that up to 80% of participants who bet their money on their ability to lose weight, end up losing their bets. Cawley and Price (2011) looked more closely at attrition rates in a real-world study of one year duration (N=2407) that had three arms, the first offered no financial incentive, the second offered increasing incentive as weight loss was achieved and the third where an incentive was given when participants reached their weight loss goal. Even with these incentives in place, attrition rates were reported as up to 76.4% after one year. Having said this, it is still important

to consider incentives in research studies as reason for or against high attrition rates.

From this research it is unsurprising that attrition rates were high in study 1. The duration of the study, study design, the amount of engagement, the difficulty of diet implementation, the level of support received by the program, family, and peers, as well as time commitments, may all have played a role in the attrition rates here.

4.1.4 Predictors of dieting success and failure

Aside from limitations to the dietary intervention design, there are many other, more individual, non-design related reasons why people drop out of diet studies or cease dieting in general. Hughes and Walker (2011) carried out a systematic review of the literature on attrition rates in weight loss groups. They found that those who dropped out were likely to lose less weight during their weight loss program than what they had expected. In other words, they had unrealistic expectations of what they could achieve. They had a higher percentage weight loss target compared to their actual percentage weight lost. Practical issues, a loss of motivation, unsatisfactory weight loss results and previous failures were the cited reasons for attrition.

Practical issues and unsatisfactory weight loss results (slow weight loss) were also cited as reasons for attrition in a review of the research by Grave et al. (2006). Sato (2020) found that diet failure is associated with a hedonistic response to food, and they proposed that in order to have diet success, environmental controls need to be put in place to reduce food cues. A study by

Meule et al. in (2011) found that food cravings are positively associated with less dieting success. They are directly related to the success or failure of a diet. Following this, Crichton et al. (2012) suggest that compliance to diets in dietary interventions can also be an issue, particularly when the diet restricts certain foods, food groups or offers less food variety over the study duration. Greenberg et al. (2009) presented similar findings, specifically in their low carb diet group as carbohydrates such as breads, pastas and cereals were restricted.

In the DIRECT study carried out by Greenberg et al. (2009), participants were randomised to a low fat, Mediterranean or low carbohydrate diet (20 grams per day for two months and 100 grams per day from then on). Dietary adherence was measured in all participants through a complete adherence score. This score was calculated using 24 hour recalls of food with a subgroup of participants at two time points throughout the study, as well as asking all participants at the end of the study to state their adherence throughout. Overall, adherence was greater on the low carbohydrate diet compared to the low-fat diet during the initial six months, after this, there was no difference between groups. These findings are the opposite of what Crichton et al. (2012) stated in their study. Overall attrition rates for the DIRECT study were 15.5%. Attrition rates were higher in women (29% compared to 14% of men) the predictors of drop out were having a higher baseline BMI, and less initial weight loss at six months. Holidays were also a predictor of drop out and poor adherence, but age and education had no impact. Adding to this, a study by Ortner Hadžiabdić et al. (2015), with a 32.3% drop out rate, found that of 124 participants, those with a lower education level were more likely to drop out of a weight loss program.

The participants main reason for dropping out was due to a lack of motivation to continue the study (n=19). Overall, this suggests that there are many predictors of drop out in dietary studies.

When looking specifically at studies for weight loss, weight reduction groups have high attrition rates (Jiandani et al., 2016; Ponzo et al., 2021). There appear to be many reasons for this. Ortner Hadžiabdić et al. (2015) found that the higher the initial weight, the less likely the participants would complete the weight loss program. This is in keeping with the findings from Greenberg et al. (2009). Handjieva-Darlenska et al. (2011) found that greater weight loss at week eight of their intervention was associated with lower attrition odds during the intervention and was a better predictor of weight loss maintenance. Fabricatore et al. (2009) also observed that initial weight loss during the first three weeks of treatment was a predictor of weight loss success at one year. Ponzo et al. (2021) found a 53.6% drop out (N=134) in their weight loss program with the main predictors of this being a lower BMI, increased depression score and living alone. Fabricatore et al. (2009) identified that depressive symptoms and age were significant predictors of attrition. They saw that lower baseline depressive symptoms scores were predictors of weight loss success. Moran et al. (2019) also found that depressive symptoms scores that were higher at baseline were associated with greater attrition. Their attrition rates were 47.1%.

Overall, these studies suggest that reasons for attrition vary from study to study and are dependent on many factors from study structure and design to participant demographics and perceived results.

4.1.5 Aims and predictions

In line with the above findings around drop out from diet research trials, the current study will explore factors that might shed light on attrition: both specifically from study 1 and more generally from dietary interventions. This follow up piece aims to survey participants who left the study early to ascertain reasons for non-completion, alongside exploration of baseline demographic and psychological scale measurements. There are three predictions for this study.

1. Those following the KD intervention will have higher dropout rates compared to those in the LCD group, possibly due to the KD restricting more carbohydrates, similar to the findings mentioned above by Crichton et al. (2012) and Greenberg et al. (2009).
2. Those with more depressive symptoms or lower overall psychological well-being are more likely to drop out compared to those with less depressive symptoms. This would be in keeping with the works of Fabricatore et al. (2009) and Moran et al. (2019) who found this to be true in their works.
3. There will be a greater drop out of participants once the intervention ends at 12 weeks, but before the study finished at 24 weeks due to the cessation of the online program, and the need to continue unsupported for the second 12 weeks.

On completion of this study, the outcomes, and reasons for drop out should help to advise future researchers when designing their experimental research studies, interventions, or methods of care, specifically for those with depressive symptoms.

4.2 Method

4.2.1 Design

This study looks at predictors of drop out from study 1. It follows a cross sectional survey design, utilising existent survey data from study 1 and novel study specific survey responses. Criterion variables were taken from the follow up questionnaire, such as length of time of the diet, usage of education videos and reasons for drop out. These were combined with predictor variables taken from the participant's demographic data collected at baseline (T0) and the first time point (T1) such as age, gender, ethnic background, and depressive symptom severity score.

4.2.2 Participants

Of the 384 participants who completed a time point in study 1, 39 of these were controls and therefore removed for this follow up study. There were 345 participants remaining that were part of an intervention group, KD, or LCD. A total of 22 participants completed the last time point questionnaire of the study (T4). This left 323 participants (see Table 4.1). These participants started the study, completed the screening questionnaire (T0) and day 1 questionnaire (T1), and possibly other questionnaires (T2, T3) but did not complete all questionnaires up to T4. If a participant completed T0 and T1, and dropped out at any stage after that, before the end of the study at 24 weeks, they were eligible for this follow up study. By completing at least T0 and T1 questionnaires, baseline demographics, and initial psychological well-being data was available for analysis. The full flow diagram of attrition from study 1 can be seen below (see Figure 4.1).

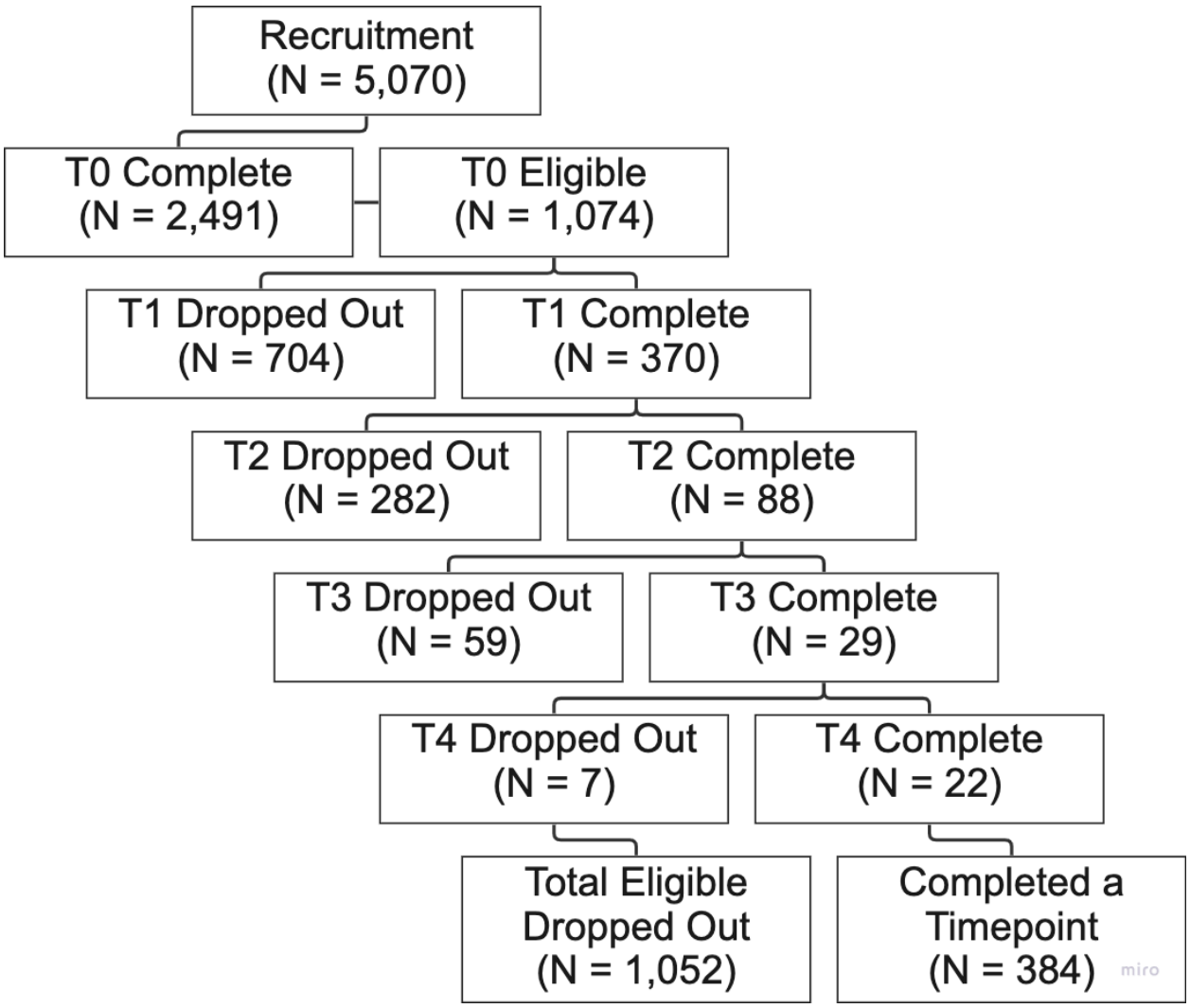

Figure 4.1: Flow Diagram of Attrition

Table 4.1: Breakdown of participants who were eligible to take part in the follow up study

Participant Breakdown	*N*
Total Participants that Completed a Time point in Study 1	384
Control Participants that Completed a Time point in Study 1	39
Intervention Participants that Didn't Drop Out	22
Remaining Participants Relevant for Follow Up Study	323

Of the 323 participants who were eligible for this study and who were contacted, 88 participants, read the information sheet, gave their consent, and started the questionnaire. This information was captured by the Qualtrics software.

4.2.3 Materials and measures

The existing variables measured were depression, depressive symptoms, perceived stress, generalised anxiety, positive and negative affect, mental well-being, body appreciation, social support, and self-compassion. See section 2.2.3 in Chapter 2 for full details of each measure. The follow up questionnaire for this study consisted of eleven questions covering the participants experience of the online platform, the intervention, and the study in general. These were a mix of quantitative and qualitative questions (see Appendix W). For example, a quantitative question was Question 3, 'How long did you follow your allocated diet for?' with answers ranging from a= 'I didn't start the allocated diet' to h= 'I'm still following the diet / a version of the diet'. An example of a qualitative open-ended question was Question 11, 'Is there anything else you would like to share with the researcher?'.

Table 4.2: Full follow up questionnaire for this study

	Question	*Answers*
Q1	Did you complete the first questionnaire when you got access to your profile?	a. Yes b. No
Q2	Did you complete the second questionnaire 6 weeks after starting?	a. Yes b. No
Q3	How long did you follow your allocated diet for?	a. I didn't start the allocated diet b. Less than a week c. 1-2 weeks d. 2-4 weeks e. 4-8 weeks f. 8-12 weeks g. 12 weeks or more h. I'm still following the diet / a version of the diet
Q4	Did you watch the educational videos on the platform?	a. Yes – All of them b. Yes – Some of them c. No – None of them
Q5	Did you find these videos useful / helpful?	a. Yes b. No
Q6	Did you track your food?	a. Yes – I tracked my food for less than 4 weeks b. Yes – I tracked my food for more than 4 weeks c. No – I did not track my food
Q7	Which app if any did you use to track your food?	a. Diabetes.co.uk Profile b. MyFitnessPal c. Carbs and Cals d. Cronometer e. Fitbit Health f. Other App (Add here) g. I did not track my food on an app
Q8	What is the MAIN reason why you dropped out of the study?	a. I found the diet difficult to stick to b. I didn't find the platform helpful c. I experienced side effects d. My circumstances changed (pregnancy, sickness etc.) e. I didn't feel good following the diet f. I continued the diet but not the study g. I found it expensive h. I didn't know what to eat i. I found social events difficult j. I worried about eating higher levels of fat k. Other (Add here)

Table 4.2: (Continued)

	Question	*Answers*
Q9	What other reasons stopped you from continuing the study? (You can choose more than one answer)	a. I found the diet difficult to stick to b. I didn't find the platform helpful c. I experienced side effects d. My circumstances changed (pregnancy, sickness etc.) e. I didn't feel good following the diet f. I continued the diet but not the study g. I found it expensive h. I didn't know what to eat i. I found social events difficult j. I worried about eating higher levels of fat k. Other (Add here) l. No other reason
Q10	Would you like to restart the study?	a. Yes – I would like to restart the study b. No – I would not like to restart the study
Q11	Is there anything else you would like to share with the researcher?	Open Answer Box

4.2.4 Procedure

A recruitment email was sent out to all eligible participants from the researcher instead of through DCUK (see Appendix U). Attached to this email was a link to the questionnaire which was held in Qualtrics. The information sheet and consent form were presented at the start of the questionnaire (see Appendices S and T). This detailed the reason for the follow up questionnaire and explained that it would take less than five minutes to complete online. Once the participants had read this and given their consent, they were then able to complete the final follow up questionnaire (see Appendix W).

Responses from participants were monitored and follow up emails at two weeks were sent to participants who had started but not yet completed the questionnaire to ensure completion (see Appendix V). After two months, the

questionnaire on Qualtrics was closed, and the data was downloaded, ready to be cleaned and analysed by the researcher.

The online survey software Qualtrics was used to host this questionnaire and only the researcher had access to this. All completed questionnaires were downloaded securely and directly from Qualtrics once the questionnaire had been closed. The Qualtrics software is GDPR compliant (see study 1).

In the ethics application for study 1 the researcher was approved by UREC to follow up with participants who dropped out of the program (see Appendix A). A second application was submitted to the committee with the specific follow up study procedure and questionnaire. This was then approved by the ethics committee (see Appendix D).

4.2.5 Analysis

Once the data was downloaded from Qualtrics, entries by participants who had not completed the questionnaire were removed (N=24). The researcher searched for duplicates and two further participants were removed (N=2), See Table 4.5.

Email addresses were then matched with the unique IDs given at the start of study 1. Each complete follow up questionnaire entry was then matched to the data from study 1. This left 62 participants with a complete baseline questionnaire (T0), day 1 questionnaire (T1) and follow-up questionnaire. The full dataset was then transferred from excel into SPSS V27 ready for analysis. Using the data from baseline, time point 1 and the follow up questionnaire,

demographic variables were analysed and reasons for dropping out were identified. Descriptive statistics and frequencies were also run.

The demographic data which consists of both categorical and continuous data was analysed using a combination of analysis of variance (ANOVA) and chi-squares. These tests were used to determine the relationships between variables and drop out status and to see if there were differences across groups. A comparison of demographic variable ranges and means across the three groups, those who completed the study, those who dropped out and didn't complete the follow up study and those who dropped out and did complete the follow up study was also created.

Then, the data from the psychological measures and variables used in study 1 was analysed using analysis of variance (ANOVA) tests to identify whether there were significant effects found between the groups.

4.3 Results

4.3.1 Demographics and differences between groups

The breakdown of eligible participants for the follow up study (N=323) by group was Ketogenic Diet (N=241) and Low Carb Diet (N=82). These participants started and completed parts of study 1 but did not finish it. A further breakdown of groups was, Keto Diet – Healthy (N=170), Keto Diet – Depressive Symptoms (N=71), Low Carb Diet – Healthy (N=55) and Low Carb Diet – Depressive Symptoms (N=27) as seen in Table 4.3 below. Out of those who were eligible, the Keto Diet group (74.6%) was almost triple the size of the Low Carb Diet group (25.4%), and the Keto Diet – Healthy group had the most participants at

N=170. This is similar to the day 1 (T1) participant and group breakdown in study 1 where the Keto Diet group accounted for 66.7% and the Low Carb Diet group 23.2%.

Table 4.3: Breakdown of eligible for follow up study participants by group

Eligible for Follow Up (N=323)	*Keto Diet*	*Low Carb Diet*
Healthy	170 (52.6%)	55 (17%)
Depressive Symptoms	71 (22%)	27 (8.4%)
Total	241 (74.6%)	82 (25.4%)

To fully understand the number of participants who dropped out altogether from the study in each group, see Table 4.4 below. In the Keto Diet group, 94% of participants dropped out and 92% of participants dropped out of the Low Carb Diet group before the end of the intervention at 12 weeks (time point 3).

Table 4.4: Breakdown of participants per intervention who dropped out as a % of total participants per group

	Total Started in Group	*Dropped Out No Follow Up*	*Dropped Out Followed Up*	*Total Dropped Out as % of Total Started in Group*
Keto Diet	256	190	51	94%
Low Carb Diet	89	71	11	92%

The full breakdown of participants who started and completed the follow up study is seen in Table 4.5 below.

Table 4.5: Breakdown of participants who started, were removed, and completed the follow up study

Participants	*N*	*%*
Eligible for Follow Up	323	100.0%
Started Follow Up	88	27.2%
Non-Complete Dropped Out	24	7.4%
Removed - Duplicates	2	0.6%
Healthy Keto Group	38	61.3%
Healthy Low Carb Group	10	16.1%
Mental Health Keto Group	13	21.0%
Mental Health Low Carb Group	1	1.60%
Total 100% Complete	62	100.0%

Of the 62 participants who completed the questionnaire, 51 were from the Keto Diet group (82.3%) and 11 were from the Low Carb Diet group (17.7%). Forty-eight participants were from the Healthy group (77.4%) and only 14 were from the Depressive Symptoms group, representing only 22.6% of the total sample.

The demographical data which consists of both categorical and continuous data was analysed across all three groups. Then the psychological measures data from baseline in study 1 was analysed across all three groups. The PHQ-9 data was used both as a categorical variable in a categorical analysis, comparing the numbers in each intervention group scoring above the threshold for depressive symptoms (see Table 4.7), as well as a continuous variable (see Table 4.8).

Table 4.6: Comparison of variable ranges, means and standard deviations in those who completed the study, dropped out and didn't complete the follow up study and dropped out and did complete the follow up study

	Didn't Drop Out Completed Study (N=22)	Dropped Out No Follow Up (N=261)	Dropped Out Followed Up (N=62)
Measured		X (M, SD)	
Age	31-65 years (M=50 years, SD=9.61)	19-65 years (M=48 years, SD=9.18)	25-63 years (M=50 years, SD=7.71)
Body Mass Index (BMI)	23-42kg/m^2 (M=30.2kg/m^2, SD=5.51)	19-53kg/m^2 (M=30.7kg/m^2, SD=5.67)	20-44kg/m^2 (M=29.8kg/m^2, SD=5.04)
Waist	74cm-105cm (M=90cm, SD=10.39)	57cm-120cm (M=93cm, SD=14.08)	69cm-112cm (M=94cm, SD=11.55)
Weight	62kg-115kg (M=85.4kg, SD=15.63)	53kg-141kg (M=83.9kg, SD=16.48)	48kg-127kg (M=82.5kg, SD=14.96)

Table 4.7: Number of participants and percentage of total sample in those who completed the study, dropped out of the study, dropped out and didn't complete the follow up study and dropped out and did complete the follow up study

	Didn't Drop Out Completed Study (N=22)	Dropped Out (N=323)	Dropped Out No Follow Up (N=261)	Dropped Out Followed Up (N=62)
Measured	N (% of column N)			
Intervention: Keto Diet	15 (68.2%)	241 (74.6%)	190 (73%)	51 (82%)
Intervention: Low Carb Diet	7 (31.8%)	82 (25.4%)	71 (27%)	11 (18%)
*Psych Health Group (PHQ-9): Healthy	14 (63.6%)	225 (69.7%)	177 (67.8%)	48 (77.4%)
*Psych Health Group (PHQ-9): Depressive Symptoms	8 (36.4%)	98 (30.3%)	84 (32.2%)	14 (22.6%)
Gender: Females	18 (81.8%)	271 (83.9%)	218 (84%)	53 (85.5%)
Gender: Males	3 (18.2%)	48 (26%)	39 (15%)	9 (14.5%)
Depression or Anxiety Diagnosis	4 (18.2%)	46 (14.2%)	34 (13%)	12 (19.4%)
Anti-depressant Medication Prescribed	2 (9.1%)	36 (11.1%)	27 (10.3%)	9 (14.5%)
Education - Undergraduate	11 (50%)	131 (40.6%)	107 (41%)	24 (38.7%)
Ethnicity - White British	22 (100%)	275 (85.1%)	223 (85.4%)	52 (83.9%)

*Patient Health Questionnaire (PHQ-9) variable is continuous in this instance

Univariate ANOVAs were carried out on the demographic continuous variables across all three groups (those who dropped out and didn't do the follow up (N=261), those who dropped out and did do the follow up (N=62), and those who completed the study at T4 (N=22). There were no significant effects found between the groups for age, BMI, waist measurement or weight measurement (for all effects, $p>.05$) (see Table 4.6 above). This shows that for the continuous demographic variables, there is not much difference between groups. Though there is an over-representation of ketogenic diet participants in both drop out samples, this is reflective of the initial sample distribution in study 1.

A comparison of frequencies was then carried out on the categorical variables data. Chi-square tests were performed to test the goodness of fit, assess the relationships between the categorical variables and drop out status and to see if distributions differed across groups. The categorical variables tested were gender, education level, ethnic group, depression or anxiety diagnosis, antidepressant use, intervention diet type and psych health group, healthy or depressive symptoms via the categorical measure of the PHQ-9.

Table 4.8: Breakdown of participants per psych health group who dropped out as a % of total participants per group

	Dropped Out	*Did Not Drop Out*	*Total*
Healthy	225 (94.14%)	14 (5.86%)	239
Depressive Symptoms	98 (92.45%)	8 (7.55%)	106

No significant relationships were found between the variables and drop out status, specifically those who didn't drop out and completed the study and those who dropped out in total (for all measures, $p>.05$). Those who dropped out of the study in total were split into two groups, those who dropped out and didn't complete the follow up and those who dropped out and did complete the follow up (see Table 4.7). Further analysis was carried out across these drop out groups and no relationships were found between the variables and drop out status (for all measures, $p>.05$). The data suggests that for these variables, there was no association with drop out status. Therefore, diet type, psych health, gender, depression or anxiety diagnosis, antidepressant use, education level and ethnicity were not predictors of drop out.

Groups that had a higher percentage of participants with a depression or anxiety diagnosis either completed study 1 or completed the follow up study. Those with a lower percentage of those with a depression or anxiety diagnosis dropped out of study 1 and did not complete the follow up study (see Table 4.7) showing that more people with depression and anxiety diagnosis stayed in.

Table 4.9: Psychological measures (means and standard deviations) at baseline (Study 1) in those who completed the study, dropped out and didn't complete the follow up study and dropped out and did complete the follow up study

Psychological Measures	Completed Study (N=22)	Dropped Out No Follow Up (N=261)	Dropped Out Followed Up (N=62)
	Mean (SD)		
Patient Health Questionnaire (PHQ-9) (continuous)	4.23 (4.74)	3.92 (4.40)	3.39 (4.60)
Berlin Social Support Scale (BSSS)(SUM)	53.0 (7.59)	50.8 (8.06)	52.1 (9.03)
Body Appreciation Scale (BAS-2)	3.19 (1.08)	2.84 (.96)	2.85 (.97)
Perceived Stress Scale (PSS)	14.29 (8.42)	14.42 (6.24)	13.85 (7.57)
Positive and Negative Affect Scale – Positive (PANAS)	30.62 (9.77)	31.86 (8.25)	31.53 (8.92)
Positive and Negative Affect Scale – Negative (PANAS)	16.95 (7.91)	17.14 (6.12)	16.92 (6.56)
Warwick Edinburgh Mental Well-being Scale (WEMWBS-S)	22.76 (5.52)	22.52 (3.57)	23.05 (4.59)
Generalised Anxiety Disorder (GAD-7)	3.38 (4.34)	4.16 (3.83)	3.94 (4.45)
Centre for Epidemiological Studies Depression (CESD)	11.38 (10.93)	12.52 (9.31)	12.52 (11.55)
Self-Compassion Scale (SCS-SF)	3.38 (.97)	3.24 (.83)	3.13 (.88)

For the psychological variables, univariate ANOVAs were carried out on the data across all three groups. There were no significant effects found between the groups for depressive symptoms, stress, positive and negative affect, mental well-being, generalised anxiety, depression, social support, self-compassion, or body appreciation (for all effects, $p>.05$) (see Table 4.7). This suggests that there doesn't seem to be anything in the psychological measures data that points to reasons of drop out.

Frequencies for those who completed this follow up study, the Dropped Out Followed Up group (N=62), stated that 44 participants (71%) watched some or all the educational videos on the online platform and 18 participants (29%) did not. Of the 44 participants who watched the videos, 38 found them useful and helpful (61.3%) and 6 participants did not (9.7%).

When it came to tracking or logging food eaten, 35 participants (56.5%) said that they tracked their food with 27 participants (43.5%) saying that they did not. Of the 35 participants who tracked their food, 21 participants tracked for less than four weeks, and 14 tracked for more than four weeks.

Further analysis showed that 48 participants (77.4%) self-reported that they completed the first questionnaire at time point 1 in study 1. This was the first day of the allocated interventions. Fourteen participants (22.6%) said that they did not complete this questionnaire. For the second questionnaire at time point 2, six weeks into the intervention and the halfway point, 23 participants (37.1%) stated that they completed the questionnaire, and 39 reported that they did not (62.9%). This large drop off in the first six weeks suggests that predictors of

drop-out may be found in the initiation of the diet or logistics of the study itself. It is important to note here that participants may have then gone on to complete the later questionnaires, but simply missed or did not complete the second questionnaire at time point 2.

Finally, analysis of the length of time that participants followed their allocated diet for stated that, 18 participants (29%) did not start their diet at all. This may be the same group of participants who did not complete the questionnaire at time point 1 as mentioned earlier. Thirty-four participants followed their diet for up to 12 weeks, or time point 3 which was the end of the intervention. Ten participants (16.1%) reported that they were still following the diet, or a version of the diet when they completed the follow up survey, approximately six months after the end of study 1, meaning that they had been following their diet for approximately one year in total (see Table 4.10 below).

Table 4.10: Length of time those who completed the follow up study followed the allocated diet in study 1

Time	*N*	*Percent*
I didn't start the allocated diet	18	29%
Less than a week	9	14.5%
1-2 weeks	4	6.5%
2-4 weeks	7	11.3%
4-8 weeks	12	19.4%
8-12 weeks	2	3.2%
I'm still following the diet / a version of the diet	10	16.1%
Total	62	100%

4.3.2 Reasons for dropping out – Qualitative

The process of analysis for this data was determined once all the data had been collected. The purpose of waiting until all data was received was so that the researcher could decide the best way to analyse the data to draw the best story for the participants. This study was added to help complete the narrative of the high percentage of participants who dropped out of the first study, study 1. The main and other reasons for dropping out were collated into an excel spreadsheet. In-depth analytic techniques could not be used as comments left by participants were generally quite succinct. However, a brief analysis of the qualitative data could be carried out.

Table 4.11: Single choice primary reason why participants dropped out of Study 1

Primary Reason	*N*	*Percent*
Found the diet difficult to stick to	11	17.7%
Circumstances changed (sickness, pregnancy etc.)	10	16.1%
Continued diet but not study	5	8.1%
Found it expensive	3	4.8%
Didn’t find the platform helpful	1	1.6%
Experienced side effects	1	1.6%
Didn’t feel good following the diet	1	1.6%
Didn’t know what to eat	1	1.6%
Found social events difficult	1	1.6%
Worried about eating higher levels of fat	1	1.6%
Other	27	43.5%
Total	62	100%

Of the 62 participants who dropped out and completed this follow up study, 53 (85.5%) participants gave feedback on both their primary and secondary reasons for dropping out of the study (see Table 4.11). Those who chose 'Other' were asked to share their answer (see Table 4.12). Each row in the table below represents one participant (N=1).

Table 4.12: Single choice primary reason why participants dropped out of Study 1 (Other-Text)

Primary 'Other-Text' Reason
Family bereavement
Followed until holiday time
Did not receive any information from you (the researcher)
I do not have diabetes
I was not in the right place emotionally
I found I was obsessing about preparing food and spent a disproportionate amount of time thinking about food
I found it difficult to get enough fibre
I found the process confusing; I mistook the emails for spam
I found the email in my junk mail, having not heard from you after signing up I assumed I had not been selected
I got busy and forgot as a working mum it was difficult, so I followed my own low carb diet
I never received anything and have no idea what any of this is. I would have loved to get involved
I was unable to log on
It was very confusing as to what I was meant to be doing, eating, and tracking
My head wasn't in the right place to follow a plan at that time
Too many e-mails and not enough time

Table 4.13: Multiple choice other reasons why participants dropped out of Study 1

Other (Multiple choice) Reasons	*N*
I found the diet difficult to stick to	9
I found social events difficult	7
I didn't know what to eat	5
I worried about eating higher levels of fat	5
My circumstances changed (pregnancy, sickness etc.)	4
I continued the diet but not the study	4
I didn't find the platform helpful	3
I didn't feel good following the diet	3
I experienced side effects	2
I found it expensive	1
Other-Text	18
- Can't remember	1
- Communication unclear as to when to start	1
- Depression	1
- Doing the diet with everyone else in the family became unsustainable	1
- I just forgot to complete the questionnaire when it was sent as I was out of the country	1
- It was hard to integrate it with cooking for the family	1
- Not in a good place emotionally	1
- Time and other commitments	1
- Wasn't the right time for me	1
No other reason	18

Reasons for drop out were reviewed and each reason was labelled with an overarching theme to better understand the data. Once labels had been allocated to the reasons, they were reviewed, grouped, and mini themes were created. These themes represent the reasons for drop out from study 1. The following themes were identified.

4.3.3 Main Themes

Table 4.14: Summary table of main themes identified and the number of participants whose quotes fell under these categories

Main Theme	*N*	*Percent*
Diet Too Difficult to Follow	32	31.1%
Change in Personal Circumstance	15	14.6%
Unclear Communication and Project Design	14	13.6%
Worried About Diet Macronutrients and What to Eat	12	11.7%
Continued the Diet but Not the Study	11	10.7%
Side Effects	8	7.8%
Cost of the Diet	4	3.9%
Poor Mental State	4	3.9%
Not the Right Time to Start	3	2.9%
Total number of reasons for drop out	103	100.0%

Diet Too Difficult to Follow (N=32): The main reason for dropping out was that the diet was too difficult to follow in general. Participants stated that the diet was 'Difficult to integrate into family life', 'Doing the diet when everyone else in the family isn't, became unsustainable' and 'It was hard to integrate it with cooking for the family'. Some 'Found it difficult to get enough fibre' and 'Got

busy and forgot as a working mum it was difficult'. Social events were also difficult to navigate for some 'I found social events difficult'.

Change in Personal Circumstance (N=15): Changes in personal circumstances was the next most popular reason for dropping out. Situations such as 'My circumstances changed (pregnancy, sickness etc.)', and 'Family bereavement' got in the way of them completing the study.

Unclear Communication, Poor Platform and Project Design (N=14): Some participants commented that communication and information provided was unclear in places. The platform and project design may have contributed to dropouts, alongside participant user error. Statement such as 'Communication was unclear as to when to start', 'I was unable to log on', and 'It was very confusing as to what I was meant to be doing, eating and tracking' were stated.

Worried About Diet Macronutrients and What to Eat (N=12): Being unsure about what to eat and the composition of the diets themselves were also a reason for drop out. 'I worried about eating higher levels of fat', and 'I didn't know what to eat'.

Continued the Diet but not the Study (N=11): Participants stated that they continued the diet but not the study. 'I followed up to my Thailand holiday in January 2020' and 'I followed my own low carb diet'.

Side Effects (N=8): Some participants mentioned that they experienced physical and psychobehavioural side effects on the diet, or they didn't feel good overall when following the program. 'I experienced side effects', 'I didn't feel good

following the diet', 'I found I was obsessing about preparing food and spent a disproportionate amount of time thinking about food'.

Cost of the Diet (N=4): The cost of the diet was also a reason for some, stating that it was too expensive to follow.

Poor Mental State (N=4): A few participants mentioned that they were not in the right mental state to start or complete the study, or it was not the right time for them. 'I found I was not in the right place emotionally but have recently started following a low carb way of life again way', 'My head wasn't in the right place to follow a plan at that time', 'I was not in a good place emotionally', and 'Depression'.

Not the Right Time to Start (N=3): It was also not the right time for some participants. They stated that there were 'Too many e-mails and not enough time', and they had issues with 'Time and other commitments'.

4.3.4 Final thoughts and feedback from participants on the study

Participants were asked at the end of the follow up questionnaire if there was anything they would like to also leave feedback to the researcher about the study in general. 29 participants (46.8%) contributed feedback for the researcher. There is a collection of feedback on the study in Table 4.15 below.

Table 4.15: Feedback on the study from participants who dropped out of the study but completed the follow up questionnaire

Participant	*Feedback*
1	I am vegan so please could it be tailored to suit.
2	I believe in the benefits of this diet, and I am sorry I didn't finish the study for you, but I found I couldn't follow the Keto diet and get as much fibre as I would like in my diet. I am currently trying to reduce the carbs in my diet, but I do not try to follow a full keto diet.
3	I decided to follow a similar low-carb diet with a small group - as I found doing it entirely online very difficult - I wanted some company!
4	I found out I had an under active thyroid which was giving me issues with mental & physical health and found it difficult to continue the programme because of this.
5	The diet for some reason affected my digestive system very badly (mainly things like salad, beef, tomato-based meals, broccoli). I did seek medical advice, but no conclusions were arrived at.
6	This was interesting to participate in. The main reason for not continuing the study was due to time pressures.
7	Tracking food for such a long time is quite time consuming. I felt that after a couple of weeks I had a good grasp of what things were low in carbs.
8	After I stopped counting the carbs, I put more weight on than I had lost during the low carb diet. It is quite scary for me to commit to a low carb diet for life.
9	Although I'm now following a LCHF diet, I started after I dropped out of the study.
10	Being low card is difficult but like giving up smoking I just need to keep trying until I get it right.
11	I found the diet really good I wasn’t hungry at all on it, but I did struggle to lose weight I also like sweet things and missed a chocolate treat, Dark chocolate didn’t really do it for me. I think my problem was I had to many coffees with cream and got disheartened as I only lost a small amount of weight. I am now on Slimming World and have lost 5 and a half pound in 2 wks. Thanks for allowing me to join your trail I wish you every success with your study.
12	I have always found it difficult to log meals and exercise and don’t find it very motivating.

Table 4.15: (Continued)

Participant	*Feedback*
13	I have literally just today started on Slimming World with a friend so these two may not be compatible, even though I am theoretically interested in restarting. I was looking for an expected email that had not arrived when I found this one in my junk folder. I'm truly sorry that it would appear that I defaulted out of the study - I would have liked to have taken part.
14	I have lost weight but now plateau.
15	I lost weight.
16	I started off doing a very low-calorie diet then switched to no carb and then low carb which i stuck to for the last 5 months and lost weight that way.
17	I still try to maintain the principles of the diet and have found it helpful.
18	I was going through a bad divorce.
19	I watched a few videos tried to do the diet but found it too difficult especially when my family weren’t following it.
20	I would like to have been better organised, but I had a lot of work situations that prevented this. I also had treatment for skin cancer that kinda threw me. However, several situations have been resolved and I look forward to concentrating more on my dietary choices.
21	I'm sorry I didn't follow the diet. I have had great results previously when I followed the keto diet. However, I have lacked willpower and self-esteem.
22	It's me that would like to be more proactive.
23	My circumstances changed shortly after I applied. Subsequently they changed again and in September, after a shock weigh in (86kg) and blood pressure check with my GP, I used the resources from this study to begin a Keto way of eating which I am still following now (current weight 71.7kg) and love. If it is still useful to you, I would be happy to take part in any other research.

Table 4.15: (Continued)

Participant	Feedback
24	My partner is type 2 diabetic, and I was able to influence his food choices with my behaviour and the positive results I have achieved I find the sugar withdrawal very hard to do at first but once you have achieved this you no longer crave sugar at all and find the taste displeasing.
25	No, it was a great diet to start with and worked well just didn't suit my lifestyle.
26	Or is expensive also hard for lunchtimes at work when you only have 30 mins to get to shop and eat something usually sandwiches or carb rich food available. on reflection i needed more time to prepare lunch rather than buying at local corner shops where choice is limited.
27	Sadly, my mum was taken seriously ill during the study time and passed away, I was not in a good place to follow the regime.
28	The only reason I really stopped was Christmas and laziness!! I know am realising I have to put in the effort to receive weight loss results!! I keep expecting a miracle!!!
29	There was a lot of measuring and stuff with food prep which was very off putting. It's also very difficult to change a lifetime of mindset on eating fats. I have actually worked in medical research and am aware of what drug companies did to manipulate opinion on safe cholesterol levels but, nonetheless. I hope you have enough recordings for your research.

4.4 Discussion

4.4.1 Summary of aims and predictions

The aim of this study was to investigate the dropout rates across all interventions and participant groups observed in study 1 and to establish whether there were any key predictors in drop off from the dietary intervention groups or from specific participant types. Study 1 experienced high levels of attrition which made in depth analysis difficult in some cases. Therefore, study 2 was added to this program of research to determine and understand the predictors of drop out. It followed a cross sectional survey design, utilising existing survey data from study 1 and novel study specific survey responses.

From the results, it is clear that the data in this study is a representation of the entire study 1 sample, as no marked differences were observed in the demographics of the sample or in the baseline psychological profiles. Therefore, the findings and interpretations made here can be generalised to the wider sample, of those who completed the study, and those who dropped out.

There were three main predictions for this study.

1. The first prediction was that those following the KD intervention would have higher dropout rates compared to those in the LCD group, possibly due to the KD restricting more carbohydrates.
2. The second prediction was that those with more depressive symptoms or lower overall psychological well-being were more likely to drop out compared to those with less depressive symptoms.

3. The third prediction was that there would be a greater drop out of participants once the intervention ended at 12 weeks, but before the study finished at 24 weeks due to the cessation of the online program, and the need to continue unsupported for the second 12 weeks.

The first prediction was that those following the KD intervention would have higher dropout rates compared to those in the LCD intervention, possibly due to the KD restricting more carbohydrates, similar to the findings mentioned above by Crichton et al. (2012) and Greenberg et al. (2009). In other words, more participants would drop out from the KD intervention over the course of the study. This study found that there was no association between dietary intervention and drop out status, so diet type did not prediction drop out status. Looking at the dietary intervention groups independently, Table 4.4 above reports that 94% of those who started the Keto Diet intervention (N=256) dropped out by the end of the intervention at week 12 (N=241). In the Low Carb Diet intervention (N=89), 92% of participants dropped out (N=82).

Based on these drop out percentages 94% and 92%, this suggests that intervention type, specifically the KD intervention, was not a predictor of drop out as both groups experienced similar attrition rates. This is in keeping with the findings of Crichton et al. (2012) and Greenberg et al. (2009) who suggested that compliance to diets that restrict certain foods groups would be lower and attrition rates would be higher. In this study, both the LCD and KD restrict carbohydrates significantly below the recommended daily intake of at least 200g (Macdonald, 1999) with the KD (<50g) restricting further than the LCD (90-130g).

The second prediction was that those with more depressive symptoms or lower overall psychological well-being were more likely to drop out compared to those with less depressive symptoms. This would be in keeping with the works of Fabricatore et al. (2009) and Moran et al. (2019) who found that those with more depressive symptoms had higher attrition rates. This study found no significant association between depressive symptoms as determined by the PHQ-9 and drop out status. Therefore, depressive symptoms did not predict drop out. This is not consistent with the findings from Fabricatore et al. (2009), Moran et al. (2019) and Ponzo et al. (2021) discussed earlier, who found that increased depression scores were predictive of higher attrition rates.

Interestingly this study found that, in the two more engaged groups; those who completed the study, and those who dropped out but completed the follow up, there were more participants with a depression or anxiety diagnosis compared to those who dropped out. Those with the depression or anxiety diagnosis were therefore likely to have fallen into the 'depressive symptoms' groups and had higher levels of depressive symptoms and lower psychological well-being. The group who dropped out and did not complete the follow up had the lowest number of participants with a depression or anxiety diagnosis (N=34, 13%) and therefore most of this category were likely to have fallen in the 'healthy adults' groups, with lower levels of depressive symptoms and higher psychological well-being. It may be that those with lower psychological well-being stayed and continued to participate because they were fulfilled by the study in some way.

Perhaps those with higher psychological well-being, and lower depressive symptoms scores (healthy adults group) didn't feel the need to continue to

engage with the study as their well-being wasn't poor enough for them to warrant following such a diet or intervention. This is in keeping with the results of a new systematic review looking at the effects of low carbohydrate diets on psychological outcomes. They found that the ketogenic diet had the same impact on psychological well-being as any other diet in those without physical or mental health issues. In other words, the ketogenic diet didn't improve psychological well-being in those who were already healthy (Sindler et al., 2023).

This suggests that those who stayed in the study, had a reason to do so, over, and above simply taking part. Either they experienced a psychological or physical (e.g., weight loss) benefit from the intervention or they found some meaning in taking part in a study with others and being part of something bigger than themselves. Some of the participants who stayed in the study will be interviewed in the next chapter. Understanding their journey throughout this study may help the researcher to better understand the reasons for sticking to the dietary intervention.

The third prediction was that there would be a greater drop out of participants once the intervention ended at 12 weeks, but before the study finished at 24 weeks due to the cessation of the online program, and the need to continue unsupported for the second 12 weeks. This study found that of those who started their diet, 34 participants followed their diet for up to 12 weeks, at intervention end, by which time they had dropped out. Two participants followed their diet for 8-12 weeks before stopping. Only ten participants continued on past the 12-week mark and beyond 24 weeks to the follow up study. So, although more participants dropped out before the intervention ended at 12 weeks, only two

participants dropped out at the intervention end. This was the smallest number of participants to drop out at any point in the study. Overall, 29% didn't start the intervention, 54.9% followed it up to 12 weeks and then dropped out, and 16.1% continued until the end of the study. Therefore, the majority of participants dropped out during the first 12 weeks, which is the opposite of what was predicted. From the reasons given in this study, participants stated that they dropped out because they found the diet difficult to stick to (17.7%), their circumstances changed (16.1%) or they dropped out for other reasons (43.5%). These findings are in keeping with that of Crichton et al. (2012) whose participants stated that they dropped out because the diet was difficult, or they had other time commitments. Therefore, it cannot be suggested that the end of the intervention and initiation of unsupported intervention for a further 12 weeks had any impact on dropout rates.

4.4.2 Limitations

There are some limitations to this drop out study. The total number of participants originally recruited for study 1 were significantly higher than any other dietary intervention studies that had been carried out at the time of the study design. Despite this, the dropout rates at time point 3 (intervention end) and 4 (end of study) in study 1, meant that the researcher was unable to carry out the analysis initially proposed as the sample sizes became too small to accurately analyse.

The participants that completed this study, dropped out of the main study (study 1) at some point, but still completed this follow up questionnaire. 323 participants were eligible for this follow up study and only 27.2% of them started

the questionnaire. 62 participants completed the follow up questionnaire and were analysed here. This is 19% of those who were eligible to take part. 19% of those who dropped out of study 1 were recontacted and completed this study.

This study was developed post hoc and therefore has its own limitations. Had more participants been recruited, attrition rates considered, and actions put in place to minimise drop out, this study would not have been added to this program of research. As the original study (study 1) was not originally focused on drop out or attrition rates, there may have been other predictors of attrition that were not included in the initial design of the study.

The demographic details for the participant dropouts at each time point, per group in study 1 were also not recorded. As this study was designed during the analysis of study 1, the original dataset had already been cleaned. This meant that all duplicates, incomplete responses, and drop-outs were removed before analysis began. Therefore, the number of participants that dropped out at each time point was recorded but it is unclear which dietary intervention or psych health group they belonged to. The complete flow chart of attrition available to the researcher is seen in Figure 4.1. This is a limitation to this research as understanding who dropped out of which group and which time point may have helped the researcher to understand better the predictors of drop out.

4.4.3 Future directions

These future directions of research cover both the dietary approach as well as the mode of intervention. Future RCTs and trials should expect high attrition rates and make sure to identify the possible areas of attrition when designing

the study. This is important as otherwise, the attrition rates, particularly in the later part of the trials, make it more difficult to analyse and less likely to find any significant results.

Recruitment retention and enhancing compliance could be bolstered in future in many ways. Firstly, over recruiting initially for the study is imperative as well as recruiting a larger sample of males, which is in keeping with the findings from Crichton et al. (2012).

Secondly, in terms of logistics, minimising the time between screening, consent, and initiation of the program will help. This supports the suggestions of Crichton et al. (2012). It will also be important to make sure that all participants receive, and open important trial information sent to them. This may mean that a research assistant is assigned the task of tracking emails, read receipts, and loading remote content. They may then re-send important information when necessary if they don't believe it has been opened or completed. Using a research assistant will keep the trial blind from the researcher if an RCT approach is being followed.

Thirdly, future trials and interventions should adhere to a minimum trial period of 12 weeks if carrying out research in outpatients or a community real life setting. This allows for individuals to learn about the diet, get into a state of ketosis and maintain it to see results. For some, it may take a few weeks to learn how food is impacting their ketones and they may have social occasions that get in the way of their adherence. This suggestion is supported by a new systematic review of the literature that stated all interventions should be at least

12 weeks long to allow for adaptation and to give enough time to see results (Sindler et al., 2023).

As there is an increased risk of those with moderate to severe psychiatric illnesses such as bipolar disorder, experiencing a deterioration in mental state in the first few weeks of implementing a ketogenic diet, it would be prudent for future researchers to take a gradual approach to reducing carbohydrates and reaching the ketotic state, especially if the individual is taking psychiatric medications. To support this, intervention platforms could benefit from providing further regular psychoeducation and support that takes a step by step approach over the 12 weeks to keep individuals engaged and motivated to continue.

In terms of support, future research would benefit from allocating a member of the research team to monitor a 'contact-us/get-support' email account or chat box. Participants should be encouraged to easily contact and communicate with the research support throughout the study. They should be able to have their questions answered on the logistics of the program, for example questions on how to log in to the platform, or how to navigate to their profile. To take it one step further, there could be designated researchers or supports to contact participants first, and directly as proposed by Crichton et al. (2012), especially for such a long study where the second half there is less support. This means that the researchers act in a preventative fashion, as opposed to a responsive manner.

Finally, future research should carefully select their participants. In this study, participants were blinded to their intervention and unaware of the exact reason

for the research. Had participants known that the study was measuring the impact of the ketogenic diet on depressive symptoms and psychological well-being, perhaps participants would have better adherence to the intervention. Perhaps those who fell into the depressive symptoms groups would also have shown better adherence to the intervention because they are searching for something to improve their symptoms. The ketogenic diet is a novel therapeutic intervention for those with moderate to severe psychiatric illness where in some cases they may have become resistant to some standard medications. They want to feel better and reduce both their physical and mental health symptoms. They have a WHY. It is very difficult to change diet totally, so the why and reason for doing so needs to be strong. This, for some, was just not strong enough. It seems that those for whom the diet did work – stuck to it.

Therefore, future research should fully inform their participants on the intervention and the possible changes that can be expected with this dietary approach. It may even serve the researchers better as the participants can be engaged in the research and actively contribute to the research findings by sharing their accounts of the intervention along with any improvements or changes experienced. These suggestions should help to advise future researchers to consider these reasons before designing research studies, interventions, or methods of care, specifically within the mental health population.

Chapter 5: Study 3 - Attitudes Towards and Accounts of the Ketogenic Dietary Intervention Experience (Qualitative Thematic Analysis)

5.1 Introduction

5.1.1 Background

When researching ketogenic diets for psychiatric conditions, case studies of patients following a ketogenic diet with positive outcomes on their mental health have been published as far back as the 1960's (Pacheco et al., 1965). Research into the ketogenic diet's effects on bipolar depression type 1 (Saraga et al., 2020) and bipolar depression type 2 (Phelps et al., 2013) in the past decade has shown the diet has mood stabilising effects and can reduce the need for psychiatric medications. More recently, a study using the ketogenic diet for serious mental illness in an inpatient hospital setting of 31 patients, found 43% clinical remission and 64% of patients discharged on less medication than when they started (Danan et al., 2022). The research into the ketogenic diet for psychiatric diseases is growing rapidly thanks to the work of these researchers and clinicians such as Dr. Chris Palmer who has made 'metabolic health is brain health' a mainstream phrase through his book 'Brain Energy' (Palmer, 2022). The RCTs are in progress to investigate whether the ketogenic diet can be used as a therapeutic medical intervention for psychiatric illness. However, the research available at present is predominantly quantitative in nature.

This research carried out a review of the qualitative literature looking at the experiences of participants who are following any diet to better understand the

barriers they faced. Poraj-Weder et al. (2021) looked at the experience of those who had tried to lose weight and the reasons why it is so hard for some people to lose it. They found that some participants came off their diet because they felt it was too restrictive to be followed long term. Other disagreed with the recommendations made by the dietitian and therefore did not see the results they wanted. Both of these outcomes suggest that in order for a diet to work it needs to be up to the individual to create their diet within a given framework, rather than being prescribed a diet plan. The individual needs to understand how a diet works and must learn how to implement it into their lifestyle for the best outcomes. Cradock et al. (2021) used qualitative approach to understand the barriers that influence diet behaviour in a population with T2D. They found that themes of lacking energy, lacking motivation and poor or low mental state were barriers to sticking with a healthy diet and physical activity. In a thematic analysis by McDonald et al. (2022) exploring constructions of healthy eating, the theme of tempting hyperpalatable foods was presented. The idea of cravings and desiring foods and having to stay strong in a bid to staying health was expressed. In addition to this they found that certain tactics had to be used to stay on track day to day such as meal planning and preparing food ahead of time. They also covered the challenge of social engagements and found that individual's preferred to shy away from attending the event so that they didn't need to explain their nutritional approach to others and were not tempted by what they believe to be unhealthy foods.

With regards to the low carbohydrate and ketogenic diet qualitative literature, it is only within the last five years that qualitative studies on the ketogenic diet

have been published. This may be a result of the ketogenic diet gaining popularity in recent years as a dietary approach to lose weight.

Harvey et al. (2018) looked at healthy adults, non-obese, non-diabetic, following a ketogenic diet with MCT oil supplementation (N=28), specifically the 'lived experience' of such individuals over three weeks. They found that individuals experienced benefits in well-being, mood, sleep, and sugar cravings and that these improved gradually over the duration of their study. They found that mood, energy, and cognition were low at the start of the study, most likely due to a reduction blood glucose without the increase in ketones, as the participants had not yet reached ketosis. This was also true for satiety levels, hunger, and the desire to eat, as well as sugar cravings, all of which improved as time went on and participants achieved a state of ketosis, where ketone levels were increased and providing energy for the body. Individuals who came off plan or who were non-compliant experienced negative effects in the form of a "food hangover".

Sleep quality also improved which is to be expected as research suggests that following a higher carbohydrate diet negatively impacts sleep by increasing sleep length but reducing its quality by spending more time in rapid-eye-movement (REM) compared to slow-wave sleep (SWS) (Benton et al., 2022). According to a systematic review, individual's following a low carbohydrate diet tend to spend more time in SWS and experience an increase in the duration of deep sleep (Vlahoyiannis et al., 2021).

Using thematic analysis, Newson and Parody (2022) looked at the experience of low carbohydrate diets in those living with T2D. They found that in ten participants, who had been following a LCD for at least five months, they experienced a lack of hunger, gained confidence, felt resilient, calm and more energetic. Although they felt that starting the LCD was difficult, it was easier over time, and soon became a lifestyle.

Finally, Wong et al. (2021) looked at the ketogenic diet amongst those with type 1 and type 2 diabetes, who followed a ketogenic diet for between six to 19 months (N=14). Using thematic analysis, they found that individuals experienced greater glycemic control, weight loss and satiety. Participants also experienced improvements in cognition, specifically concentration, a reduction in chronic pain levels, an increase in well-being, energy, and improvements in sleep. Individuals reported no hunger and stated that the KD was easier to follow than other diets, however they did initially express difficulty getting used to the idea of eating a KD as the foods eaten are not in keeping with conventional nutritional guidelines. Individuals reported some keto flu symptoms at the start of the diet such as fatigue, headaches, dizziness, and constipation but these symptoms were temporary and soon passed. These findings support the work of Bostock et al. who found that keto flu symptoms were apparent when starting the diet but that they were transient (2020).

According to Wong et al. (2021) Newson et al. (2022) and Bostock et al. (2020) the diet implementation can be difficult initially, but soon the diet becomes easier to follow and progresses into a lifestyle. The findings from this study reflect these previous reports.

From this literature, it is clear that the ketogenic diet can lead to improvements in mental health and relief from psychiatric symptoms in some people. The exact cohort of people that the KD will benefit is yet to be determined, although there are hypotheses. Many of the clinical outcomes of following the ketogenic diet are known, as seen in Chapter 1. The benefits, if a patient responds to the diet, can be life changing, and the safety of the diet has been confirmed (Bravata et al., 2003; Castellana et al., 2020; Ludwig, 2020; Moriconi et al., 2021), but whether the diet is easily implemented and sustainable in the real-world within the general population is uncertain.

Research is required to investigate the accounts, perspectives, and experiences of those following a ketogenic diet to better understand their journey to improve their physical or mental health. This will help researchers to better inform care pathways and provide the right support to individuals at the right time.

The previous chapters have covered and explored the effects of the ketogenic diet on psychological well-being and the results from the studies have produced quantitative outcomes that will inform clinical applications and future research. During the design phase of this research project the researcher included a qualitative element to gain a richer understanding of diet and study experiences. It was proposed that this additional narrative would add a depth to the research findings that is not found with quantitative findings alone. This study follows up with nine participants who followed the ketogenic dietary intervention arm of this research study. Follow up was close to a year later as the final time point of the study was at six months (T4, week 24).

5.1.2 Aims and predictions

The aim of this study is to review the accounts of participants who have completed the ketogenic dietary online intervention and program and to identify any common themes relating to their journey. This study will focus specifically on the health of participants prior to the start of the program, the challenges, and obstacles they faced implementing the diet and any physical or psychological changes, either positive or negative that they experienced throughout the program. Aside from directly discussing their accounts of the KD intervention, the interviews will cover participant's overall health and well-being in a broader sense and will touch on areas such as their relationship with food, their general health, and their mental and physical state prior to starting the ketogenic diet.

5.1.3 Original contribution

This study will complement the quantitative studies in this program of research. Through reflexive thematic analysis, the accounts and attitudes of participants following the ketogenic dietary intervention will be explored. Though there are a few studies directly exploring the experiences of those following a low carbohydrate or ketogenic diet, this will be the first study to explore the narrative through the lens of mental health and psychological well-being. The findings will inform future research directions into the application of a ketogenic diet either through online programs or via healthcare professionals in clinical practice. The data gathered is crucial to fully understanding if and how an online platform and dietary intervention could help those with depressive symptoms and poor psychological well-being.

5.2 Methods

5.2.1 Design

The study was an interview-based research piece, using face to face semi structured interviews of participants drawn for the pool of ketogenic dieters in study 1, and using Braun and Clarke's reflexive thematic analysis process to draw out, create, and analyse themes (Braun & Clarke, 2012). Reflexive thematic analysis takes an experiential approach and was chosen to understand the views, perspectives, and perceptions of participants following the ketogenic dietary intervention (Braun & Clarke, 2014).

5.2.2 Participants

A sample of nine participants who had followed the ketogenic diet (KD) intervention were recruited for this study. Participants were recruited from the study 1 sample. There were five participants from the 'healthy adults' group and four participants from the 'depressive symptoms' group. Out of the five in the 'healthy adults' group, one participant had a diagnosis of depression from their GP, and they were taking antidepressants for more than three weeks. However, when randomised to a dietary intervention, they had a PHQ-9 score of 3, meaning they were allocated to the healthy adults group rather than the depressive symptoms group.

In the healthy adults group, there were five females and one male, and in the depressive symptoms group there were three females and one male. The mean age overall was 51 years (SD 8.12). The mean age for healthy adults was 52 years (SD 10.23) and for depressive symptoms it was 49 years (SD 5.47). All

nine participants were renamed for the purpose of this analysis in order to maintain their anonymity. Reference names are seen in the table below along with their group allocation, age, and gender.

Table 5.1: Demographics of participants, anonymised name, psych group, age, and gender

Participant Number	*Anonymised Name*	*Psych Group KD*	*Age*	*Gender*
1	Amari	Healthy	36	Female
2	Anika	Healthy	63	Female
3	Diane	Healthy	58	Female
4	*Harriet	Healthy	54	Female
5	Mark	Healthy	50	Male
6	Jessica	Depressive	56	Female
7	Philip	Depressive	43	Male
8	Sarah	Depressive	47	Female
9	Whitney	Depressive	50	Female

*Participant had a diagnosis of depression but showed very few depressive symptoms on the PHQ-9 and so allocated to healthy group

5.2.3 Materials and measures

For the semi-structured interviews, open ended interview questions with a series of prompts were developed by the researcher and approved by the University of East London Ethics Committee in order to extract the full journey from the eligible participants (see Appendix E).

Examples of the questions included in the interview were 'how had you been feeling psychologically and emotionally before starting this program?' and 'please can you describe your journey on the diet?', with prompts such as; 'what were reasons for joining the program?', 'how do you think diet played a part in

how you felt?', 'what was your opinion of yourself?', 'how did you feel in the first few days?' and 'how has your mental state or mood changed?'.

Zoom software, which is GDPR compliant, was used to carry out the interviews. NVivo qualitative analysis software (NVivo 12 for Mac) was later used by the researcher to aid in the organisation of transcripts and carrying out the thematic analysis. Finally, MIRO software was used to help the researcher visualise the themes and create thematic trees as seen in Figure 5.1, 5.2, and 5.3.

5.2.4 Procedure

There were two criteria for participants to be eligible for this study. Firstly, participants must have ticked 'yes' to the following question in the study 1 consent form, 'I am happy to be contacted for future research studies by the researchers or by Diabetes.co.uk'. Secondly, participants must have at least completed the questionnaire sent to them at time point 3 of study 1. This questionnaire was sent 12 weeks after the start of the trial and marked the end of the online intervention. Participants must have completed at least 12 weeks of the trial to be eligible for this study because it was imperative that they could give a full account of the intervention from start to finish. There were 18 participants in the keto diet group who completed the questionnaires at 12 weeks. Those who completed time point 4, the final time point at 24 weeks, were also eligible and there were 15 participants at this point. Overall, there were 33 participants in total from the keto diet group who were eligible for this study.

The email addresses of those who were eligible were made available to the researcher by the study collaborators Diabetes.co.uk. No other identifiable data

was given to the researcher at this time. Participants were contacted by the researcher once study 1 had come to an end, more than six months after the study began. An email, using the university's email server, was sent out to all eligible participants, asking them if they would like to take part in this follow up study. Initially, participants must have completed all 24 weeks to be eligible for the study. However, due to high attrition rates across the study, those what had completed up to week 12 were also eligible. An information sheet and consent form were attached to the email, (see Appendix Y). A total of two follow up emails were sent to eligible participants until recruitment was complete.

Once participants had been recruited, and had signed the consent form, the researcher agreed a time and date to carry out the interview via Zoom. Interviews were approximately 20 minutes long, with some a little longer based on how much the participant wanted to share. Interviews were conducted via Zoom with the researcher based in a quiet, private university meeting room. All interviews were audio recorded for later transcription following informed consent at the start of the call.

Participants were encouraged to share their journey of following the online dietary intervention and the positive and negative effects they encountered during their dietary change. Following the interviews, all participants were sent a debrief sheet (see Appendix AA) explaining the reasoning for the interview and study overall.

Interviews were then transcribed into Word documents and saved on the researcher’s password protected university drive. Full transcripts were then

uploaded to data analysis software NVivo to assist with the qualitative analysis. Once uploaded, the audio recordings were subsequently deleted.

5.2.5 Position

An essentialist and realist approach to the data was taken, with the language used by participants to share their accounts of the intervention taken at face value, with no further in-depth interpretation of the meaning of language used seen as necessary. What participants say is their experience and reality (Braun & Clarke, 2006). Then, an inductive or 'data-driven' approach was taken as there were no specific research questions and no pre-defined themes for this study. This was an exploratory analysis where the themes became analytical outputs and were reflective of the data collected and were therefore free from the researcher's analytical preconceptions (Braun & Clarke, 2019). Themes were actively identified at the semantic level, meaning that no further interpretation of the data was carried out beyond what the participants had shared. Themes were then described and further interpreted. This position and approach is similar to that used by Newson et al. (2022) who used thematic analysis to investigate the experiences of those with T2D following a low carbohydrate diet.

5.2.6 Reflexivity statement

At the time of research project design, the researcher was working in acute inpatient psychiatric services as an assistant practitioner on both male and female wards. The researcher also took the position of ketogenic nutritional consultant in a private limited company from 2017-2023, the duration of this research project. Here, the researcher disseminated the current ketogenic and fasting literature into layman's terms and educated the public with this

information over a period of six years. The researcher also worked 1:1 and via groups with clients to initiate a ketogenic diet and fasting protocols, based on the scientific literature for the goals of fat loss and improved general health. The researcher has also personally followed a ketogenic diet since 2014. The initiation of this diet is what prompted this research project. In the final year of this research project, the researcher worked with clients who were implementing the diet with the goal of improving their mental health. Overall, this experience and these events may have aided the researcher in the design of this study and may naturally have shaped how the researcher developed codes and themes for the data in this study.

5.2.7 Ethical approval

Ethical approval was granted from the University of East London, UREC 1718 87 on the 4th of July 2018. The approved semi structured interview schedule can be seen in Appendix E.

5.2.8 Analysis

An inductive thematic analysis of the interview transcripts was carried out following the six-phase framework set out by Braun and Clarke (2006), to review the shared accounts of participants.

Transcripts were initially coded line-by-line and sorted. The researcher became familiar with the data by reading and re-reading the transcripts before generating initial codes. These preliminary codes were assigned to the data to describe the content. The researcher then searched for consistent patterns and developed themes from the codes across all interviews after a period of

familiarisation with the collected data which is in keeping with the work of Terry et al. (2017). Once themes were constructed, they were repeatedly reviewed, defined, and renamed. Figure 5.1 below shows the initial themes and sub-themes emerging from the data. As the researcher continued to review the data, themes and sub-themes merged further to create Figure 5.2 which produced six main themes. This process continued and with further refinement and renaming, the researcher reached the stage where they were confident with the final groupings. There were six main evident themes with three to six sub-themes each, see the final Figure 5.3. A total of six themes were identified from this sample. The findings were kept to six themes so that the analysis stayed coherent, and that the researcher could provide a meaningful overview of the data. This is in keeping with the guidance from Braun and Clarke (2012). The findings were then written up and finalised.

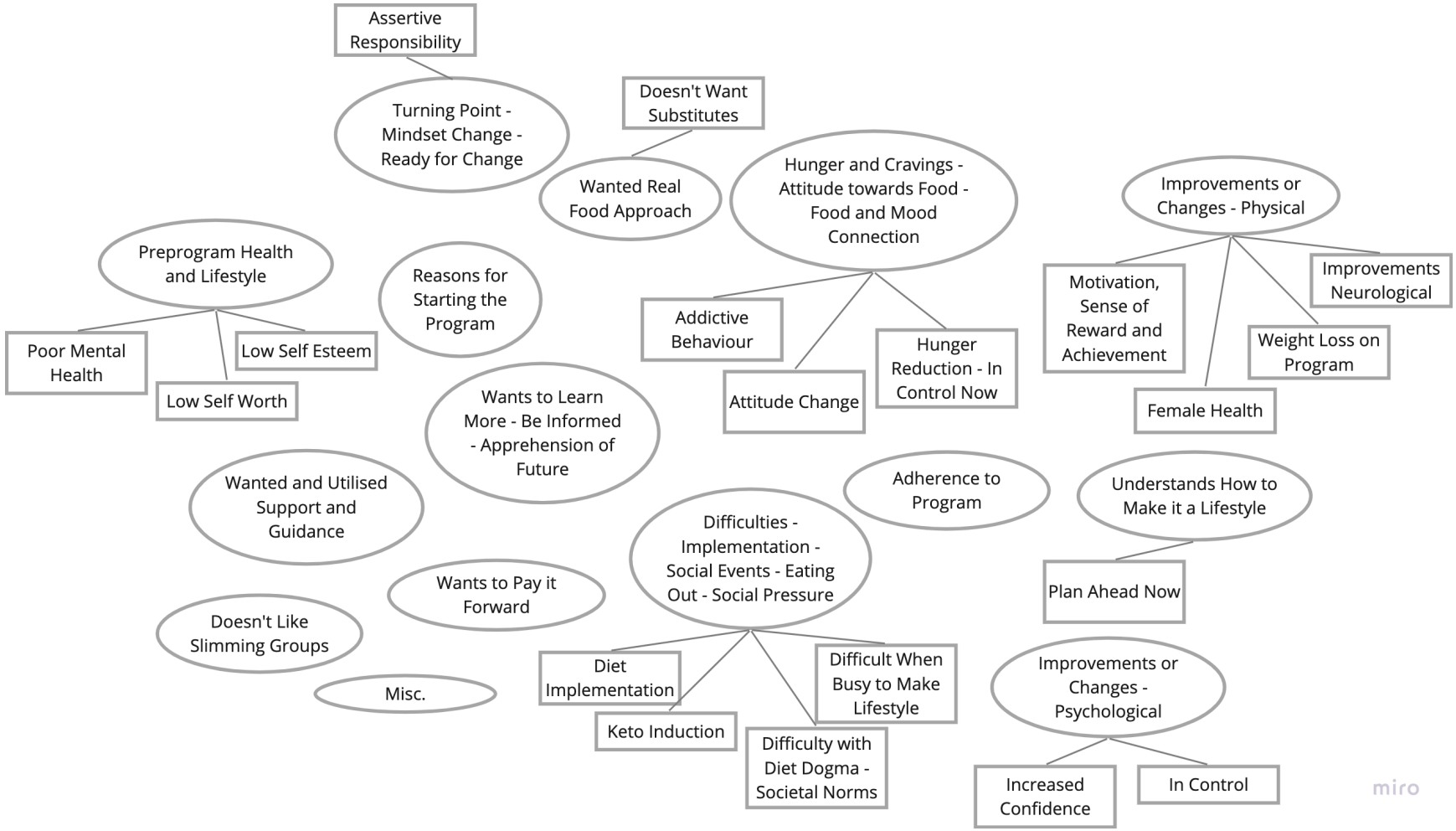

Figure 5.1: Initial thematic map showing emerging themes (circles) and sub-themes (rectangles)

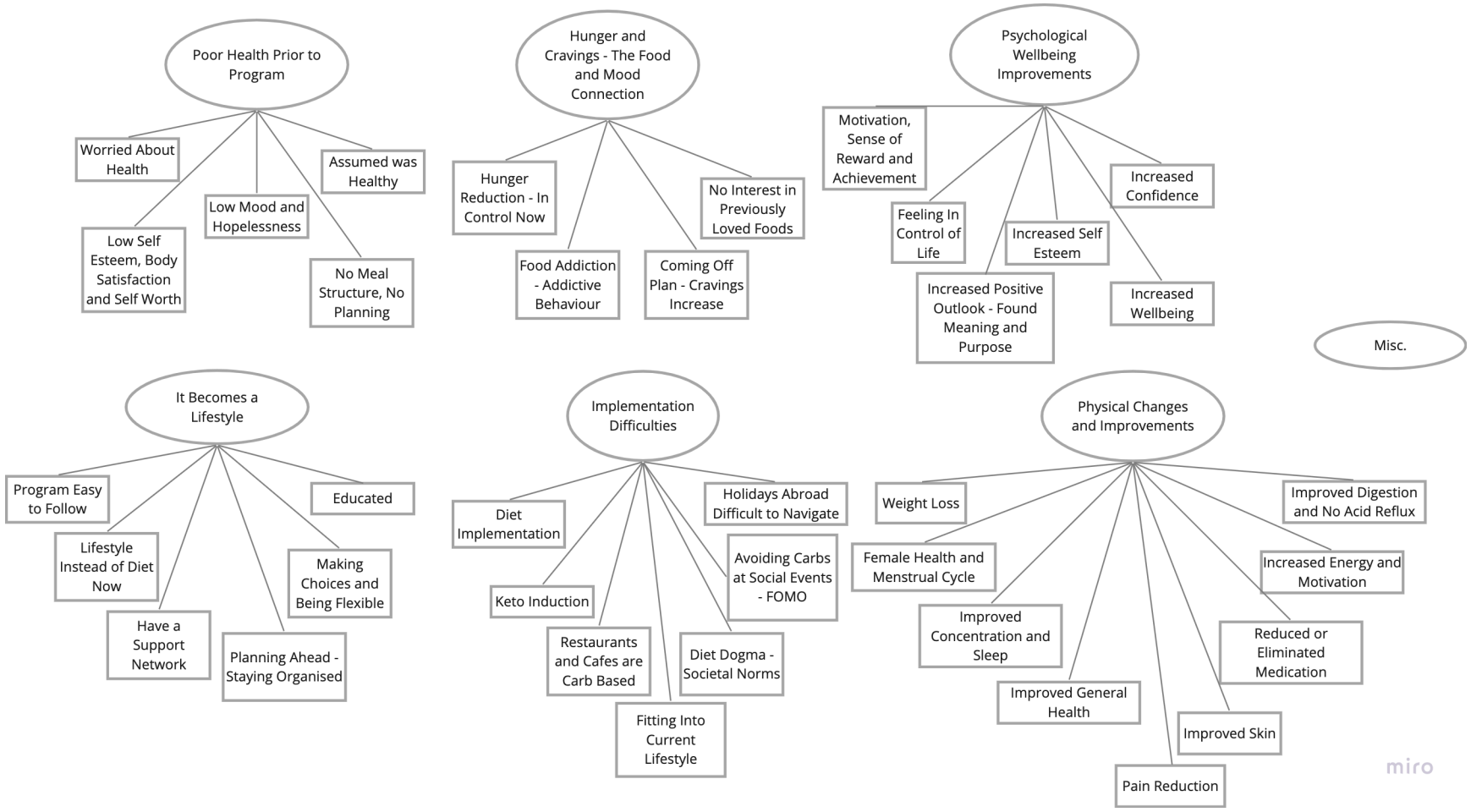

Figure 5.2: Thematic map showing six main themes in progress (circles)

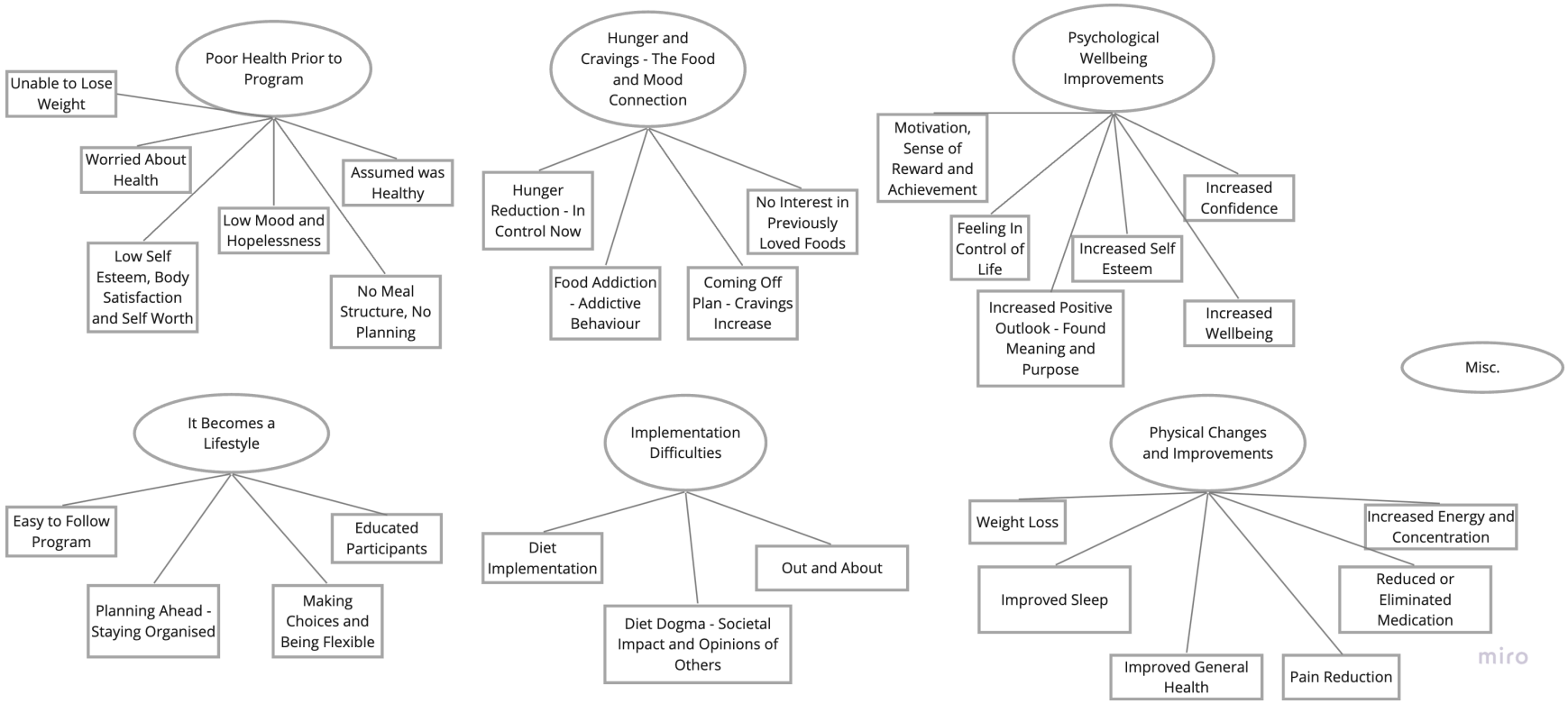

Figure 5.3: Final thematic map showing six main themes (circles)

5.3 Findings in Relation to Groups and Previous Research

Six core themes and 28 subthemes were created during this analysis as seen above in figure 5.3. The six core themes in order from highest referenced to lowest referenced were, (1) Poor health prior to program; (2) Hunger and cravings – the food and mood connection; (3) Psychological well-being improvements; (4) It becomes a lifestyle; (5) Implementation difficulties; and (6) Physical changes and improvements. Direct quotes from participants have been included to help illustrate each theme and subtheme and, in some cases, the psych group they were allocated to has been identified to better understand if a subtheme was predominantly representative of one specific group. Identifying each participant group, as healthy or depressive symptoms, is not typically qualitative in approach, however, in some findings relating to psychological well-being it is interesting to note who experienced improvements or deteriorations. Participants in general felt that they were healthy, but the intervention made many reflect on their health prior to starting the study and adopting the ketogenic diet.

5.3.1 Theme 1 - Poor health prior to program

This theme is characterized by participants stating that they felt generally healthy, however as the theme was refined, physical and psychological health issues arose from the data which suggested that people were not as healthy as they had initially assumed.

5.3.1.1 Subtheme - Assumed was Healthy

The first question in the interview asked how the participants health was before starting the program. Four participants out of nine, "assumed they were healthy" and that they ate in a generally "healthy" way. Diane believed that her health is "pretty good in general", both now and before they started the program. Whitney stated that she couldn't remember the last time she purchased a ready-made meal as she always prepares her meals at home alluding to the fact that she followed a healthy diet overall. Mark shared his thoughts when grocery shopping:

> You know, I'd go round the supermarket and look at people's trollies and think ooh no you don't want to be eating all that crap because I thought we were, well we were, we do, eat relatively sensibly. (Mark)

Some participants were following a standard western diet prior to starting the ketogenic diet. Other diets such as the Mediterranean diet, which eliminates processed foods like the ketogenic diet, are associated with greater psychological well-being compared to the western diet (Firth et al., 2020). Perhaps some participants experienced this when moving from the standard western diet to the ketogenic diet.

5.3.1.2 Subtheme - No Meal Structure, No Planning

Though answers to the interview questions about health varied from good to bad, the overarching observation was of poorer health prior to initiating the program. There appeared to be a lack of meal structure and little planning of food or meals in advance which led participants to graze through the day, eat on the go, or eat less healthy options based on what was available when they

were faced with hunger. This was reported by two participants in the depressive symptoms group and one in the healthy group. The lack of meal structure and food planning was felt by Sarah who shared that because she only had to cook for herself, she didn't, and for Harriet, she would spend the day "eating rubbish" and skipping dinner as a result. For Whitney, a morning routine with no meals planned appeared to be normal:

> *So then I wouldn't have time for breakfast so would just go to work and drink coffee…There is that, if there's biscuits going round, or cake, you would have that before your lunch. (Whitney)*

Participants appeared to have a daily self-care routine that lacked a meal structure or food planning stage. The perceived lack of time to plan meals or prepare food is associated, unsurprisingly with a higher intake of fast and convenient food (Escoto et al., 2012). On the other hand, meal planning has been linked with improved diet quality and less obesity (Ducrot et al., 2017) and structured meals may increase the success of weight loss (Eom et al., 2022) and therefore overall health if employed consistently.

5.3.1.3 Subtheme - Unable to Lose Weight

Although the topic of weight was not part of the interview questions, in the context of diet change and previous health, weight came up multiple times across the interviews. Some participants stated that their weight issues ran in the family:

*My grandfather's nickname was jumbo fist, he was quite charismatic character, but he was about 24stone and 6 foot 6! So, he was a giant of a man and lived till 77 but I actually attended a family birthday this weekend, my aunt's birthday and on my mother's side of the family with the exception of 1 they are all people who have battled with their weight. (*Mark)

And that they had carried excess weight since childhood.

When I was at junior school and we were doing a Mary and Joseph Christmas play, and I was Joseph and I had a Mary and she said to me, you look like you're pregnant. (Mark)

Eight out of the nine participants stated that they had tried many diets and dietary changes in the past but for one reason or another, they didn't work long term. They mentioned many well-known diets that they had followed, such as, the Ashcan diet, Slimming World, Weight Watchers, Atkins, Juice fasts, 5:2 diet and diet classes in the hopes of "finding something" (Whitney) that worked, but "nothing worked" (Amari). Mark's statement sums up the eight participants' experience when he said:

I've tried all sorts of things; I've tried slimming world and weight watchers. I've tried all sorts of bits and bobs and it's kind of yoyo fad dieting. (Mark)

So, although some participants stated that they were generally healthy prior to starting the program, they still felt it necessary to seek out and try to follow popular diets to improve their health. Furthermore, for Amari, this was the one thing that she still couldn't master in their life.

*This is the one area, the one thing. (A*mari*)*

5.3.1.4 Subtheme - Worried About Health

Alongside this, there appeared to be an underlying feeling prior to the program, of worries about current and future health, understandably. Again, this questions how participants truly felt about their overall health prior to the program. Though just under half of the participants stated they felt generally healthy, once the researcher dug a little deeper there appeared to be ongoing health concerns amongst many. Philip stated that though he had not been morbidly obese, he had always been on the "wrong side of ok" and that was a concern for him. The idea that some participants needed to take medications for their ailments was also a cause for worry. Amari stated that she didn't want to take the medication and it "doesn't make me feel nice". Anika shared the reality of her worrying situation:

The only thing that can stop the neuropathy is medication unfortunately…they said it was something I was going to have to be on. (Anika)

When participants were asked to share more about their experience of health prior to the program, it became clear that there were both significant negative physical and psychological symptoms present in their everyday lives. Physically, participants experienced extreme tiredness, fatigue, and lethargy throughout the day.

I was really struggling in meetings at work, and I was constantly falling asleep, and I kept thinking, what on earth is wrong with me! (Harriet)

Tired is an accurate word of how I would describe myself, sluggish and just tired. I didn't have a lot of energy anymore, restless, you know. (Sarah)

Prior to the dietary intervention their cognition and ability to concentrate was also impaired, they lacked focus and often experienced symptoms such as brain fog. Mark stated that he had always had a low attention span, and that he still struggles with that now. Philip shared his more debilitating experience:

Whether it's a funk or fog I don't know, so this is where I sort of started, I couldn't really sort of keep any concentration and any focus or goal…I've always enjoyed learning, but I couldn't focus, I couldn't retain any attention to what I was doing…I was getting frustrated with myself. (Philip)

Alongside this, participants also experienced negative physical symptoms. Amari shared that she was constantly dealing with "stomach cramping, IBS pain and acid reflux". This physical response may have been a result of the psychological distress participants were encountering (Qin et al., 2014), following a western diet (Raskov et al., 2016) or a combination of both.

5.3.1.5 Subtheme - Low Self-Esteem, Body Satisfaction and Self-Worth

Psychologically, extremely low self-esteem, poor body satisfaction and little self-worth were evident in four of the nine participants. Worthlessness is a symptom identified in the diagnosis of depression and research shows that poor body satisfaction predicts worse depression and mood outcomes (Choi & Choi, 2016; Hasin et al., 2018). Three participants from the depressive symptoms group stated that they felt "terrible about myself" (Jessica), that they were "feeling so

rotten" (Whitney), and "my opinion of myself has never been terrific" (Philip). One participant from the healthy group shared that:

I couldn't even look at myself in the mirror, really, really, low self-esteem. (Amari)

This was followed by "rock bottom" confidence (Jessica), a lack of motivation, and the feeling they were "stuck in a rut". Understandably, day to day energy was limited and carrying out simple daily routines and tasks were a struggle for some participants. As Jessica put it, "I couldn't motivate myself to do anything". Whitney shared her thoughts:

Yeah, so I suppose a lack of motivation, you just get into that rut don't you, you feel lazy so you just, you can't get up…and just felt stuck in a rut. (Whitney)

This lack of motivation, and low energy that participant's experienced ties back to their difficulty of following a routine that supports a healthy lifestyle and may have been a contributing factor to their lack of daily structure with regards to meal timing and food planning. Whitney again shared an example of this:

Not getting out of bed on time to get myself ready for work to get to work…Yeah just feeling pretty lazy actually. (Whitney)

5.3.1.6 Subtheme - Low Mood and Hopelessness

For some participants, their mood was extremely low which is a symptom necessary for the diagnosis of depression (Hasin et al., 2018). From the healthy group, Anika felt "quite depressed really", and from the depressive symptoms group, Philip experienced a sense of hopelessness.

I was beginning to worry about, not depression itself but being in a rut if you know what I mean…I felt pretty hopeless, I wasn't suicidal, I just couldn't work out what was wrong with me. (Philip)

Jessica even felt a lost sense of meaning and purpose in their life.

I was just getting really down about, well where is my life going and what was there left for me to do…but I couldn't find my niche in life…you lose your identity really…you just think, oh well, who am I then? Where do I fit in? (Jessica)

These low feelings and experiences were to be expected in some participants as they showed mild to moderate depressive symptoms at the start of the study which is why they were placed in the depressive symptoms group. However, their accounts of daily life prior to the program are clearly impactful. What is interesting is that there is a positive relationship between the western diet, and major and persistent depression (Jacka et al., 2010) which could in part explain their perceived low mood. The western diet is also associated with metabolic syndrome which as stated earlier, is associated with depression (Dunbar et al., 2008; López-Taboada et al., 2020; Zinöcker & Lindseth, 2018). Overall, these findings suggest that poorer physical and mental health was experienced prior to starting the ketogenic diet.

5.3.2 Theme 2 - Hunger and cravings – the food and mood connection

The second theme from this data is Hunger and Cravings – The Food and Mood Connection. This theme starts by explaining how participants experienced hunger and cravings during this program, followed by their experience of an increase in self-awareness where they were able to make the connection between eating certain foods, and that foods impact on their bodies both physically and mentally.

5.3.2.1 Subtheme - Food Addiction – Addictive Behaviour

Many participants noted that consuming sugar through sweets, chocolates, or baked goods, had a negative impact on their physical and psychological health. They found that when they ate sugar or carbohydrates, they "crave it more" (Whitney). Harriet shared how her cravings can impact her behaviour around sugar:

> *If I don't have any sugar, I don't crave it but the minute I have some, then I just go off the scale again. (Harriet)*

When she attempted to eliminate the sugar from her diet, she experienced emotional withdrawal like symptoms. This may sound extreme, but sugar addiction (Avena et al., 2008), has been shown to be equally or more addictive than other substances such as cocaine (Ahmed et al., 2013; DiNicolantonio et al., 2018; Lenoir et al., 2007) and food addiction has been recently considered a valid diagnostic construct (Gordon et al., 2018). Research suggests that the western diet can promote addictive eating behaviours due to the composition of many ultra-processed convenience foods which are both high in fat, salt and sugar, the combination of which are not found in natural whole foods (López-

Taboada et al., 2020). Interestingly a recent case series shows promise for treating Binge Eating Disorder and food addiction symptoms with a ketogenic diet (Carmen et al., 2020). A pilot study by Rostanzo et al. (2021) of five participants using the ketogenic diet as a treatment for binge eating and food addiction in women found that after following a ketogenic diet no cases of food addiction or binge eating were recorded, and all participants improved.

In the current data, there were three accounts from participants on their experience of sugar withdrawal.

I have to go through that real craving few days where I feel like I need to be locked in a room so I can't have any, and then I'll be fine. (Harriet)

How your brain just thinks, it makes you believe it will be ok to have one, I can account for this it will be ok, but no it won't be one, it never ever is, and even now, I know that, the sensible side of me knows that but the craving and desire was so strong. (Harriet)

I could demolish a packet of biscuits without even thinking about it, I could honestly, if the biscuits are in the house, I can eat them, they are in the house and they're there and they're calling me all the time. (Jessica)

These accounts of sugar withdrawal are similar to the behaviour effects noted in other addictions. Research suggests that highly processed foods such as sugar can trigger addiction-like symptoms and behaviours, including withdrawal when restricted or reduced in some people (Parnarouskis et al., 2020; Schulte et al., 2018). These behaviours are linked to alterations in the brain's neurochemistry, such as the dopamine pathway, which is also altered by other addictive substances (Avena et al., 2008). In rat studies, the withdrawal symptoms from

sugar were found to be similar to symptoms of morphine or nicotine withdrawal (Colantuoni et al., 2002). Alongside this, physical symptoms of withdrawal were also experienced, and one participant could feel the impact of sugar on their blood glucose levels. Diane said:

Weird headachy thing when I feel my sugar go up. You know what I mean, it's like a sugar spike kind of feeling, I feel a bit muddy headed and a bit groggy. (Diane)

Another participant realized that they were experiencing a change in blood glucose levels post sugar intake. They realized after they had eaten some sugar, that they were experiencing the sugar spike. They had heard about it happening before and had thought "really does that exist?" (Harriet).

5.3.2.2 Subtheme - Hunger Reduction – In Control Now

Once participants had started the ketogenic diet, hunger levels appeared to drop, cravings dissipated, and they felt more in control of their diet. This is in keeping with previous research which has shown that cravings for starchy foods, and sweets disappear (Cohen et al., 2018), appetite is suppressed, and satiety levels are heightened on a ketogenic diet due to the physiological state of ketosis (Gibson et al., 2015; McClernon et al., 2007; Nickols-Richardson et al., 2005).

If the ketogenic diet is implemented correctly, and ketosis is the goal, ketone bodies are produced and begin to rise, reaching 1-2mmol/L after approximately 48-96 hours of low carbohydrate intake (Pinckaers et al., 2017). Ketones have appetite suppressing effects and therefore it is expected that hunger levels will drop (Paoli et al., 2015; Roekenes & Martins, 2021) once ketones begin to rise. Physical cravings should also reduce once blood sugar levels regulate and

ketones rise (Anguah et al., 2019; Harvey et al., 2019), leaving only emotional cravings such as eating in response to negative emotions (Dakanalis et al., 2023; van Strien, 2018) such as when anxious or bored, or even when happy (Braden et al., 2018).

Participants began to experience the drop in hunger and the reduction in frequent and bothersome food-related thoughts. Though they expected to be hungry following this diet, as they had been on previous diets, the hunger occurred only once or twice, if at all. This is in keeping with the findings from Newson et al. (2022) whose participants also acknowledged a reduction in hunger. Participants stated, "I just don't seem to get hungry at all" (Jessica) and "I'm actually eating less now than I was before" (Mark), and "I don't even think about food" (Harriet). Philip shared his thoughts:

It seems to be really easy, it's like the simplest thing in the world is to not eat, rather than worry about it…I'm not a scientist, but I put that lack of hunger down to the lack of carbs. (Philip)

Similar to hunger, although participants were expecting to crave certain foods, little to no cravings were experienced. Some were experienced in the first few days as mentioned above, but not to the extent that was expected. Amari stated that:

I thought I might crave, I don't know something savoury or something sweet and I really haven't. It's been fine. (Amari)

Over the duration of the program, cravings appeared to reduce with ongoing low carbohydrate intake and little sugar. One participant stated succinctly, "Because I'm not having it, I'm not craving it" (Whitney). This is to be expected as

physiologically, once sugar is ingested, blood sugar rises and ketones drop (Wolever & Miller, 1995). Blood sugar and ketone levels have an inverse relationship (Courchesne-Loyer et al., 2017). This blood sugar spike will decrease once more and leave the individual looking for more sugar and carbohydrates to increase their blood sugar levels. This is known as postprandial hunger (Wyatt et al., 2021). The presence of ketones are protective in this way. If there are no ketones present, the blood sugar levels drop following a meal, and cravings and hunger will return until such time as the ketones begin to increase past 0.5mmol/L to exert their appetite suppressing effects, similar to when the ketogenic diet is initiated. Psychologically, once sugar is ingested after a period of restriction, a "binge" may occur, which can then lead to "withdrawal" symptoms. Individuals may experience cravings for more high sugar foods which they will need to avoid until the cravings pass, and ketosis ensues. This behaviour was previously reported by Avena et al. (2008). They stated that rats with intermittent access to sugar were found to binge on the sugar when available, similar to other substances of abuse in addiction models.

5.3.2.3 Subtheme - No Interest in Previously Loved Foods

Three participants from the healthy group and one from the depressive symptoms group shared that as time went on, they no longer wanted or liked the taste of anything sweet, "I think my body is used to not having anything sweet in my life now" (Amari). This is in keeping with the research which shows that taste intensity can change, and that sweet receptors can become sensitized as there is no longer a frequent influx of sweet tastes (Wise et al., 2016). Harriet sums up the experience:

Because I have such a sweet tooth, once I stopped that I was amazed at how I could just, I had no interest in anything sweet. (Harriet)

Though cravings were reduced or even eliminated when following the diet, cravings could return for two reasons. Firstly, if carbohydrate filled foods were observed and looked appetizing, such as at social events, or other events where it was difficult to remove them from sight. Sarah mentioned how her workstation was surrounded by chocolate bars. Having these sugary treats around throughout the day when emotions and stresses can occur and at times overwhelm, is not ideal. Research has shown that willpower to resist sugar as a pick me up is difficult when feeling stressed or overwhelmed throughout the day (Yau & Potenza, 2013). These foods are better off 'out of sight and out of mind'. Mark said:

I think a lot of the time I'm not hungry or craving anything and then you see something, and you go hmm. (Mark)

5.3.2.4 Subtheme - Coming Off Plan – Cravings Increase

Secondly, if participants came off plan or increased their carbohydrate intake enough to come out of ketosis, their blood glucose, cravings, and hunger would increase, and some participants felt like they were "back to square one" (Harriet).

On the Saturday, we had pizza and, on the Monday, not only did I get that horrible hunger, but I was in a tetchy mood. (Philip)

As Philip mentioned, not only did coming off plan increase his cravings and hunger again, but for some participants, their mood and physical health were

negatively impacted as they likely experienced symptoms of keto induction or keto flu as they moved back into a state of ketosis. Philip followed on with:

I've really noticed the difference to my mood. I notice now, the next day, I'm really irritable and again I'm putting it down to eating too much or eating too much of the wrong things. (Philip)

One participant mentioned that they experienced quite severe side effects from eating a lot of carbohydrates in one sitting at a wedding:

The day after, I came out in a rash, so my eye swelled up and yeah, just dreadful and that week felt just a bit rotten really. (Whitney)

Understandably, for most participants, their interest in previously loved foods soon decreases and they no longer miss foods they used to eat either because of how their body now responded to those foods or because their tastebuds and food preferences had changed. Wise et al. (2016) reported that a reduction in sugar intake led to an increase in perceived sweetness however, research is unclear as to whether a reduction in sugar intake changes food preferences. The draw towards foods high in sugar or carbohydrates is no longer present and participants stated that going without old favourites "doesn't bother me anymore" (Sarah), they have "no interest in anything sweet" (Harriet) and well, "I don't feel like it" (Whitney). Mark shared how certain he was about the dietary change:

I really don't miss anything and in fact the thought of eating a plate of pasta now or potatoes fills me with dread. (Mark)

It appears that participants have experienced a shift in their attitude towards the diet and their approach to food and the role food plays in their life. They appear to have a heightened sense of self awareness that wasn't apparent prior to starting the program. The chaos and decision fatigue around 'dieting' day to day is no longer present. Mark shared that he could go out to a restaurant and "just get on with it without making a fuss" and Jessica felt that food is no longer the be all and end all of the day, "I don't think about it like I used to", "It has been a complete revelation to me," said Whitney. The increase in self-awareness is summed up well by Philip who said:

Now I can catch myself when I know I'm tetchy about nothing in particular, I'm aware of that now. (Philip)

Overall, participants experienced a significant reduction in their hunger and cravings which only increased when tempted or if they veered off plan with higher carbohydrates either on purpose or by accident. Participants observed and were later able to identify the negative effects that increased sugar and carbohydrate intake had on their mood and psychological well-being.

5.3.3 Theme 3 - Psychological well-being improvements

This theme discusses the psychological changes and improvements that participants experienced over the course of the program. Most interestingly, what appeared to be relatively low self-reported well-being prior to the start of the program, seemed to increase over the duration of the study.

In contrast to the findings from study 1, many participants on the ketogenic dietary intervention appeared to experience psychological well-being improvements which may have been due to the biological impact of ketones on the brain as covered in Chapter 1. However, improvements were not universally observed.

It is important to consider that naturally, as weight loss may have been a secondary goal for participants in the current study, it may be that any reductions in weight, and the perception of these achievements, were the main drivers of the experience of increased well-being, suggesting a psychological impact on the outcomes.

5.3.3.1 Subtheme - Motivation, Sense of Reward and Achievement

An increase in motivation, determination, achievement, and a sense of reward was felt by some participants. In theme 1, "poor health prior to program", participants stated that other diets had not worked for them and that they felt they lacked motivation daily. Since following the program, participants said that they were "determined" now (Sarah) and that "It's nice to feel you are doing something good for yourself" (Diane). Participant Amari shared her account of the diet:

It's just worked amazing well compared to anything else I've ever tried I feel great, I feel fantastic with it. (Amari)

5.3.3.2 Subtheme - Increased Positive Outlook – Found Meaning and Purpose

It appears that the sense of hopelessness, previously described by three participants, had disappeared. A sense of meaning and purpose was found, along with increased positivity. Hopelessness has been shown to be a risk factor for suicidal ideation, which is one of the symptoms needed for a diagnosis of depression according to the DSM-V (Beck et al., 1975; Ribeiro et al., 2018).

Therefore, by eliminating the sense of hopelessness and finding a sense of meaning, the risk of suicidal ideation may be reduced, which in turn reduces the number of diagnostic symptoms present (Hasin et al., 2018).

Participants shared that they felt "a lot more positive and cheerful overall" (Jessica) and that it has given them "more of a positive outlook and helps me focus on my objectives" (Mark). Anika's account showed the renewed sense of hope:

I think my outlook on life is better on the grounds that I don't think I'm going to end up sort of in a wheelchair or whatever, so I think I do feel more energised and it's made me feel more positive. (Anika)

These improvements suggest an increase in aspects of psychological well-being such as mental well-being and depressive symptoms, however, in study 1, a significant improvement in these measures was not found in the data. This lends to the importance of a qualitative arm to support a quantitative based study.

These reported perceived improvements in depressive symptoms would be in keeping with the findings from Tillery et al. (2021) who reported a reduction from moderately severe depressive symptoms to no symptoms in a depression case study of the ketogenic diet. These findings are also in keeping with the improvement in mental well-being found by Unwin et al. (2022) and the decrease in depression found by Danan et al. (2022) when following a low carbohydrate and ketogenic diet. The observed improvements also support the reports of antidepressant effects found in mice models following a ketogenic diet (Gumus et al., 2022; Sussman et al., 2015).

5.3.3.3 Subtheme - Increased Confidence and Self Esteem

Alongside these improvements, some participants' confidence that was lost prior to the program, began to make a comeback and self-esteem improved also. Two participants from the depressive symptoms group mentioned that they felt better about themselves and that they feel more confident since following the program, "feeling better about myself is its own reward" (Philip). Jessica struggled prior to the program with low confidence, and since then she shared that:

> *When I left work my confidence was just rock bottom, I just though oh where is me gone? And now I just feel that me is coming back really. (Jessica)*

These improvements may be related to the diet change and the effect of ketones, but they may also be attributed to a sense of achievement in meeting their weight loss goals and improving their physical health.

5.3.3.4 Subtheme - Increased Well-being and Feeling in Control of Life

Increases in well-being, a sense of calm, equilibrium, and patience were also observed amongst at least five participants which is in keeping with the earlier mentioned work by Harvey et al. (2018). Experiencing calmness when in ketosis is not a new phenomenon and research suggests that this may be because ketones can reduce neuronal excitability (Lutas & Yellen, 2013). Perhaps this is what participants experienced when they mentioned a sense of calm, patience, and less frustration. This increased sense of calm and tranquility experienced by participants is the opposite of agitation which is a symptom necessary for the diagnosis of depression (Hasin et al., 2018).

It is also possible that the routine associated with following the ketogenic diet gave participants a greater sense of control over their diet and their health. Perhaps they were able to form healthy habits as once established, routines and habits require little effort to maintain (Arlinghaus & Johnston, 2019). This may have contributed to increased patience with others as they were less worried and experienced less frustration and decision fatigue when it came to self-care and diet choices, leading them to exhibit a sense of increased well-being.

Whitney stated that she is "no longer in the same place as when I started, much happier" and Mark summed up his heightened well-being:

You know the song Park Life by Blur, where it says you should cut down on your pork pies mate get some exercise, and it talks about the birds and it giving him an enormous sense of well-being, and that always resonates with me in my head, it should be called "pork life" not park life, the enormous sense of well-being that you get. (Mark)

Overall, improvements in psychological well-being were observed by many participants from both the healthy adults group and those with depressive symptoms. Improvements were noted in aspects of psychological well-being that were low prior to the program start, for example self-esteem, motivation, confidence, and a sense of meaning and purpose. The improvements experienced here are in keeping with the findings stated earlier from Harvey et al. (2018), Wong et al. (2021) and Newson et al. (2022).

These psychological improvements may have been a result of the dietary changes and ketone effects on a biological level. However, on a psychosocial level, improvements may also have been a consequence of achieving their weight loss goal, taking control of their health by following a diet, or contributing their data as part of a wider research study.

5.3.4 Theme 4 - It becomes a lifestyle

This theme discusses how the diet becomes a lifestyle over time for participants. There were some initial implementation difficulties that will be discussed later (see section 5.3.5), but overall, it appears that participants were able to easily follow the diet once they understood how to apply and integrate it into their life. On average it takes 66 days or 9 weeks to create an automatic habit, which suggests that for those who continued the study for the duration of the intervention (12 weeks), they may have created a new habit, of following the diet (Arlinghaus & Johnston, 2019). Perhaps this is what helped them to turn it into a lifestyle. These findings are in keeping with the qualitative findings of Newson et al. (2022) who looked at the experience of a low carbohydrate diet in those with T2D. Their participants stated that the diet was difficult initially but then it became sustainable. Participants also noted that they no longer craved carbohydrates and looked at the low carbohydrate diet as a lifestyle.

5.3.4.1 Subtheme - Educated Participants and Easy Program to Follow

Participants shared that the diet wasn't that difficult "once you get the hang of it" (Diane), and that "it doesn't seem like particularly hard work" (Sarah). Over time it became a lot easier to understand what participants could and couldn't eat and it therefore became a lot more "instinctive" (Anika). Mark stated that:

> *This is so easy to do, it's a no brainer and I don't know why it isn't out there. (Mark)*

However, in order for it to become a lifestyle, education about the diet, how it works and how to implement it was crucial. Initially, participants followed education videos provided in the program, learnt to read product labels, and

understand them, and calculated carbohydrates, calories and/or macros using a notebook or an online tracker app such as MyFitnessPal or Cronometer. Over time, and with practice, the need to do this all the time reduced. This may be because participants had learnt the macronutrient composition of most of their foods and therefore only needed to do this when eating something that they wouldn't usually eat, such as when out at restaurants or on holidays. Cadario et al. (2022) found that in the general population, individuals tend to eat the same breakfast every day while seeking more variety for other meals. This lends to the idea that once participants found one or two suitable breakfast options; the frequency of tracking may have dropped. It is not certain, but perhaps this also happened for other meals in the day.

5.3.4.2 Subtheme - Planning Ahead – Staying Organised

Prior to the program start, some participants mentioned that they had no meal structure or food plan and that they often ate what was in front of them at work and therefore would later skip meals. After some time following the program, many participants found that the key to staying on track was to plan ahead and stay organized, and in some cases, cook or prepare food at home ahead of time such as making their own protein bars without sugar. Planning ahead and preparing food at home is not specific to the ketogenic diet however, as research shows that these actions are important for any dietary program to be successful (Wolfson & Bleich, 2015). Meal planning and preparing food ahead of time is associated with a healthier diet overall (Ducrot et al., 2017).

Harriet shared that checking the menu and knowing where you will or can eat when out and about is a good way to keep this diet easy. Sarah stated that:

Even going into town, having an afternoon, you can't have your cake and your coffee, you've just got to think ahead of what you're going to eat. (Sarah)

Eating out in restaurants and cafes was therefore no longer difficult or confusing. Participants were able to find meals on the menu that fit the ketogenic diet, or they would swap carbohydrate filled sides for leafy greens. Simple side swaps, switching a beer for a vodka and diet soda, skipping the bread, or leaving the chips behind meant that participants could still eat out and spend time with others, "you can order the food, just don't eat all of the carbs that come with it" (Diane). Whitney's account was that:

There's always something you can have without all the carbs – like chicken. (Whitney)

5.3.4.3 Subtheme - Making Choices and Being Flexible

But for some, flexibility was key and ultimately the choices lay with the participants. Perhaps mastering this flexibility helped to keep them on track long term. These results replicate the findings from Newson et al. (2022) whose participants also mentioned that they allowed themselves some flexibility from time to time. There is research to suggest that when it comes to substance use recovery pathways, there are "moderators" and there are "abstainers" (Eddie et al., 2022). It could be suggested that in the context of carbohydrates there are those who were able to have some carbohydrates from time to time, but remain on track, seeing progress, without hunger and cravings. These individuals may be "moderators", and those who stick 100% to the ketogenic diet are "abstainers". This emphasizes the importance of making it a lifestyle for the diet to work. Sarah shared how it has become a lifestyle for them:

I'm not eating crisps and I've had a piece of cake today because well, you're only human. (Sarah)

Participants were able to overcome implementation difficulties and navigate social situations in order to maintain the improvements in their physical and psychological health. Initially they may have been motivated by physical appearance changes but over the long term it appears it was other physical or psychological changes that kept them on track. Society may feel that the ketogenic diet is too restrictive or difficult to follow, however, not only did participants in this study state the opposite but carrying on with the diet appeared to be worth it given the health improvements they experienced.

If I'm left to my own devices, I'm absolutely fine. (Philip)

Having a greater "Why" for following the diet after the end of the program is key. Overall, this subtheme suggests that without the pressure of others, participants were able to make personal choices and decisions in line with their health goals.

5.3.5 Theme 5 - Implementation difficulties

This theme identifies and discusses three main areas where difficulties were encountered when implementing the diet. As with any new diet or way or eating, a transition period is expected with some teething problems along the way. Learning about the macronutrients of foods, what to eat and when to it, all of this requires time. The ketogenic diet is no different. It takes time to learn about carbohydrates and the levels of these in each food and how they affect your individual blood glucose and ketone levels. In a study by Campbell et al. (2019) looking at the implementation of ketosis in those with bipolar disorder, 22% of participants mentioned they encountered an adaption period before they experienced any positive effects from the diet.

5.3.5.1 Subtheme - Diet Implementation

The first challenge area was initiating the diet and getting into a state of nutritional ketosis. Participants found that it took some time before they felt they knew what they were doing. This is in keeping with the works of Campbell et al. (2019) who found that 10% of their participants had difficulties implementing the diet initially.

In the first week to two weeks of implementing the ketogenic diet, there is a transition into ketosis which can give rise to some negative symptoms. This is better known as “keto induction” or experiencing the “keto flu” although it bears no similarity to the viral flu. These negative symptoms are transient and do not last long (Bostock et al., 2020). From the data, as expected, some participants experienced these keto induction symptoms. These short-term symptoms experienced included increased hunger in the first few days, wanting to urinate

more than usual, loose bowels, and reduced energy to carry out day to day tasks. These symptoms "didn't last very long at all" (Jessica), and "went away on their own" (Harriet). In addition to this, interestingly, Amari observed that her menstrual cycle impacted her ketone levels, and she experienced a drop in ketones.

> *My hormones seem to knock the ketones I think, I found that quite tricky, especially the first time because I wasn't expecting it…I thought it was that I was eating more inadvertently but I absolutely haven't, it's my cycle, whatever my hormones are doing effect my cycle. (Amari)*

Though there is almost no research on the effects of the ketogenic diet on the female reproductive system, there is research to show that hormonal changes can alter and increase blood glucose levels, which in turn will decrease ketone levels at certain points in the menstrual cycle (Barata et al., 2013; Diamond et al., 1989; Widom et al., 1992). Further research on the impact of glucose and ketones on the menstrual cycle is needed.

5.3.5.2 Subtheme - Out and About

After these symptoms subsided and participants entered a state of ketosis, the challenge participants then faced was how to fit the diet into their current lifestyle and how to overcome obstacles along the way. The second challenge area was trying to avoid carbohydrates day to day while out and about. Avoiding carbohydrates at social events was a challenge, especially as some felt they were missing out in some instances such as when others are eating dessert at a social lunch. Some participants simply didn't want to come across as rude to their work colleagues. These situations eventually become easier once the lifestyle is

implemented but initially it can be difficult. Philip experienced this challenge when out for lunch with a friend:

I go and see a friend or something like that I find I'm having to say no to cheesy chips. (Philip)

Alongside this, many participants felt that restaurant and café meal options were predominantly carbohydrate based, which made it difficult initially to navigate the menu and choose ketogenic friendly options to enjoy. Participants mentioned that at the start of the diet, "it's not great trying to keep the carbs low" (Diane) when out, and that if you stop anywhere, "most of the things available are sandwiches and sort of carb based foods" (Anika). Diane said that:

The other options are there, it's just, everything comes with piles of carbs quite honestly. (Diane)

This challenge also extended to holidays abroad where access to usual foods was restricted. Being "away from home was difficult" (Sarah) in the early days of the diet, for example, one participant stated that although restaurants had menus, "they are very limited" (Jessica) and "hotel options are not always all you might hope for" (Diane). However, once participants learnt what to eat and began to plan ahead, these challenges resolved.

5.3.5.3 Subtheme - Diet Dogma, Societal Impact and Opinions of Others

The third and final challenge area was overcoming societal norms and diet dogma, and this extended to the opinions of others like friends, family, and work colleagues. Though this is similar to Theme 4 - subtheme 3 "making choices and

being flexible", this subtheme relates to the impact of society and the outward world on the individuals' food choices and decisions.

Following a diet that encourages the consumption of some foods that have been vilified in society (such as eggs, butter, bacon, and red meat) was difficult for some participants (Astrup et al., 2020). This is understandable as mainstream nutritional advice has often been confusing and conflicting for people (Vijaykumar et al., 2021) which is not helped by the lack of adequate nutritional training for doctors to educate their patients (Mogre et al., 2018). The idea of eating fat and reducing the amount of fruit in the diet was "really odd" and a "tricky thing to get your head around" (Amari). Diane had the same experience when it came to eating eggs:

I'm not sure, I was concerned about the wisdom about eating quite so many eggs. (Diane)

The pre-held beliefs about what foods to eat and not eat, as well as when to eat, extended to participants' friends, family, and colleagues too. Once the participants were able to implement the diet it became the opinions of those around them that became the challenge. One participant mentioned that they felt pressured to eat the food given to them by a friend and "it was like, back to square one" (Harriet) with regards to hunger and cravings. Mark experienced this when out with friends:

They'll ask me why aren't you eating and I'll say well I'm not hungry and then I don't know if we will end up going down a rabbit hole. (Mark)

Philip also noted that he had no issue when on his own but that:

If there are other people around or if I go and see a friend or something like that, I find I'm having to say no to cheesy chips. (Philip)

Overall, participants were able to navigate and overcome these three main challenges when implementing the diet. However, from this data, it is clear that following this diet is not as simple as eating set foods at set times.

Food and eating for many in society is a social occasion in the presence of other people. Eating with family in the evenings or eating with friends at the weekends has been shown to facilitate social bonding and increases satisfaction with life (Dunbar, 2017). It has been reported that individuals are influenced by what and how much those around them eat (Cruwys et al., 2015). For example, there is research to suggest that eating with a partner who chooses 'unhealthy' foods, may negatively influence an individual's decision to eat 'healthy' foods (Robinson & Higgs, 2013) and that societal norms can also have a negative impact on an individual's food choice and intake (Higgs, 2015).

A study by Vue et al. (2008) found eight 'need states' in which individual's eat which range from a basic need for food, to social expression, celebration or to gain recognition suggesting that individuals eat for both physical and emotional or social needs. This suggests that there are other lifestyle obstacles and motivations, outside of just food as fuel, that get in the way of following a 'healthy' diet and can derail even the most focused individuals. Attempting to follow a diet that is different to those around you can be difficult, especially during the implementation phase.

5.3.6 Theme 6 – Physical changes and improvements

This theme discussed the physical changes and improvements experienced by participants while following the ketogenic diet.

5.3.6.1 Subtheme - Weight Loss

Weight loss was experienced by all participants, this is to be expected as weight loss is a popular side effect of implementing a ketogenic diet due to the drop in appetite and hunger hormones (Gibson et al., 2015).

> *I mean I was, virtually, I was a 16-18 and I've just recently bought myself a new pair of jeans and I can get in a M&S size 12 and I just stood there and cried really. (Jessica)*

5.3.6.2 Subtheme - Reduced or Eliminated Medication

Following on from this, three participants were able to reduce or eliminate medications that they had been taking prior to starting the program. One participant always took acid reflux medication but "since the first week of being on this diet I haven't taken any, not one" (Amari).

> *I was on blood pressure medication and I'm not on that anymore… before it was quite high and I was on 5mg of a tablet every day, I've not taken it now for 5 weeks. (Sarah)*

These improvements are supported by the current literature which shows that blood pressure can be better regulated (Castellana et al., 2020) and acid reflux resolve (Austin et al., 2006).

In fact, digestion improved for many participants, and they are "convinced it is a change in eating" (Amari). Participants observed less bloating as a result of

implementing the diet which is in keeping with research that suggests the ketogenic diet improves symptoms of IBS, including abdominal pain (Austin et al., 2009). However, further research is needed in this area.

I don't feel that kind of, underwater kind of foggy, bloaty lethargic feeling, yeah where you would eat stuff and just feel rubbish after it as well until its digested. (Whitney)

5.3.6.3 Subtheme - Increased Energy and Concentration

Concentration and energy levels improved for some participants whereas prior to starting the program these levels had been low. One participant who had been a student and studying throughout the program stated that:

I feel like I can concentrate a lot better because before I could never study on a night, it would have to be during the day because by 7 or 8oclock at night I was just completely drained whereas now I'm quite happy to keep reading until 9 or 10 o'clock at night. I just feel like everything is, concentration levels are much better. (Sarah)

Four participants stated that they have more energy overall and that they "feel a lot more energised" to do day to day things like walk their dogs (Jessica) or go to yoga (Anika). One reason for this may be that energy levels when in ketosis and keto-adapted, remain stable throughout the day and do not rely on glucose to provide energy as there is a consistent supply of fat store derived ketones to use as energy (Ma & Suzuki, 2019). Campbell et al. (2019) found that 25% of their participants experienced increased energy when following a ketogenic diet for their bipolar symptoms. Research by Sheng et al. (2022) suggests that losing body fat improves fatigue symptoms so their weight loss may also have contributed to increased energy. Overall, this improvement in both energy and

concentration is encouraging as both lack of energy and reduced concentration are two of the five symptoms needed to be given a diagnosis of depression (Hasin et al., 2018).

5.3.6.4 Subtheme - Improved Sleep

Sleep also improved for many participants on this diet. Some participants were struggling in meetings and were constantly falling asleep during the day. This appeared to resolve the longer they were following the diet and may also have been a result of their now stable energy levels. The literature suggests that some people experience a reduction in sleep duration when following a ketogenic diet, for example the sleep seven hours now instead of nine, but their sleep quality stays the same or improves, in that they wake up refreshed and more energised than before, therefore reducing morning sleepiness (Hallböök et al., 2012; Masi et al., 2022; O'Hearn, 2021; Siegmann et al., 2019; Ünalp et al., 2021). One participant shared their sleep improvements:

> *I'm sleeping better, I struggle with insomnia and have done for four years and I'm definitely sleeping better. (Amari)*

It is important to note that for some people, sleep may get worse before it gets better, especially in the first few weeks of the diet as the body moves into a state of ketosis (Bostock et al., 2020; Masood & Uppaluri, 2018). For those with depressive symptoms or other diagnosed psychiatric illnesses this can be dangerous as sleep deprivation or untracked alterations can increase negative psychiatric symptoms such as mania, hypomania, and psychosis (Hensch et al., 2019; Lewis et al., 2017; Reeve et al., 2019; Umlauf & Shattell, 2005). Therefore, it is important to always work alongside a medical practitioner when

deciding to implement a ketogenic diet with the goal of reducing psychiatric symptoms and improving overall mental health. Overall, this improvement in sleep and reduction of insomnia symptoms suggests that another symptom of depression needed for diagnosis can be improved with a ketogenic diet (Hasin et al., 2018).

5.3.6.5 Subtheme - Pain Reduction

With regards to pain, a decrease was experienced by some participants. One participant had been taking analgesics on a daily basis and was able to reduce the need for these significantly. Another participant experienced pain reduction in their joints. Anika shared her improvements:

> *It's my joint pain, because I've got osteoarthritis and it's both of my hips and I used to get horrendous pain in that, and I barely notice it now it's just every now and again which is just not very often at all. I think it's the pain reduction more than anything. (Anika)*

These improvements are consistent with research that has found that a ketogenic diet can reduce chronic pain (Field et al., 2022), rheumatoid arthritis pain (Ciaffi et al., 2021) and osteoarthritis (OA) inflammatory pain (Kong et al., 2022). See Chapter 1, Table 1.6 for biological effects of ketones on inflammation and pain.

5.3.6.6 Subtheme - Improved General Health

Finally, participants noted a host of other general health improvements such as a reduction in heart palpitations, normalization of blood lipids and improvements in vision:

It would be anecdotal, but everyone has that one part of themselves that is dodgy and mine is my eyes, but there have been points in the past where I've been looking at the computer screen in the morning and I've struggled to see, vision is quite cloudy whereas I don't seem to think that so often these days. (Philip)

Improvements in skin were also noted by participants which has also been seen in the literature (Campbell & Campbell, 2019; Paoli et al., 2012; Zinn et al., 2017). One participant shared their thoughts:

I would never ever dream of going out without make up before and now I just you know, if I'm going out, sometimes I do sometimes I don't so...my skin is better my skin is a lot clearer. (Jessica)

Overall, participants reported experiencing significant physical health changes and improvements, most of which are supported by the ketogenic diet literature. Although this study is focused on psychological well-being it is important to mention the physical changes experienced by the participants and acknowledge that they will also contribute to the psychological well-being and overall health of participants following the diet.

5.4 Discussion and Final Remarks

5.4.1 Findings in relation to current literature

In the current literature there are very few qualitative studies that explore the accounts and lived experience of those following a low carbohydrate or ketogenic diet. Only one study looked specifically at healthy, non-obese, non-diabetic participants (Harvey et al., 2018) and no studies were found that looked specifically at a depressed population following a low carbohydrate or ketogenic diet. This explorative qualitative study is the first to examine the accounts of following a ketogenic diet in both healthy participants and those with depressive symptoms.

Through this qualitative study, participants stated the strengths and limitations on the ketogenic diet as well as their accounts and feedback of using an online platform to improve their health. Potential improvements for the online platform were identified alongside ways in which to increase engagement with the programs and online community across all populations. Though this is a qualitative study, what is interesting is that there were some subthemes where the contributing participants were predominantly females or from specific psych health groups, healthy adults, or depressive symptoms group.

From theme 1 - "poor health prior to program", nearly all participants (n=8) were unable to lose weight on other diets in the past, having tried many diets before enrolling in this study. Later in theme 6 - "physical changes and improvements", all participants (n=9) in this study experienced weight loss. This is to be expected and is in keeping with the work of Wong et al. (2021) whose

participants reported that the ketogenic diet was easier to follow than other diets and they experienced weight loss as a result.

The theme 1 subthemes, "low self-esteem, body satisfaction and self-worth", and "low mood and hopelessness" were predominantly reported by those in the depressive symptoms group. In addition to this, those who experienced the theme 3 subtheme of "increased confidence and self-esteem" at the end of the intervention were also all from the depressive symptoms group. This suggests that those with depressive symptoms experienced improvements in these areas over the duration of the intervention. Although no qualitative studies have looked at this population in relation to the ketogenic diet, the findings are in keeping with the thematic analysis carried out by Newson et al. in (2022) whose participants with type 2 diabetes experienced increased confidence levels.

It is interesting to note that those who expressed the theme 2 subtheme of "food addiction – addictive behaviour", were all females. In the binge eating literature, a study by Levallius et al. (2022) looking at addictive like behaviours across genders found that 42% of females reported binge eating compared to 21% of males. To support this, a mouse study by Wei et al. (2021) reported that female mice are more likely to have an addictive phenotype for sugar compared to male mice. Hussenoeder et al. (2022) carried out a survey (N=1,474) exploring anxiety and food addiction across genders and found that episodes of anxiety increase food addiction in females but not males. This may be because eating sweet foods in excess has been shown to reduce the effects of stress in females and not males (Macedo & Diez-Garcia, 2014). Further to this, females are more likely to report emotional eating, or eating because of anxiety compared to males

(Thompson, 2015). Perhaps the females in this study experienced higher levels of addiction-like behaviour as a result of this phenotype or in order to reduce anxiety and stress. Further research is necessary to fully understand this finding.

Overall, the accounts and obstacles that these participants faced while implementing the ketogenic diet are mostly consistent with the current literature and the researchers experience supporting individuals following a ketogenic diet. These accounts appear to cover most, if not all the challenges that are to be expected when starting the diet or implementing a lifestyle change like this.

What is most interesting is that although the sample in this study was small, improvements were observed in the symptoms (agitation, energy, concentration, and sleep) and risk factors for the symptoms (e.g., hopelessness) that are necessary for a diagnosis of depression by the DSM-V. Therefore, future research is warranted on larger sample sizes to better understand whether a ketogenic diet can reduce the severity or prevent the onset of these symptoms. This may ultimately reduce the chance of receiving a diagnosis of depression.

5.4.2 Limitations and contribution to research

There is one limitation evident for theme 4 - "it becomes a lifestyle". Perhaps it only became a lifestyle for these participants because they completed the entire study and continued with the diet for six months at least up until they were interviewed for this study. This suggests that for those who started the diet, and saw improvements, it may have motivated them to stay on the diet indefinitely, in which case the diet then became a lifestyle for them. This is important to note

as it shows that the diet, if it works, can become a lifestyle, however if no improvements are seen, the diet may remain a struggle or be stopped entirely.

The large number of participants that dropped out before the end of the main research study, study 1 (N=323), may have had a different experience with the diet, and in some cases a more negative one. From the accounts of those who dropped out and were followed up in study 2, this appears to be true. The main reason for dropping out of the study was that the diet was too difficult to stick with or that they had a change in personal circumstance. Difficulties integrating the diet into family life and doing the diet when others in the family are not, make it difficult for this diet to become a lifestyle without guidance and support from professionals or mentors to overcome these challenges.

It is also important to discuss the topic of weight loss as a possible confounder in this study as all participants experienced weight loss. It could be argued that these participants saw improvements in their mood and psychological well-being as a result of their weight loss or fat loss and not because of the impact of ketones on psychological functioning. This may be true as this is the only diet these participants have followed that has worked long term as they stated that other diets didn't work for them. There are many proposed reasons for this, but it is most likely the reduction in hunger, appetite and cravings experienced on the ketogenic diet as a result of the presence of ketones, that make it easier to maintain long term. It is true that other diets can work for weight loss, but not all diets and weight loss programs work long term as many are unsustainable (McEvedy et al., 2017). They are diets, designed to be followed for a short period of time until weight loss goal is reached, they are not lifestyle changes. When

the diet ends, the old lifestyle returns, along with the weight in many cases. This can lead to cycles of weight loss and weight gain (Bacon & Aphramor, 2011). Therefore, even if participants saw mood and psychological well-being improvements solely from the weight loss they experienced, at least their well-being improvements, their weight loss, their reduced hunger and all the other benefits they mentioned in this study can be maintained with this lifestyle.

From the participants accounts in this study, it appears that the benefits and positive outcomes of this diet outweigh any negative side effects experienced. This is encouraging for those who are looking for adjunctive therapies to address and improve their depressive symptoms, or if they are simply looking to increase their overall physical and psychological well-being. However, further qualitative research is needed to develop a greater understanding of the challenges and obstacles that face individuals who start a ketogenic diet, for any health goal.

Further to this, understanding the individual tolerance and both the physical and mental response to diets in the wider community, specifically to the ketogenic diet, is warranted in order to design personalized approaches to dietary implementation. These tailored approaches should address, reduce, or eliminate both the personal and social challenges faced by so many when starting this diet, so as to make it easier to implement and maintain long term.

Overall, future ketogenic dietary protocols can be better informed from these results. Implementation difficulties at the onset of the diet should be accounted for when designing new protocols. Individuals should be informed as to what to expect and support from peers, mentors or coaches should be available

throughout the first few weeks at least until hunger and cravings reduce and individuals are comfortably in ketosis.

In terms of risks for success and maintenance, the data from this study suggests that the implementation period was the most difficult to progress through.

Therefore, alongside peer or mentor support, resources should be created to accompany future protocols. These resources could cover topics such as staying organised and planning ahead, eating out and about, how to manage social situations and how to overcome other lifestyle obstacles such as diet dogma.

Once participants made the diet a lifestyle, they presented as knowledgeable and educated on how to follow the diet but also were able to make personalised choices and include some level of flexibility which made it easier to maintain.

From these results, it is clear that the ketogenic diet can be beneficial for more than simply weight loss. As is known from the epilepsy and type 2 diabetes research the ketogenic diet can exhibit strong therapeutic effects for many illnesses. These results suggest that the ketogenic diet can improve many aspects of physical and psychological well-being such as sleep, energy, concentration, pain, and confidence. Medication reduction and even elimination while following the ketogenic diet can be achieved in some cases. Therefore, future promotion of the ketogenic diet should reflect this and be personalised to individuals who may benefit from its effects.

Additionally, if the diet is presented in a personalised manner, tailored to the individual and targeting their specific symptoms, it may result in better adherence generally, but more specifically for those with poor mental well-being.

Overall, the results of this study will aid researchers to better understand how a low carbohydrate and ketogenic diet can be applied in people's daily lives either by using an online program or with the support of mentors, coaches, and health professionals such as psychologists, dietitians, and nutritionists. The benefits, drawbacks, and changes to aspects of psychological well-being that may be experienced by participants, which has been indicated but relatively undetailed through the quantitative arm of this research work, are now better understood.

Chapter 6: General Discussion

The ketogenic diet puts the body into ketosis, a metabolic state which burns fat and ketones for energy, rather than glucose. Evidence suggests that the KD produces significant metabolic changes in the body that influence mood and depressive symptoms. According to previous research, the presence of ketones in the body has been shown to be neuroprotective and may improve symptoms of depression. The theoretical basis for this is that the ketones provide an alternative energy source to the brain which can regulate many biological processes that have become dysregulated due to biological or psychological factors.

The complete array of biological mechanisms by which the KD works is not yet known and the conclusions from the literature are mixed, however, research suggests that ketogenic diets should be considered as an intervention for some psychiatric conditions (Brietzke et al., 2018; El Karkafi et al., 2023). As there are a host of biochemical actions and reactions observed when in a ketogenic metabolic state, there is enough research to warrant a closer look at the possible effects on affect and other aspects of psychological well-being. A review by Leichsenring et al. in 2022 of over 3,500 RCTs suggests that the effect that psychotherapy and pharmacotherapy have on psychiatric disorders is limited and that more research is necessary to identify other novel treatments for these illnesses (see Chapter 1).

To date, many of the studies on KD and psychiatric conditions have focused on mechanisms of action in rodents and mice, and less so in humans. Though

human studies have recently been published they are predominantly case studies or initial pilot studies (Needham et al., 2023; Palmer, 2017); no randomized control trials have been carried out to investigate the impact of the ketogenic diet on psychological well-being or depressive symptoms. There is also no quantitative or qualitative literature comparing the effects of a KD to a LCD in a depressed population.

The overall aim of this research project was to investigate the impact of the KD on psychological well-being using a KD intervention, a LCD intervention, and a control group to compare outcomes.

In study 1 it was anticipated that those following the KD would experience increased ketone levels by default from following the prescribed macronutrient breakdown. Increased ketone levels are reported to have mood stabilising effects in humans (Brietzke et al., 2018; Campbell & Campbell, 2019; Norwitz et al., 2020) and mood elevated effects in mice and rodents (Ari et al., 2016; Hollis et al., 2018; Kraeuter et al., 2020; Murphy et al., 2004; Olivito et al., 2023). As a result, it was proposed that the KD would show concomitant significant improvements in affective state (depression, anxiety, positive and negative affect), stress and mental well-being compared to the LCD. It was also predicted that the LCD would show some improvements in affective state (depression, anxiety, positive and negative affect), stress and mental well-being compared to those in the control group, but not as much as the KD.

In study 2 it was predicted that those following the KD would have higher dropout rates than the LCD, and that those with greater depressive symptoms

would be more likely to drop out compared to those who were healthier. It was also proposed that there would be a greater drop out of participants once the intervention ended at 12 weeks but before the study ended at 24 weeks due to lack of ongoing support from the online program.

In study 3, the purpose was to review the accounts of participants who completed the KD intervention and to identify any common themes relating to their journey that also may compliment the quantitative outcomes found in study 1. Below is a brief overview of each study outline:

Study 1

- A randomised control trial with quasi experimental design
- Participants with mild to moderate depressive symptoms and low depressive symptoms were randomised and initiated either a LCD, a KD or a control diet
- The dietary interventions were run through an online education platform for 12 weeks, followed by 12 weeks of unsupported continued diet. The control diet was maintained for a total of 6 weeks
- Exploration at baseline (T0), day 1, week 6, week 12, and week 24 included questionnaires and psychological measures

Study 2

- Due to study 1 attrition rates, study 2 was added to investigate reasons for attrition and to better understand how to reduce attrition rates in future research studies

Study 3

- Participants in the KD group were interviewed to gain a richer understanding of the diet and study experience
- Qualitative thematic analysis was carried out on the data to explore participants' attitudes and accounts

The focus of this thesis was to understand the impact of the ketogenic diet on depression and psychological well-being. The findings from this work show that the ketogenic diet did not improve quantitatively measured depressive symptoms or aspects of psychological well-being, although some improvements in physical and mental health were noted in the qualitative interviews (see Chapter 5).

To summarise the main results of this quantitative and qualitative research, see Figures 6.1 and 6.2.

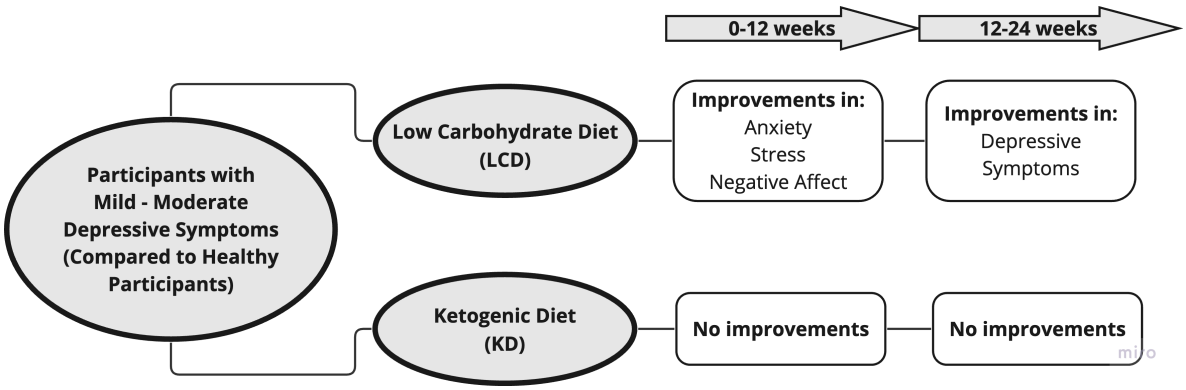

Figure 6.1: The main results of study 1: Changes in well-being and depressive symptoms over time as a function of diet type in participants with mild to moderate depressive symptoms

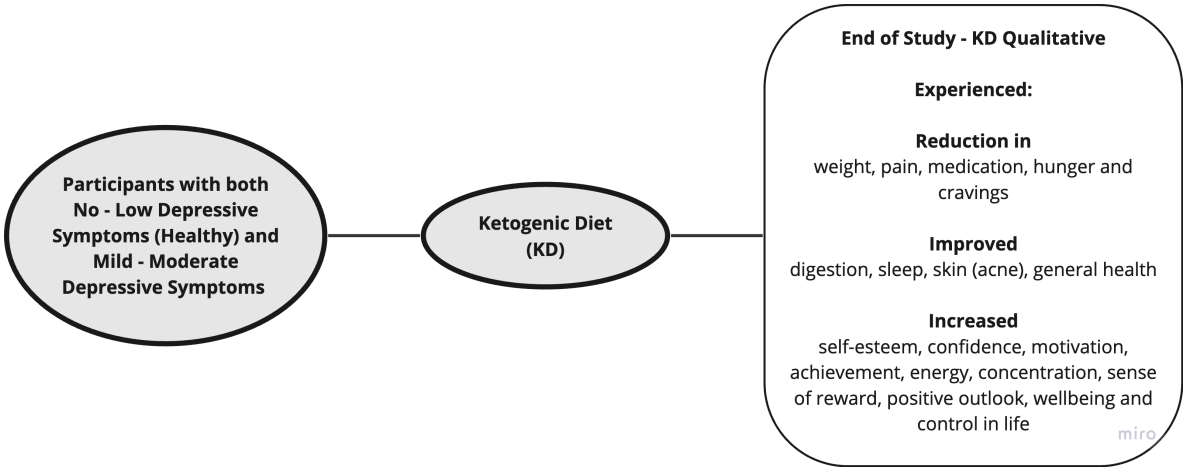

Figure 6.2: The main results of study 3: Reported benefits of adhering to a ketogenic diet among both healthy and mild to moderately depressed participants

6.1 Study 1: Ketogenic Diet vs Low Carbohydrate Diet Randomised Trial

The quantitative arm of this research investigated the impact of a KD on depressive symptoms and aspects of psychological well-being in an otherwise healthy group of participants. In order to do this, participants were split into two groups, depressive symptoms (mild to moderate) and healthy adults (low to no depressive symptoms). They were then assigned to a ketogenic diet, a low carbohydrate diet or a control group which was diet as usual in order to compare the diet outcomes on psychological well-being.

It was expected that those following both the KD and LCD would show greater improvements overall compared with the wait list control group in both the healthy adults and depressive symptoms groups. There were three predictions for this study:

1. Lowering carbohydrate intake to initiate ketosis (KD), will improve psychological well-being in people with mild to moderate symptoms of depression

2. Lowering carbohydrate intake without initiating ketosis (LCD), will improve psychological well-being in people with mild to moderate symptoms of depression

3. The ketogenic diet will show greater improvements in psychological well-being in those with mild to moderate depressive symptoms compared with a low carbohydrate diet. The ketogenic diet will have a greater impact

because of the ketones that are produced which are not present in the low carbohydrate diet

For prediction 1, when all time points were analysed, the results of this study found that the KD did not produce improvements in aspects of psychological well-being in those with mild to moderate symptoms of depression. This is not consistent with the findings from Danan et al. (2022) whose subjects (n=7) with major depressive disorder all experienced a reduction in depression symptoms using the HAM-D from levels of severe depression to no depression. Findings are also not consistent with the current evidence from rodent studies which report anxiolytic effects (Murphy et al., 2004). For prediction 2, the results found that from T1 to T2 at six weeks, compared to controls, the LCD did not significantly improve aspects of psychological well-being. However, with more time, when analysed over the 12 weeks of study intervention the LCD significantly reduced anxiety, stress, and negative affect. Over the full 24 weeks, a significant decrease in depressive symptoms was found in those with mild to moderate depression. Therefore, a decrease in anxiety, stress, depressive symptoms, and negative affect were found when compared to baseline, although the LCD intervention did not improve all measures of psychological well-being. In their research, Unwin et al. (2022) used a low carbohydrate dietary approach - a food plan that followed a low carbohydrate approach was given to participants in those with food addiction - alongside education and psychosocial support. The results reported an improvement in mental well-being from low to population norms over a 10-14 week period. Although scorers on the specific measure of mental well-being did not effectively change in the current study, other changes

in affective state mentioned above clearly indicate that there were improvements in some dimensions of psychological well-being.

For prediction 3, no significant improvements were reported in the KD intervention when compared with the LCD intervention. Instead, it was participants in the LCD intervention with mild to moderate depressive symptoms, that experienced greater improvements in psychological well-being compared to those in the KD intervention. There is currently no comparison study available of KD and LCD in humans to compare these results with.

When compared with the research available on the KD, these results are surprising and not consistent with the data that shows following a KD of <20g of carbohydrates per day can achieve clinical remission in some cases of persistent mental illness (Danan et al., 2022). With this in mind, perhaps significant improvements may be apparent and more profound with a KD intervention in those with severe depressive symptoms or treatment resistant type illness, who also present with at least one indicator of poor metabolic health as seen in Danan's work. Or perhaps, individuals need to present with severe depressive symptomatology rather than mild to moderate depressive symptoms. Alongside this, maybe reaching nutritional ketosis is not always necessary in order to experience a meaningful and significant improvement in depressive symptoms and other aspects of psychological well-being.

From additional analysis on the study 1 data, there were three further predictions. The first prediction was that participants with higher perceived social support would experience greater improvements in aspects of psychological

well-being across both KD and LCD interventions. However, aspects of psychological well-being did not significantly improve in those with greater social support compared to those with less. This is not in keeping with the works of Bardach et al. (2011) and Van Weel et al. (2005) who reported that those with greater social support were psychologically healthier than those with less.

A second prediction was that those with lower levels of body appreciation would see greater improvements in psychological well-being compared to those with higher levels across the LCD and KD interventions. Significant improvements in positive affect, mental well-being and depressive symptoms were found in those with lower levels of body appreciation compared to those with higher levels. This is in keeping with the findings of Winter et al. (2019).

Finally, a third prediction was that self-compassion would improve more in those with higher levels of depressive symptoms compared to those with lower levels across both dietary interventions. The results showed no significant improvements in self-compassion with levels staying constant in the group with lower levels of depressive symptoms. Therefore, it is clear that following a dietary intervention alone is not enough to increase rates of self-compassion.

When looking at these results, the LCD significantly reduced anxiety, stress, negative affect, and depressive symptoms over 24 weeks compared to baseline. From this, it can be suggested that the LCD could be implemented as a treatment or adjunctive treatment for those with mild to moderate depression. The current standard of care for mild to moderate depression is talking therapy as a first line approach, with antidepressants alongside if necessary. With talk therapy,

specifically CBT, individuals with mild to moderate depression will need 8-16 sessions of CBT as standalone or alongside antidepressant treatment. The number of sessions depend on the patient's responsiveness to the therapy (Gautam et al., 2020). The number of individuals referred to the UK's IAPT service is approximately 1.5 million per year with treatment carried out on less than half of all those referred. Non-attendance to appointments is a significant limitation of this service (Sweetman et al., 2023).

With regards to antidepressant efficacy, Fournier et al. (2010) reported that there is little evidence that antidepressants have greater effects than placebo when decreasing severity of depressive symptoms. From a systematic review in 2014, there was not enough evidence to support or refute the efficacy of antidepressant use for mild to moderate depression (Cameron et al., 2014).

From the results of this study, the LCD could be offered as a treatment or an adjunctive treatment for those with mild to moderate depression.

6.2 Study 2: Understanding Drop Out and Attrition Rates

This additional study investigated the high dropout rates experienced in study 1, in a bid to identify predictors of drop out alongside the exploration of baseline demographics and psychological scale measurements.

There were three predictions for this study;

1. Those following the KD intervention would have higher dropout rates compared to those in the LCD group, due to the fact the diet requires individuals to restrict their carbohydrate intake even more severely than the LCD possibly due to the KD restricting more carbohydrates, similar to

the findings mentioned in chapter 4 section 4.1.4 by Crichton et al. (2012) and Greenberg et al. (2009).

2. Those with more depressive symptoms or lower overall psychological well-being were more likely to drop out compared to those with less depressive symptoms. This would be in keeping with the works of Fabricatore et al. (2009) and Moran et al. (2019) who found this to be true in their works (see Chapter 4 section 4.1.4).

3. There would be a greater drop out of participants once the intervention ended at 12 weeks, but before the study finished at 24 weeks due to the cessation of the online program, and the need to continue unsupported for the second 12 weeks.

For prediction 1, it was found that diet type was not a predictor of drop out with 94% of participants dropping out of the KD and 92% dropping out of the LCD by the end of the study. As both the KD and LCD reduce carbohydrates considerably, these findings are supported by the literature which suggests that restricting certain food groups would increase levels of attrition and reduce compliance (Crichton et al., 2012; Greenberg et al., 2009).

For prediction 2, it was found that depressive symptoms and poorer mental health did not predict drop out as hypothesised. There was a higher rate of dropout (69.6%) amongst those with lower levels of depressive symptoms, (i.e., those in the 'Healthy' group), compared to those with higher levels of depressive symptoms (30.4%) (see Table 4.3). This is therefore not consistent with the literature that states higher depression scores are predictive of higher attrition

rates (Fabricatore et al., 2009; Moran et al., 2019; Ponzo et al., 2021). As discussed in chapter 4, it was thought that this effect may have occurred because those with poorer psychological well-being were fulfilled by the study in some way compared to those with greater psychological well-being whose depressive symptoms were not enough to warrant them following such a diet or intervention. Sindler et al.'s (2023) systematic review of the effects of carbohydrate restricted diets on psychological outcomes reported that the KD had the same impact on psychological well-being as any other diet in those with little to no psychiatric symptoms, and the results from this study are reflective of Sindler's findings.

In relation to prediction 3, the majority of participants who dropped out of the study, did so before the end of the dietary intervention at 12 weeks for reasons such as the diet being difficult, or they had other time commitments. These findings are not in keeping with the study prediction but are supported by the work of Crichton et al. (2012) whose participants found it difficult to restrict certain food groups and therefore attrition rates were increased.

6.3 Study 3: Attitudes Towards and Accounts of the Ketogenic Dietary Intervention Experience

The qualitative arm of this research explored the accounts of those following the ketogenic diet intervention in two groups, healthy adults, and those with depressive symptoms. This is the first study to look at the personal accounts of the ketogenic diet experience in people with symptoms of depressive illness.

The aim of the study was to identify any common themes related to participants journeys following the KD. The study focused on the health of participants prior to the program and the challenges and obstacles they faced during the intervention. Health in a broader sense was also covered such as participants relationship with food and their general health.

A reflexive thematic analysis produced six core themes and 28 subthemes from the data. The six core themes were (1) Poor health prior to program; (2) Hunger and cravings – the food and mood connection; (3) Psychological well-being improvements; (4) It becomes a lifestyle; (5) Implementation difficulties; and (6) Physical changes and improvements.

The main findings were that participants experienced a combination of physical and mental health improvements from previously being unable to lose weight, to losing weight with ease and starting the study with poor self-esteem to finishing with increased self-esteem and confidence. Therefore, for those who started the diet, and saw improvements, it motivated them to stay on the diet indefinitely, in which case the diet then became a lifestyle for them, but for those who didn't improve, the diet remained a struggle and may have been stopped entirely. These findings are in keeping with the limited qualitative works in this area (Campbell & Campbell, 2019; Newson & Parody, 2022; Wong et al., 2021). These accounts appear to cover most, if not all the challenges that are to be expected when starting the diet or implementing a lifestyle change like this.

6.4 Synthesis

To fully understand what this research means in a wider sense, it is important to synthesise these results and findings.

From the results of the quantitative study 1 and qualitative study 3, there appears to be a contradiction between the lack of impact of a KD on psychological well-being in study 1, compared to the positive KD effects experienced by those interviewed in study 3. Of those that were interviewed in study 3, five participants were considered healthy with low to no levels of depressive symptoms, and four participants were considered depressed with mild to moderate levels of depressive symptoms.

All nine participants interviewed in study 3 experienced positive outcomes both physically and psychologically from implementing the ketogenic diet with many improvements and comments shared, not related to mental health. For these individuals to have followed the intervention for 24 weeks and continued it post research study suggests that they found it worthwhile as otherwise they would have stopped. With this in mind, there may be an element of selection bias here as participants experienced a positive outcome and were therefore more likely to complete the interview to discuss their positive experience.

The psychological improvements noted, and the comments shared by participants do not overlap entirely with the aspects of psychological well-being measured in study 1. For example, experiencing a regained feeling of control in life, alongside a new sense of reward and achievement. This highlights a greater richness of psychological experiences beyond those items assessed in the self-

reported questionnaires collected at each time point. This suggests that there are some psychological benefits of the ketogenic dietary intervention that are not easily captured with single factor measures such as depression scales. The improvements in depressive symptoms noted in the qualitative study, suggest that the depression rating scales used in study 1 may have their limitations. For example, these single factor measures have lower reliability overall due to the reduced number of response categories in each measure (Allen et al., 2022). In addition, Bech (2006) suggests that the scales tend to be diagnostic rather than effective at measuring real change in depressive symptoms over time. This has also recently been reported in the literature by Demyttenaere (2020), who suggest that such scales are reductionist by nature and are not able to identify and portray the complexity of each individual. They also report that what is assessed by the scales is not always what matter to individuals.

To add to this, future research could take a larger group of individuals on a KD to see if these results are replicated. The outcomes of the accounts captured in this qualitative study could be used to generate a scale which could then explore the commonality of these experiences in a larger cohort of individuals following a ketogenic dietary intervention. The scale could also look to see how such experiences might differ from the effects experienced by those following a low carbohydrate diet or from participant groups for example, those who do or do not exhibit improvements or those who drop out of the intervention. For other future research suggestions see section 6.7.

Some of the comments from the interviews in study 3, can inform the results from the drop out study (study 2). In study 2, it was found that those who stayed

in the study had a reason to do so, over and above simply taking part. The findings from study 3 support those of study 2. From the qualitative interviews, all participants experienced weight loss which had previously been difficult for them to achieve. Many suffered with poor physical and mental health prior to starting the intervention and over the course of the study, aspects of both physical and psychological health appear to have improved. Therefore, it is understandable why participants may want to continue the intervention and the diet post study. For many in study 3 who had completed the intervention and continued the diet, the KD was easy to follow once implemented and it became a lifestyle for them. However, for many in study 2 who discontinued the diet, dropped out of the study, and were followed up, they found the diet difficult to stick to and struggled to make it a lifestyle.

From study 2, it was also found that participants were most likely to drop out during the first 12 weeks and the main reason cited for this was because the diet was difficult to stick to. From study 3, participants shared that they experienced some implementation difficulties initially. Starting a new diet, understanding what to eat when out and about, and navigating diet dogma alongside the opinions of others was a challenge. These challenges experienced in the early weeks of the intervention may have led those in study 2 to drop out because they found the diet too difficult to stick to. However, it is unclear why some people stayed on the diet and found it easy, while others found it difficult.

6.5 Novel Contributions

The quantitative study reported in this thesis is the first randomised control trial to measure the impact of the ketogenic diet on depression and aspects of psychological well-being compared to a more common low carbohydrate diet. It was unexpected that the LCD would have such a positive impact on psychological well-being, compared to the KD, despite the presumed absence of ketones. This suggests that some improvements in psychological well-being can be found by following a less restrictive LCD. This raises the possibility that a LCD may be used as a preventative measure or a treatment approach for depressive symptoms. Though further research is needed both on the LCD and KD interventions, it gives individuals the option to try a non-invasive, non- medical, dietary intervention adjunct to standard care that may improve their psychological well-being.

The quantitative arm of this research was also an online dietary intervention for potential psychological well-being improvements. This online digital intervention is novel in nature as to date, research has focused on digital interventions for physical health improvements such as T2D or for therapeutic applications such as Cognitive Behavioural Therapy (CBT) (Summers et al., 2021; Venkatesan et al., 2020).

The qualitative study is the first to look at the accounts of a depressive population and their experience following a ketogenic dietary intervention. From this study, participants experienced benefits that were not unusual on the ketogenic diet, such as a reduction in acne, pain, acid reflux, and medications, and improved skin, sleep, and eyesight. Unlike many reports on the ketogenic

diet in other areas of research such as epilepsy, participants who completed the qualitative study found the diet easy to adhere to. Alongside this, the narrative from female participants pointing towards a possible increase in addictive behaviour when implementing a ketogenic diet compared to males is interesting and requires further focus.

Finally, this program of research is a reflection of a real-life intervention. Randomised control trials (RCTs) are the gold standard in research and testing, and their results are highly accurate and contribute to the development of many standard treatments in health care. They are the best-case scenario for truly understanding how a treatment can impact health, but they suffer from a degree of artificiality as they are usually located on a ward or in a secure setting, and if not, they are at least highly controlled by many researchers and their research teams. This clinical environment therefore is not natural. RCTs exploring mental health interventions may often fail to account for how to take care of, or treat, health in the real world when balancing competing priorities such as health, career, families, partnerships, and finances, among others. Although this program of research experienced its limitations, seen in the next section 6.6, it was embedded in the community and is therefore more reflective of the efficacy of interventions outside of the RCT clinical arena. Overall, it has greater ecological validity compared to a standard RCT.

6.6 Limitations

As with all research studies, it is important to identify and discuss the limitations to this work. The five main limitations discussed below are, recruitment and maintaining engagement, control group (wait condition) time in the study, no mandatory request to track carbohydrates, no objective ketone measurement, and no weight change control.

Recruitment for the main study (see Chapter 2) was challenging, possibly due to the strict inclusion and exclusion criteria and the need to recruit those with mild to moderate depressive symptoms. Attrition rates were high during the intervention, the first 12 weeks, potentially due to some project design issues and the diet being too difficult to adhere to, as stated by participants in study 2. Recruitment, retention and enhancing compliance could be bolstered in future in many ways. Firstly, over recruiting initially for the study is important, which is in keeping with the findings from Crichton et al. (2012).

The addition of extra education may be helpful for those starting the intervention, both on the science of how the intervention may work to improve psychiatric symptoms and what to expect at each timepoint when implementing the diet, may be beneficial. This would keep participants engaged and would help them to understand if what they are experiencing or feeling is normal during the intervention.

Alongside this, providing support from a mentor, peer, or coach either through email and/or video calls to help answer questions and set expectations at each

stage may help with retention of participants. The addition of possible rewards and incentives could bolster retention also.

The control group remained in the study for six weeks. They were used as a wait condition where they eventually gained access to the program. During the recruitment phase, participants were told that they would wait until recruitment was complete before starting their intervention. However, this six week waiting period was actually their contribution to the study as a control/wait condition participant. From the results it is clear that the six week period was too short and this limited the interpretation of the findings. For example, there may have been benefits of the KD which may have been observed when compared with the wait/control group, despite not been seen when compared with the LCD data. Future use of control groups should be for the duration of the entire study to allow for group comparisons across all time points.

In this study there was no mandatory request of participants to track daily food and macronutrient breakdown on an app or in a logbook for their own education or for researchers to review and analyse. This is important when initiating any dietary intervention such as a LCD or KD where it is necessary to count the number of carbohydrates consumed per day. It may be that the carbohydrates target for the KD was not low enough to initiate ketosis in all participants.

Accuracy is important here as a few extra carbohydrates per day will lower ketone levels and reduce the chances of being in a state of ketosis and experiencing the possible benefits of a ketogenic metabolic state.

Related to the above point, there was no objective measure of compliance and adherence to the low carbohydrate or ketogenic diets in the current work, due to the prohibitive costs of providing blood ketone monitors to all participants at the start of the study.

Providing an objective ketone measurement was attempted at the beginning of the project. Once the recruitment of participants for study 1 had started urine ketone dipsticks were shipped out by DCUK to a subsample of participants following both the LCD and KD intervention. They were told to use them regularly and to note if the dipsticks changed colour. It was explained to them that they were not aiming for a colour change, just observing the result.

Urine ketone dipsticks can give a binary 'in' or 'out' of ketosis by measuring AcAc when excreted in the urine. However, this measure is not very reliable as there are many other factors that can interact with the result, including hydration status (Gibson et al., 2020). Therefore, later in the study it was decided that the results of the urine dipsticks would not be reliable enough to determine if participants in the KD group had reached a state of ketosis.

Alongside this, the researcher applied for and was granted funding to provide KetoMojo blood ketone monitors, the gold standard of ketone measurements, to a subsample of participants (Gibson et al., 2020). However, logistically it was too late in the intervention to follow through with this. This left the participants without an objective ketone measurement despite the efforts of the researcher.

For many individuals, carbohydrates must be decreased to below 50g or even 20g to initiate ketosis. However, this can vary between individuals. It is possible

that those on the LCD (90-130g) may have been in ketosis at times, and those on the KD (<50g) may have been eating a higher amount of carbohydrates that kept them out of ketosis and therefore unable to experience the potential benefits of the ketones on their mental state. Daily fluctuations in ketone levels may also have increased the likelihood of coming in and out of ketosis. If too much time is spent out of ketosis, the individual may have experienced symptoms of keto flu again when re-entering this metabolic state. This may have adversely affected their mental state and the measures of these. The gap between the two recommended carbohydrate target ranges, LCD and KD should have allowed for individual variance, however the researcher cannot be sure.

The body weight of participants was collected at baseline and at each time point throughout the study. However, when cleaning the data for analysis, there was some ambiguity related to whether the correct measurements were added by the participants at each time point. Many weight measurements that were added appeared to have been incorrectly submitted (e.g., submitted weight as 76 pounds, instead of 76 kilograms). Therefore, due to these widespread inaccuracies, the researcher was unable to effectively measure and analyse weight change or control for it over time.

As weight change was not controlled for, it could be argued that these participants saw improvements in their mood and psychological well-being as a result of their weight loss or fat loss. For many participants sharing their accounts in study 3, the KD was the only diet these participants had followed that worked long term as they stated that other diets had not worked for them in the past when it came to losing weight.

Although when recruited participants were told that the study would be about how diet can impact mood, the motivations of participants to take part in the study were not recorded and therefore are unclear. It is likely that there were participants who wanted to do the study for weight or fat loss rather than for the studies original purpose. In future, this should be recorded at the beginning of an intervention.

To summarise, in order to extend this work, it would be valuable to recruit a larger sample of participants, extend the control group for the duration of the study to compare with other diet groups, ask participants their motivations for taking part, and advise them to track both carbohydrate intake and ketone levels daily, so the researchers can control for weight change over time. It may also be worthwhile recruiting participants who want to trial the KD intervention specifically to improve their mood and well-being. If designed and controlled correctly, this could include participants with more severe depressive symptoms, compared in groups to those with mild to moderate or no to low levels of depressive symptoms as suggested in section 6.1.

6.7 Implications for Future Research

Having reviewed the limitations of this work, perhaps one or two of the most important implications for future research would be participant selection and the design of the dietary intervention itself. Firstly, the precise selection of participants based on groups identified to be the most responsive to the intervention, such as those with severe or treatment resistant depression and those with high levels of inflammation, a diagnosis of atypical depression and/or metabolic syndrome, would be ideal. Secondly, the design of the dietary intervention should include daily tracking of carbohydrates and ketone levels for at least 12 weeks. The addition of education and guidance through the online intervention along with support, and medical supervision from an experienced professional is imperative. These implications for future directions of research cover both the recruitment strategy and the design of the delivery mode of the intervention.

6.7.1 Participant selection

The term depression encompasses a range of symptoms and subtypes (Nguyen et al., 2022). Future research may benefit from better understanding the heterogeneity in both clinical and sub-clinical samples as this will aid in participant selection and recruitment for intervention studies and future treatment.

A depression diagnosis often comes with certain features called ‘specifiers’. The specifier ‘atypical features’ includes many symptoms that would be classed as unusual. In other words, it is a specifier for a group of miscellaneous symptoms

that don't really fit anywhere else. Within a diagnosis of depression with atypical features, there are symptoms of significant weight gain, an increase in appetite, hypersomnia or excessive sleepiness or sleeping more than usual at night, along with leaden paralysis, a feeling of heavy arms and legs (Kennedy, 2008). Those with a diagnosis of depression with atypical features, specifically experience significant weight gain and an increase in appetite. It could be proposed that these individuals may be part of a subgroup that would be most responsive to a dietary and metabolic intervention such as a ketogenic diet. This is yet to be tested. Individuals diagnosed with depression and atypical features account for approximately 18-43% prevalence of depression (Sen et al., 2021).

It is important to research these subgroups of depression in future and analyse the different specifiers of depression. There appears to be differences in inflammatory profiles and markers between subgroups. There is at least one group of those diagnosed with depression who present with all of the features of an inflammatory response (Miller & Raison, 2016). So perhaps this subgroup is associated with a particular specifier.

In depression with melancholic features, with melancholia as the specifier, IL-6 and IL-1β are present and elevated compared to controls (Yang et al., 2019). However, IL-6 was not found to be elevated in those with atypical depression compared to controls (Dunjic-Kostic et al., 2013). CRP was reportedly elevated in those with non-melancholic depression (Yang et al., 2019), but it was unclear which specifier of depression this referred to. Reduced Tumour Necrosis Factor-Alpha (TNF-α) levels were observed in both melancholic and atypical depression patients compared to healthy controls (Dunjic-Kostic et al., 2013). Interestingly,

Schmidt et al. (2016) suggested that the pro-inflammatory markers are not pro-depressive but that they are related to the regulations of symptoms and the severity in depression patients. This suggests that there is something else happening downstream in each specifier and subgroup of depression that is not yet fully understood. If this is true, then this suggests that the specifiers, inflammation levels and the status of treatment response must be reviewed before deciding on a course of treatment or suitable intervention.

From the Netherlands Study of Depression and Anxiety (NESDA) cohort, those with melancholic depression, secreted different levels of the hormone cortisol compared to those in the atypical or control group. Cortisol is a hormone that is crucial for the body's response to any type of stress, and it has potent anti-inflammatory properties (Hannibal & Bishop, 2014). Higher levels of cortisol in melancholic type depression compared to atypical depression were also found by Karlovic et al. (2012).

Those in the atypical group were found to have higher levels of inflammation measured by inflammatory markers such as CRP, IL-6, and TNF-α and higher Body Mass Index (BMI) scores and waist measurements compared to those in the melancholia or control group.

Increased inflammatory markers have been associated with atypical symptoms of depression (Lamers et al., 2018), and with suicidal depression (Black & Miller, 2015). However, not all depressed patients exhibit increased inflammation levels. In one study by Lynall et al. (2019) they found that two thirds of their participants expressed elevated levels of inflammation and more depressive

symptoms compared to one third who had lower inflammation levels. Interestingly, within the larger more depressed group there appeared to be further subgroups lending to the idea that although inflammation is present in many cases of depression, there may be more than one mechanism or root cause for the inflammation itself. For example, it was found that a subset of depressed patients have altered immune systems and increased levels of inflammation (Irwin & Miller, 2007; Maes, 2008; Miller et al., 2009; Miller et al., 2003). Further to this, a recent study suggested that there could be more individuals with depression and activated immune systems than research currently states (Sforzini et al., 2023). Researchers found that in the genes of those with depression, there is an immune response that is independent of CRP levels, and the response is present even where inflammation isn't identified through CRP. This suggests that there are more depressed individuals with immune reactions than first reported. From this it can be suggested that atypical depression has many metabolic abnormalities in its physiology that differ to depression with other specifiers (Lamers et al., 2012; Penninx et al., 2008).

These reported features of atypical depression are also consistent with the DSM that states overeating and an increase in appetite are characteristics of this specifier. By overeating and responding to the increase in appetite, higher BMI scores and waist measurements are to be expected. If these are not controlled, obesity will ensue. Obesity increases the risk of developing metabolic disorders such as type 2 diabetes (T2D) 10-fold compared to those who are of normal weight (Koopman et al., 2009). High BMI scores and increased waist measurements, particularly a waist to height ratio measurement of >0.5 are also

associated with increased risk of cardiovascular disease (CVD) and T2D (Ross et al., 2020). It should be noted that waist circumference measurements are more accurate than BMI scores and increasing waist measurements are a characteristic of obesity (Darsini et al., 2020).

According to the World Health Organisation (WHO), in 2016, approximately 1.9 billion people over the age of 18 were overweight or obese globally (Hill, 2018) which is interestingly similar to the amount of people who are living with a diagnosable mental health condition. The National Health and Nutrition Examination Survey 2009-2016 found that only 12% of Americans were classed as metabolically healthy. Poor metabolic health was found even in those of 'normal' weight (Araújo et al., 2019). Seven years on from this report and global metabolic health is only getting worse.

This suggests that there is at least one specifier of depression, atypical, that may be amenable to dietary and metabolic intervention with the potential of other subgroups also responding to a dietary intervention.

In addition to the antidepressant and anti-inflammatory effects of ketones in the KD, the diet can also improve metabolic health. Depression has been coined a metabolic disease because there is an association between MetS and depression (Dunbar et al., 2008). It has also been reported that MetS is a risk factor for depression and depressive symptoms, suggesting that symptoms of metabolic syndrome may be present before the development of depressive symptoms (Kim et al., 2023). This may be true for the subset of those with atypical depression rather than melancholic depression. The cohort of individuals within the

subsample of depression with specifier type atypical appears to have the characteristics of MetS such as increased appetite and weight gain compared to those with melancholia who express an alternative, opposite presentation. Those with the specifier melancholia exhibit a lack of appetite and weight loss and may be less likely to respond to this dietary intervention. Therefore, those with melancholic depression may need the current standard of care, whereas those with atypical depression may benefit from this therapeutic dietary intervention.

It is important to understand that although these individuals all fall under the depression umbrella, there are many biological roots to each specifier and therefore they may be pathophysiologically different, meaning that alternative interventions or combination of treatments may work for different depression specifiers. Therefore, it can be suggested that a dietary intervention may not be effective for those with depression associated with loss of appetite and weight loss (melancholic subtype) but may be very effective for those with an increased appetite and weight gain (atypical subtype who also happen to have metabolic syndrome, T2D and/or obesity).

Alongside this, recruiting participants who have symptoms of MetS and a diagnosis of depression may be worthwhile. Recruiting participants from DCUK and including those with T2D rather than excluding them as was carried out in this study, would not only make it easier to recruit participants overall but would also mean the MetS and depression connection could be tested further. Medical supervision would be necessary in this case, to monitor T2D medication during the LCD and KD intervention. Overall, focusing future research on this may guide

clinicians towards a more accurate and personalised way to use dietary management in patients diagnosed with depression.

In the literature, there also appears to be some autoimmune illnesses that mimic psychiatric symptoms and conditions (Endres et al., 2022) and it has been suggested that some psychotic presentations are associated with vitamin B12 deficiency, some depressive disorders with folate deficiency (Dogan et al., 2008; Hutto, 1997) and some urinary tract infections (UTIs) with neuropsychiatric disorders (Chae et al., 2015). This suggests that there are many psychiatric cases that may in fact have a non-CNS biological foundation, and therefore treating with antidepressants and antipsychotics may not be successful. It is therefore important to also understand that some depression subtypes may be more positively affected by a LCD or KD compared to others. There are many biological pathways by which depression may present and this should be considered when carrying out future research. Studies should test for these baseline issues before recruiting or starting any psychiatric treatment or intervention.

6.7.2 Intervention design

The online interventions included weekly step by step educational videos to guide and support participants; however, it did not include meet ups, check ins or other forms of support from the researcher or DCUK programme coaches in order to keep the interventions blind to the participants. From the results of research, it appears that the LCD online intervention was adequate enough to improve participants psychological well-being. However, due to the improvements and benefits noted by the participants who were interviewed on

their ketogenic diet experience, perhaps additional layers of support could be added to future interventions to see if these findings could be replicated in a quantitative study.

The intervention could be followed in tandem with a level of support or check ins with peers, a mentor or health coach in the program. This would give participants time to discuss the diet and their struggles with others, form a better understanding of how to implement it in a real-life setting, share helpful tips to overcome obstacles and challenges and create a community where individuals feel supported at all points during their journey and lifestyle change. Questions specific to the diet could be answered by mentors and health coaches and general support could be given amongst attendees. Each session could cover aspects mentioned by participants in their interviews in chapter 5. This education and support model worked well in a study on low carbohydrate diets for food addiction by Unwin et al. (2022).

In terms of intervention length, the ketogenic diet and its implementation have been shown to initiate an adaptive, hormetic stressor response in the body. Hormetic stressors are the addition of controlled, short term stressors on the body which in turn, improve overall health through a series of biological processes at the cellular and mitochondrial level (Calabrese, 2004). Examples of a hormetic stress are HIIT exercise, hot and cold exposure, calorie restriction, fasting, and the ketogenic diet because of its fasting mimicking properties (Sthijns et al., 2016). Once a hormetic stress such as the ketogenic diet is introduced, it takes the body time to adjust and carry out its cellular functions (Milder et al., 2010). It is unclear how long it takes for the body to adapt to

these stressors, as well as how long it takes to learn how to implement the diet (see Chapter 5). Therefore, it may be prudent to extend future interventions beyond 12 or 24 weeks for the greatest chance of observing any true effects of the ketogenic dietary intervention (Milder et al., 2010; Phillips et al., 2018).

With regards to selecting a depression sample, the results from study 1 suggest that the LCD has positive effects but that the KD is not effective in those with mild to moderate depression. However, future research should explore whether the KD has some effect in those with more severe depression, such as treatment resistant depression or MDD similar to that found by Danan et al. (2022). If the results were positive, this would reflect the data available on antidepressant effectiveness which shows that there is little effect beyond placebo for those with mild to moderate depression, but they are significantly more effective than placebo for more severe cases of depression (Fournier et al., 2010). Both the KD and antidepressants have anti-inflammatory properties (Maes, 2008; Tomaz et al., 2020), so perhaps this would be their shared biological mechanism of action.

Although this research did not find beneficial effects of a KD intervention for mild to moderate depression, it is important to understand the wider psychiatric literature to help inform future studies. From this research, the LCD intervention improved aspects of psychological well-being in those with mild to moderate depression, so future research should determine which intervention would help those with severe depression or treatment resistant illness and whether it would be a more carbohydrate restricted LCD, in other words, a ketogenic diet.

From the limited research on ketogenic diets and psychiatric conditions, new research has emerged using the ketogenic diet as an intervention for bipolar disorder. Research suggests that there is a small risk that those who start the ketogenic diet may experience a deterioration in mental state temporarily until their body has acclimatised to the diet. This is similar to the short-term side effects experienced by others starting the diet, also known as the keto flu. However, in those with a psychiatric condition, small changes in their sleep status and an upregulation of mitochondria and ATP during this time may increase the chances of hypomania (Harvey et al., 2009; Lewis et al., 2017). Close psychiatric monitoring may be necessary as medications may need to be adjusted in the short term to compensate. Alongside this, tracking of blood ketone levels is important as research now shows that those with psychiatric conditions may experience improvements in their mental state when aiming for levels of approximately 1-4mmol/L (Needham et al., 2023). Tracking ketones may also positively impact dietary adherence, accuracy, and compliance for the psychiatrist and/or researcher.

These suggestions and recommendations are drawn from a recent pilot study of the ketogenic diet in bipolar disorder (Needham et al., 2023). This study offered their participants (N=27) weekly online contact with a dietitian and gave them the contact details of the psychiatrist should they have any concerns or issues during the intervention. Support to participants was provided to help with adherence and managing any side effects of dietary implementation. Daily blood ketone readings were also tracked. This pilot study experienced a withdrawal rate of 23% over the eight-week trial. Researchers suggested to help retention,

future research should include dietitian input to educate participants at the start of the study, more information and education on creating ketogenic meals, and the option to join group sessions for ongoing support, similar to what has been stated above on the future directions from this research.

Future research should focus on using this dietary intervention in a remote setting along with close monitoring of mental state by an online mental health specialist such as a psychologist or therapist, tracking of ketone levels, tracking of daily carbohydrates to adjust in reference to ketone levels, and frequent 1:1 or group check ins with a health coach or mentor for a period of at least 12 weeks. It is unknown whether there may be a temporary deterioration in mental state for those with severe depression, so this approach is recommended in order to keep the individual safe and to give them the best chance of success.

Having discussed the above, it is important to note that these researchers are carrying out pioneering research, but this is not yet an established research area. There are clinicians carrying out adhoc "off label" prescribing of the ketogenic diet as a metabolic therapeutic intervention for psychiatric conditions but this therapy is not a frontline treatment for any psychiatric condition at this time. It is not currently standard care or stated in the DSM-V, nor is it a universally agreed upon diagnostic approach to managing psychiatric illness. There are no completed RCTs yet although they are underway. However, although RCT results may be favourable initially especially with regards to retaining participants for longer with incentives and support, the improvements may not hold up over time. For example, there are RCTs results that support switching antidepressants in MDD, but due to flaws in the study design and lack of generalisability and

external validity, the results are not as applicable to real world practice (Kui Chen & Mei, 2017; Paraskevas et al., 2019).

The results from this current research question how sustainable the ketogenic diet is without the clinical control of an RCT, or without ongoing support from professionals, mentors, coaches, and peers. Though study 1 experienced high attrition rates, if the results of the study are valid, they question the idea of using a ketogenic diet for psychiatric conditions overall. These findings reflect stronger ecological validity beyond the clinical setting and provide real world evidence to this area of research.

6.8 Conclusion - Final Remarks

The focus of this thesis was to understand the impact of the ketogenic diet on depression and psychological well-being. The ketogenic diet did not improve quantitatively measured depressive symptoms or aspects of psychological well-being. When followed up via interview, a small sample of those following the ketogenic diet did experience benefits to both their physical and psychological health based on their interview responses and a qualitative analysis of their accounts. Within this group there was a real sense of change and improvement, but for many in the quantitative arm of the KD intervention, this was not the case and attrition rates were high. However, the qualitative study was a small cohort of nine participants that experienced benefits from the diet and therefore they may have been prone to selection bias when taking part in the interviews. There are many other reasons for a positive outcome such as not experiencing significant adverse effects when starting the diet making it easier to continue, or perhaps having atypical depression or other biological factors that were

responsive to the ketogenic dietary intervention. Future individual factors for these effects should be explored.

Any adverse effects from the implementation of the ketogenic diet that were experienced were mild and temporary, but retention of participants overall was challenging. Therefore, from this research it can be concluded that an online ketogenic dietary program with education only is not robust enough as a standalone intervention for the improvement of depression and overall psychological well-being. It is suggested that future studies should test other aspects of support, such as dietitians, psychiatrists and peer support or mentor-led group check ins to overcome the challenges faced during the intervention and to make implementation easier.

This research does suggest that an online dietary intervention of a low carbohydrate diet of 90-130g per day can improve some aspects of psychological well-being in those with mild to moderate depressive symptoms over 24 weeks. This is relevant in light of the rising levels of depression and anxiety and difficulty accessing treatment and care both in the UK and globally. It may be that these benefits were experienced by those on the LCD because the KD was more difficult to implement. The LCD may have been an easier first step into carbohydrate reduction with participants also experiencing weight loss. Therefore, weight loss and physical health benefits can't be ruled out as drivers of these positive effects. Overall, these findings are a valuable addition to the low carbohydrate dietary literature.

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Appendices

Appendix A - Ethics 1 Quantitative

31st May 2017

Dear Erin,

Project Title:	**A ketogenic diet for depression**
Principal Investigator:	**Dr Jennie Brown**
Researcher:	**Erin Louise Bellamy**
Reference Number:	**UREC 1617 51**

I am writing to confirm the outcome of your application to the University Research Ethics Committee (UREC), which was considered by UREC on **Wednesday 22 March 2017.**

The decision made by members of the Committee is **Approved**. The Committee's response is based on the protocol described in the application form and supporting documentation. Your study has received ethical approval from the date of this letter.

Should you wish to make any changes in connection with your research project, this must be reported immediately to UREC. A Notification of Amendment form should be submitted for approval, accompanied by any additional or amended documents: http://www.uel.ac.uk/wwwmedia/schools/graduate/documents/Notification-of-Amendment-to-Approved-Ethics-App-150115.doc

Any adverse events that occur in connection with this research project must be reported immediately to UREC.

Approved Research Site

I am pleased to confirm that the approval of the proposed research applies to the following research site.

Research Site	Principal Investigator / Local Collaborator
Online questionnaire	Dr Jennie Brown

Approved Documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
UREC application form	3.0	31 May 2017
Appendix 1 - Screening Questionnaire	2.0	31 May 2017
Appendix 2 – Questionnaire T1	2.0	24 May 2017
Appendix 3 – Questionnaire T2	2.0	24 May 2017
Appendix 4 – Questionnaire T3	2.0	24 May 2017
Appendix 5 – Questionnaire T4	2.0	24 May 2017
Appendix 6 – Recruitment posters for Community and Online	2.0	24 May 2017
Appendix 7 - Participant Information sheet	2.0	24 May 2017
Appendix 7 - Consent form	2.0	24 May 2017
Appendix 8 – Ethical approval from Diabetes.co.uk	1.0	7 March 2017
Appendix 9 – Debrief Sheet	1.0	7 March 2017
Appendix 10 – Flow Chart of Method	1.0	7 March 2017
Appendix 11 – Letter to GP	2.0	24 May 2017

Approval is given on the understanding that the UEL Code of Practice in Research is adhered to.

The University will periodically audit a random sample of applications for ethical approval, to ensure that the research study is conducted in compliance with the consent given by the ethics Committee and to the highest standards of rigour and integrity.

Please note, it is your responsibility to retain this letter for your records.

With the Committee's best wishes for the success of this project.

Yours sincerely,

[redacted]

Fernanda Silva
Administrative Officer for Research Governance
University Research Ethics Committee (UREC)
Email: researchethics@uel.ac.uk

Appendix B - Ethics 2 Quantitative Amendment 1

8th August 2018

Dear Erin,

Project Title:	**A ketogenic diet for depression**
Researcher:	**Erin Louise Bellamy**
Principal Investigator:	**Dr Jennie Brown**
Amendment reference number:	**AMD 1819 04**
UREC reference no of original approved application:	**UREC 1617 51**

I am writing to confirm that the application for an amendment to the aforementioned research study has now received ethical approval on behalf of University Research Ethics Committee (UREC).

Should you wish to make any further changes in connection with your research project, this must be reported immediately to UREC. A Notification of Amendment form should be submitted for approval, accompanied by any additional or amended documents: http://www.uel.ac.uk/wwwmedia/schools/graduate/documents/Notification-of-Amendment-to-Approved-Ethics-App-150115.doc

Approved Research Site

I am pleased to confirm that the approval of the proposed research applies to the following research site:

Research Site	Principal Investigator / Local Collaborator
Online questionnaire	Dr Jennie Brown

Summary of Amendments
The researcher is looking to further recruit from other areas, including local shops, businesses and through social media. Local pharmacies have reached out to the researcher asking if they can promote the research to their customers.

Ethical approval for the original study was granted on 31st May 2017.

Approval is given on the understanding that the UEL Code of Good Practice in Research is adhered to.

With the Committee's best wishes for the success of this project.

Please ensure you retain this letter, as in the future you may be asked to provide evidence of ethical approval for the changes made to your study.

Yours sincerely,

[redacted]

Fernanda Silva
Administrative Officer for Research Governance
University Research Ethics Committee (UREC)
Email: researchethics@uel.ac.uk

Appendix C - Ethics 3 Quantitative Amendment 2

14th March 2019

Dear Erin,

Project Title:	**A ketogenic diet for depression**
Researcher:	**Erin Louise Bellamy**
Principal Investigator	**Kirstie Soar**
Amendment reference number:	**AMD 1819 22**
RRDE reference no of original approved application:	**EXP 1617 51**

I am writing to confirm that the application for an amendment to the aforementioned research study has now received ethical approval on behalf of Research, Research Degrees and Ethics (RRDE) Sub-Committee.

Should you wish to make any further changes in connection with your research project, this must be reported immediately to (RRDE). A Notification of Amendment form should be submitted for approval, accompanied by any additional or amended documents: http://www.uel.ac.uk/wwwmedia/schools/graduate/documents/Notification-of-Amendment-to-Approved-Ethics-App-150115.doc

Approved Research Site

I am pleased to confirm that the approval of the proposed research applies to the following research site:

Research Site	Principal Investigator / Local Collaborator
Online questionnaire	Kirstie Soar

University of East London

Summary of Amendments

Change of Principal Investigator: From Dr Jennie Brown to Kirstie Soar.

Medication

Participants will now be eligible to take part in the study if they are taking other medications as long as they do not have a diagnosed physical health condition. All medications must be listed in the eligibility questionnaire before taking part.

After much researching and discussion with those who work in the ketogenic diet area and implement the ketogenic diet to their patients and clients, the contraindications of regular medications are few. As participants on regular medications are working with a doctor, any changes to medication will be carried out by their doctor at their regular check-up.

The previously approved inclusion criteria: 'No diagnosed physical health condition' still stands.

The most common medication that may need altering over the course of the study is the statin medication. This is because the ketogenic diet has been shown to help regulate blood cholesterol and blood pressure.

As all participants are asked to inform and gain consent from their doctor to participate in the study there should be no issues with including these participants. The consent from doctors does not need to be evidenced but participants are encouraged to discuss the research with their healthcare provider. All participants are given a letter to take to their GP informing them of their participation and are encouraged to seek advice of doctor if they experience any side effects. (This letter was previously approved by the Ethics Board).

This change will give the researcher access to more participants and will reflect and 'real life' experience. The majority of the participants applying to take part are trying to regain their health. Diabetes.co.uk Low Carb Program has shown this to be a safe and effective approach in their type 2 diabetic population.

All participants are encouraged to seek the advice of their doctor if they do experience any side effects.

BMI

Participant must have a BMI over 18.5: A BMI of <18.5 is classed as within the underweight range. As the programs may encourage weight loss these individuals will not be included.

A BMI of >40 will not be considered as a physical health concern greater than anything else. Those who are looking to change their lifestyle and regain their health may have a BMI of >40.

The Diabetes.co.uk Low Carb Program has shown this to be a safe and effective approach in their type 2 diabetic population. All participants are encouraged to consult their doctor before starting the program and check in with them regularly throughout the program. The same applies for participants in this research study. All participants are given a letter to

take to their doctor prior to taking part. This letter explains the research to the doctor, giving them the ability to determine whether the participant is healthy enough to take part.

As the intervention focuses on a real, whole foods approach that is nutritionally complete, the researcher requests that those with a BMI of >40 be included in the study.

Those with a BMI of 18.5 or less will not be included in the study as the intervention can encourage weight loss if not followed correctly. Therefore, those will an already low BMI will not be included.

Recruitment

The Diabetes.co.uk online programs have recently been approved by the NHS to be prescribed to patients looking to improve their health (and reverse their type 2 diabetes). Due to these changes, the cost of this service will now increase from £29.99 to £70 a year which is waivered for one year when participants agree to take part in this study/research.

The researcher acknowledged that this may be seen as an incentive to take part in the study. However, given that this is a double blind RCT designed study participants do not know which group they are allocated to and are unaware of the fact that there are other intervention groups in the study.

The fact that the NHS has approved these programs for physical health improvement raises the impact potential of this study. The outcomes of this research will contribute to the evidence surrounding nutritional interventions for public mental health.

Biological Measures

Ketones (LCD and KD groups only): Ketone levels will be measured using urine keto sticks with a sub sample of participants also assessed using a blood ketone monitor.

As this research is self-funded, the researcher chose to check ketone levels of participants using the most cost effective measure: urine ketone sticks. Though these sticks are not 100% reliable, as hydration and fat adaptation (length of time on the diet) can alter the results, they are the most cost effective. The researcher was awarded a bursary from internal research funds to cover the cost of these urine sticks for both intervention groups.

However, the gold standard for measuring ketones is through the use of a blood ketone monitor as this measures blood ketones with reliability. This works the same way as a glucose monitor for diabetics. It requires a small pin prick to the finger and a drop of blood placed on a strip. The monitor then calculates the ketone reading. It is a very safe and easy way to check ketone levels.

The researcher has access to a small amount of ketone monitors in the near future. The researcher requests the permission to allocate blood ketone monitors at random to 50 participants in the Low Carb Intervention Group, 50 participants in the Control Wait List Group and 50 participants in the Ketogenic Intervention Group for a total of 150 participants.

Ethical approval for the original study was granted on 31st May 2017.

Approval is given on the understanding that the UEL Code of Good Practice in Research is adhered to.

University of East London

With the Committee's best wishes for the success of this project.

Please ensure you retain this letter, as in the future you may be asked to provide evidence of ethical approval for the changes made to your study.

Yours sincerely,

[redacted]

Fernanda Silva
Administrative Officer for Research Governance
Research, Research Degrees and Ethics (RRDE)
Email: researchethics@uel.ac.uk

Appendix D - Ethics 4 Drop Out

Dear Erin

Application ID: ETH1819-0167

Project title: A Ketogenic diet for depressive symptoms

Lead researcher: Ms Erin Bellamy

Your application to Research, Research Degrees and Ethics Sub-Committee meeting was considered on the 27th of August 2019.

The decision is: **Approved**

The Committee's response is based on the protocol described in the application form and supporting documentation.

Your project has received ethical approval for 2 years from the approval date.

If you have any questions regarding this application please contact the Research, Research Degrees and Ethics Sub-Committee meeting.

Approval has been given for the submitted application only and the research must be conducted accordingly.

Should you wish to make any changes in connection with this research project you must complete 'An application for approval of an amendment to an existing application'.

The approval of the proposed research applies to the following research site.

Research site: Online

Principal Investigator / Local Collaborator: Ms Erin Bellamy

Approval is given on the understanding that the UEL Code of Practice for Research and the Code of Practice for Research Ethics is adhered to.

Any adverse events or reactions that occur in connection with this research project should be reported using the University's form for Reporting an Adverse/Serious Adverse Event/Reaction.

The University will periodically audit a random sample of approved applications for ethical approval, to ensure that the research projects are conducted in compliance with the consent given by the Research Ethics Committee and to the highest standards of rigour and integrity.

Please note, it is your responsibility to retain this letter for your records.

With the Committee's best wishes for the success of the project

Yours sincerely

Fernanda Silva

Research, Research Degrees and Ethics Sub-Committee

Ethics ETH1819-0167: Ms Erin Bellamy (Medium risk)

University of East London

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Appendix E - Ethics 5 Qualitative

31st July 2018

Dear Erin

Project Title:	**A ketogenic diet for depression (Qualitative)**
Principal Investigator:	**Dr Kirstie Soar**
Researcher:	**Erin Louise Bellamy**
Reference Number:	**UREC 1718 87**

I am writing to confirm the outcome of your application to the University Research Ethics Committee (UREC), which was considered by UREC on **Wednesday 4 July 2018.**

The decision made by members of the Committee is **Approved**. The Committee's response is based on the protocol described in the application form and supporting documentation. Your study has received ethical approval from the date of this letter.

Should you wish to make any changes in connection with your research project, this must be reported immediately to UREC. A Notification of Amendment form should be submitted for approval, accompanied by any additional or amended documents: http://www.uel.ac.uk/wwwmedia/schools/graduate/documents/Notification-of-Amendment-to-Approved-Ethics-App-150115.doc

Any adverse events that occur in connection with this research project must be reported immediately to UREC.

Approved Research Site

I am pleased to confirm that the approval of the proposed research applies to the following research site.

Research Site	Principal Investigator / Local Collaborator
Online Skype video messaging	Dr Kirstie Soar

Approved Documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
UREC application form	2.0	20 July 2018
Participant Information sheet	2.0	20 July 2018
Consent form	1.0	20 June 2018
Diabetes.co.uk gatekeeper permission letter	1.0	20 June 2018
Debrief sheet	1.0	20 June 2018
Semi-structured interview schedule	1.0	20 June 2018

Approval is given on the understanding that the UEL Code of Practice in Research is adhered to.

The University will periodically audit a random sample of applications for ethical approval, to ensure that the research study is conducted in compliance with the consent given by the ethics Committee and to the highest standards of rigour and integrity.

Please note, it is your responsibility to retain this letter for your records.

With the Committee's best wishes for the success of this project.

Yours sincerely,

[redacted]

Fernanda Silva
Administrative Officer for Research Governance
University Research Ethics Committee (UREC)
Email: researchethics@uel.ac.uk

Appendix F - Ethical Approval DCUK

Diabetes.co.uk
Technology House
Sir William Lyons Road
University of Warwick Science Park
Coventry
CV4 7EZ

Monday 16th January 2017

To whom it may concern,

We, Diabetes Digital Media ltd. (Diabetes.co.uk), are willing to collaborate with Miss Erin Louise Bellamy and give her the permission to analyse and use anonymized data in order to answer her research queries.

All data collected will remain confidential and anonymous which is in keeping with our current practice as all data is owned by Diabetes Digital Media ltd.

Furthermore, we would like to assure you that the study has the ethical approval needed from us. More specifically, the participants will be informed about the aim of the study, the confidentiality and the anonymity of the data that will be collected and consent will be sought to take part in the study through our online system.

Kind regards,

[redacted]

Charlotte Summers

Diabetes.co.uk

Appendix G - Study 1 - Recruitment Posters and Emails With Versions

If you are **non-diabetic and aged 19-65**, and looking to improve your health, you could be eligible!

To find out more, simply go to

www.diabetes.co.uk/carbs

Participants in the study will be given **free lifetime membership** (worth £29.99) to award-winning online digital health resources, will have access to exclusive meal plans, and be coached by our health mentor, Louise.

The study involves following a set amount of carbohydrates each day for 12 weeks, using an easy to use online food diary to track your progress and completing some questionnaires on your experience along the way.

"Looking forward to helping you on your health journey."

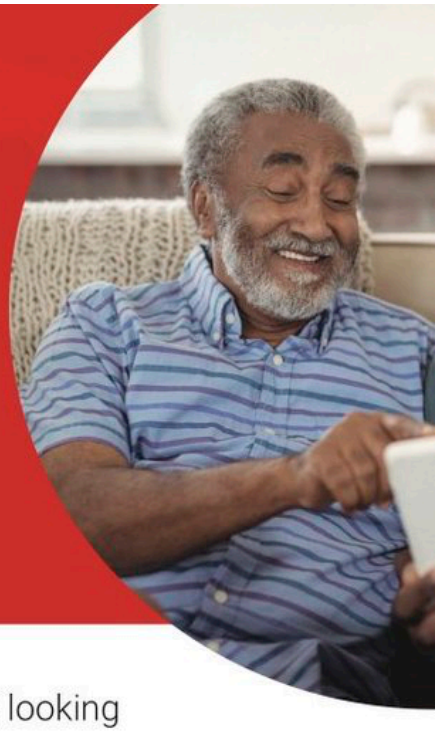
Erin and the research team

UEL University of East London

DKUEL-AUG18

Diabetes.co.uk

ARE **YOU** THE PERSON WE'RE LOOKING FOR?



There is an exciting opportunity to take part in research that could shape the way we approach health in the furture.

If you are **non-diabetic and aged 19-65**, and looking to improve your health, you could be eligible!

To find out more, simply go to

www.diabetes.co.uk/carbs

Participants in the study will be given **free lifetime membership** (worth £29.99) to award-winning online digital health resources, will have access to exclusive meal plans, and be coached by our health mentor, Louise.

The study involves following a set amount of carbohydrates each day for 12 weeks, using an easy to use online food diary to track your progress and completing some questionnaires on your experience along the way.

"Looking forward to helping you on your health journey."

Erin and the research team

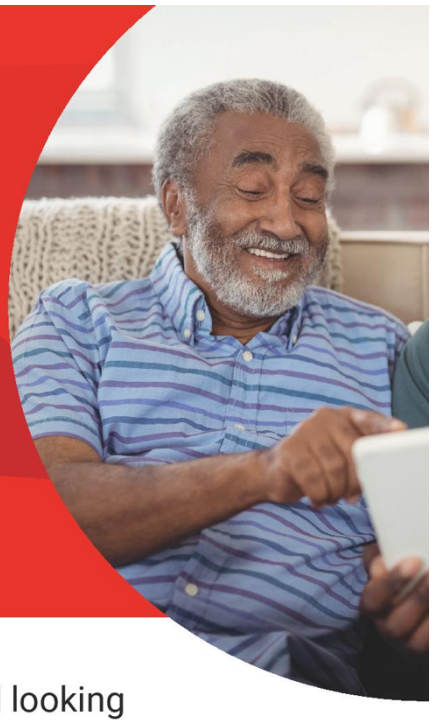
UEL University of East London

DKUEL-AUG19

Diabetes.co.uk

ARE **YOU** THE PERSON WE'RE LOOKING FOR?

There is an exciting opportunity to take part in research that could shape the way we approach health in the furture.



If you are **non-diabetic and aged 19-65**, and looking to improve your health, you could be eligible!

To find out more, simply go to

diabetes.co.uk/carbs

Participants in the study will be given **two years free membership** (worth £139) to award-winning online digital health resources, will have access to exclusive meal plans, and be coached by our health mentor, Louise.

The study involves following a set amount of carbohydrates each day for 12 weeks, using an easy to use online food diary to track your progress and completing some questionnaires on your experience along the way.

"Looking forward to helping you on your health journey."

Erin and the research team

UEL University of East London

DKUEL-MAR19

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Diabetes.co.uk
the global diabetes community

Are you the person we're looking for?

[[diabetes_segmented.firstname?? Hey]], I am reaching out to you because there is an exciting opportunity to take part in research that could shape the way we approach health in the future. We are looking for people aged 19-65 who do not have diabetes or any other physical health conditions.

Find out if you're eligible

Participants in the study will be given free lifetime membership (worth £29.99) to award-winning online digital health resources, will have access to exclusive meal plans, and be coached by our health mentor, Louise. In addition, you'll have access to an empowering community of over 310,000 people who are carving out a new approach to better health.

The study involves following a set amount of carbohydrates each day for 12 weeks, using an easy to use online food diary to track your progress.

We want you to be part of our research. Please fill out the screening questionnaire and wait to hear back from us.

Thank you,
Erin - Part of the Diabetes.co.uk Research Team

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Are you the person we're looking for?

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The study involves following a set amount of carbohydrates each day for 12 weeks, using an easy to use online food diary to track your progress.

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Thank you,
Erin - Part of the Diabetes.co.uk Research Team

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Appendix G1 - Follow Up Recruitment - 1

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Diabetes.co.uk
the global diabetes community

Did we miss each other? Gain access to the Program with a few easy steps

[[diabetes_segmented.firstname?? Hey]], I am currently working on a simple study that could change the way we look at health. I need your help - but don't worry! Your part in it will be super easy. I want to give you free access to a health app that would normally cost you £29.99.

Answer some simple questions

Participants in my study will be given free access to award-winning online health resources, such as daily meal plans, that have helped thousands of people lose weight and improve their metabolic health. You'll also get membership to an exclusive, empowering community of 350,000 people.

Once you have access, all I need you to do is follow the program (for free) and let me know what you think. If you are looking to make a lifestyle change, it couldn't be easier!

✓ Become a member of Diabetes.co.uk
Already done

2 Fill out the recruitment survey

3 Get your voucher worth £29.99

The Low Carb Program looks at reducing the amount of carbohydrates eaten, with an easy to use online food diary to track your progress and coaching from our health mentor Louise.

I want you to be part of our research. To start, simply fill out the screening questionnaire and wait to hear back from me.

Thank you,
Erin - Part of the Diabetes.co.uk Research Team
In collaboration with University of East London

UEL University of East London

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Appendix G2 - Follow Up Recruitment - 2

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Diabetes.co.uk
the global diabetes community

Did we miss each other? Don't miss your chance to gain access to the Program

[[diabetes_segmented.firstname?? Hey]], I emailed you before but I think we missed each other. I don't want you to miss out on the chance to take part in my research (and get free access to an award-winning health app).

Find out if you're eligible

Participants in the study will be given free lifetime membership (worth £29.99) to award-winning online digital health resources, will have access to exclusive meal plans, and be coached by our health mentor, Louise. In addition, you'll have access to an empowering community of over 350,000 people who are carving out a new approach to better health.

The study involves following a set amount of carbohydrates each day for 12 weeks, using an easy to use online food diary to track your progress and answering a few questions along the way.

We want you to be part of our research. Please fill out the screening questionnaire and wait to hear back from us.

Thank you,
Erin - Part of the Diabetes.co.uk Research Team
In collaboration with University of East London

UEL University of East London

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Appendix G3 - Follow Up Recruitment - 3

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the global diabetes community

Did we miss each other? Don't miss your chance to gain access to the Program

[[diabetes_segmented.firstname?? Hey]], I emailed you before but I think we missed each other. I don't want you to miss out on the chance to take part in my research (and get free access to an award-winning health app).

Find out if you're eligible

Participants in the study will be given free lifetime membership (worth £29.99) to award-winning online digital health resources, will have access to exclusive meal plans, and be coached by our health mentor, Louise. In addition, you'll have access to an empowering community of over 350,000 people who are carving out a new approach to better health.

The study involves following a set amount of carbohydrates each day for 12 weeks, using an easy to use online food diary to track your progress.

We want you to be part of our research. Please fill out the screening questionnaire and wait to hear back from us.

Thank you,
Erin - Part of the Diabetes.co.uk Research Team

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Appendix G4 - Follow Up Recruitment - 4

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Diabetes.co.uk
the global diabetes community

Did we miss each other? Gain access to the Program with a few easy steps

[[diabetes_segmented.firstname?? Hey]], I am currently working on a simple study that could change the way we look at health. I need your help - but don't worry! Your part in it will be super easy. I want to give you free access to a health app that would normally cost you £29.99.

Answer some simple questions

Participants in my study will be given free access to award-winning online health resources, such as daily meal plans, that have helped thousands of people lose weight and improve their metabolic health. You'll also get membership to an exclusive, empowering community of 350,000 people.

Once you have access, all I need you to do is follow the program (for free) and let me know what you think. If you are looking to make a lifestyle change, it couldn't be easier!

The Low Carb Program looks at reducing the amount of carbohydrates eaten, with an easy to use online food diary to track your progress and coaching from our health mentor Louise.

I want you to be part of our research. To start, simply fill out the screening questionnaire and wait to hear back from me.

Thank you,
Erin - Part of the Diabetes.co.uk Research Team

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Appendix G5 - Follow Up - Recruitment Recontact

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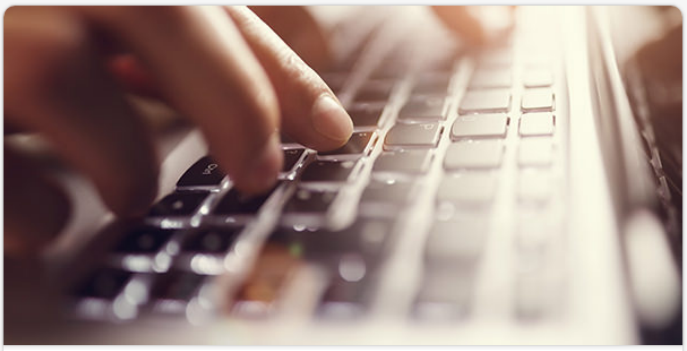
Diabetes.co.uk
the global diabetes community



Can we finish what we started?

Hi [[diabetes_segmented.firstname?? there]], how are you? The other day you showed an interest in helping me with my study, but you didn't fill out the whole survey. Was there a problem?

Jump back in

It's not too late to help change the future of healthcare. The way we look at health and lifestyle is evolving, and you can be part of that change. Your part in that change is significant!

Remember, members of the study will be given lifetime membership to an award-winning online health app that would usually cost £29.99, including access to exclusive meal plans, and will be coached by our health mentor, Louise.

In addition, you'll have access to an empowering community of over 350,000 people who are carving out a new approach to better health.

The study involves following a set amount of carbohydrates each day for 12 weeks, using an easy to use online food diary to track your progress, and answering a few questions along the way.

It's not too late to join. Simply click here to take the initial startup survey and wait to hear back from me.

Thank you,
Erin - Part of the Diabetes.co.uk Research Team
In collaboration with University of East London

UEL University of East London

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Appendix G6 - Unfortunately - Not Eligible Email

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the global diabetes community

About your part in the research...

Thank you for taking the time to complete the screening questionnaire and for showing your interest in this research.

Unfortunately you do not meet the criteria for eligible participants at this time, but we will be in touch in the future if circumstances change, or if there is any other research that I think will interest you, [[firstname.??there's always ongoing research]].

If you still want to improve your health you can head to the Low Carb Program to start your journey today. Peer-reviewed outcomes demonstrate significant health improvements for people who complete the Low Carb Program. People with type 2 diabetes **lose an average of 7.4kg**, **reduce HbA1c by 1.2% (13 mmol/mol)** and **1 in 4 people are in type 2 remission** at 1-year.

Make a new start

If you found any of the questions in this questionnaire upsetting or distressing please reach out to the following services who can support you:

Mind.org.uk
Mind provide advice and support to empower anyone experiencing a mental health problem: 0300 123 3393

Rethink.org
Rethink Mental Illness help more than 48,000 people every year through their services, support groups and helplines that are open 24/7. Different helpline number are available for different areas of the UK: 0300 5000 927

Samaritans.org
Samaritans offer a safe and confidential place to talk. They can be contacted 24/7 on 116 123.

Thanks again and best of luck in your health journey
Erin - part of the Diabetes.co.uk Research Team

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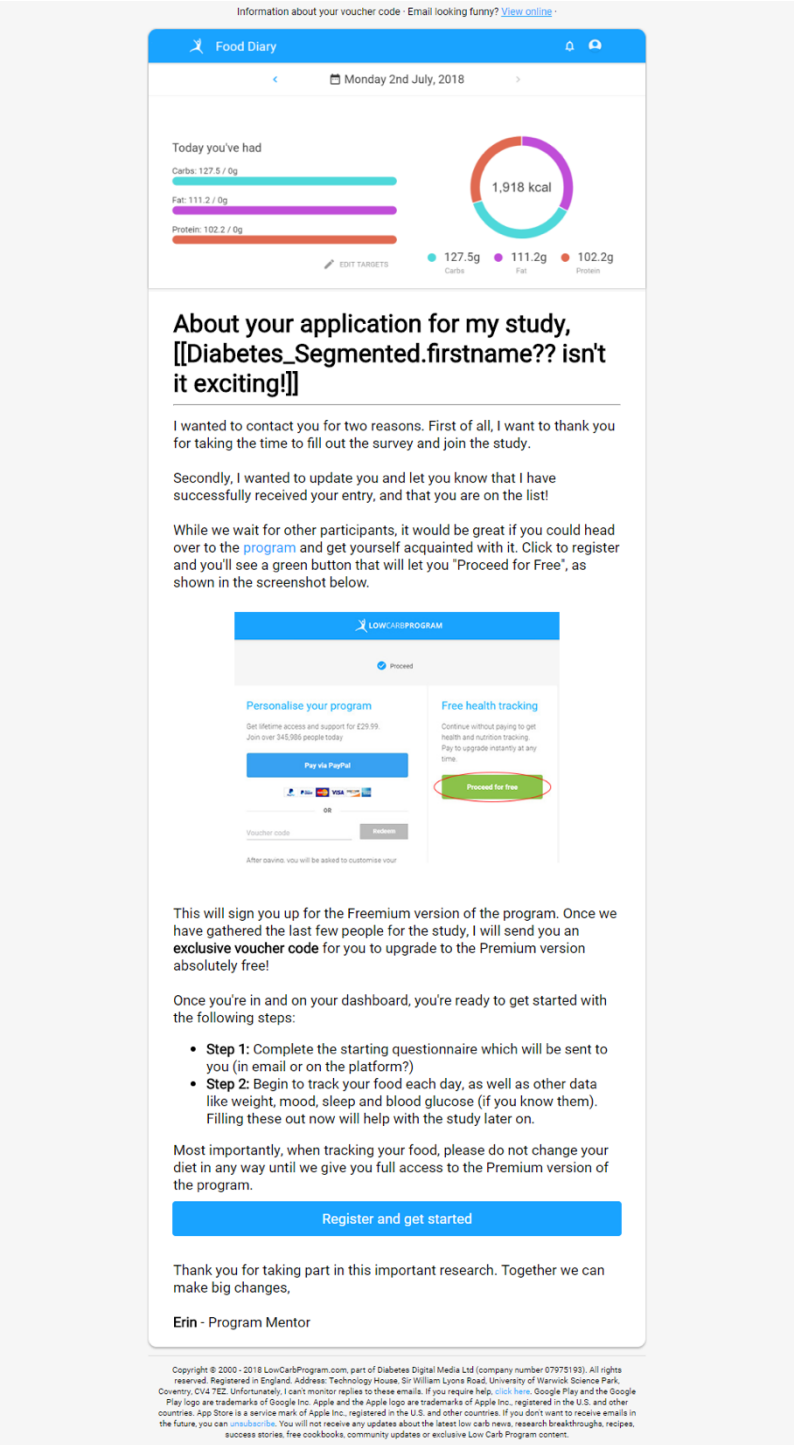
Appendix G7 - Control Group Wait List Email



Information about your voucher code · Email looking funny? View online ·

Food Diary

Monday 2nd July, 2018

Today you've had

Carbs: 127.5 / 0g

Fat: 111.2 / 0g

Protein: 102.2 / 0g

EDIT TARGETS

1,918 kcal

127.5g Carbs · 111.2g Fat · 102.2g Protein

About your application for my study, [[Diabetes_Segmented.firstname?? isn't it exciting!]]

I wanted to contact you for two reasons. First of all, I want to thank you for taking the time to fill out the survey and join the study.

Secondly, I wanted to update you and let you know that I have successfully received your entry, and that you are on the list!

While we wait for other participants, it would be great if you could head over to the program and get yourself acquainted with it. Click to register and you'll see a green button that will let you "Proceed for Free", as shown in the screenshot below.

This will sign you up for the Freemium version of the program. Once we have gathered the last few people for the study, I will send you an **exclusive voucher code** for you to upgrade to the Premium version absolutely free!

Once you're in and on your dashboard, you're ready to get started with the following steps:

- **Step 1:** Complete the starting questionnaire which will be sent to you (in email or on the platform?)
- **Step 2:** Begin to track your food each day, as well as other data like weight, mood, sleep and blood glucose (if you know them). Filling these out now will help with the study later on.

Most importantly, when tracking your food, please do not change your diet in any way until we give you full access to the Premium version of the program.

Register and get started

Thank you for taking part in this important research. Together we can make big changes,

Erin - Program Mentor

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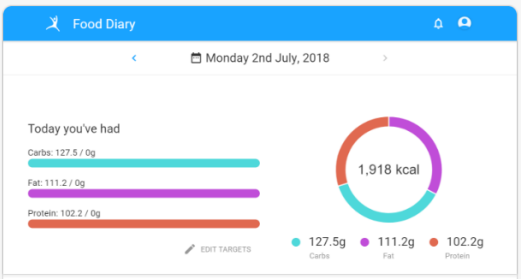
Appendix G8 - T1 LCD Group First Questionnaire and Access to Program

Information about your voucher code · Email looking funny? View online ·



About your application for my study

I wanted to contact you for two reasons. First of all, I want to thank you for taking the time to fill out the survey and join the study. I'm excited to give you access to the health app!

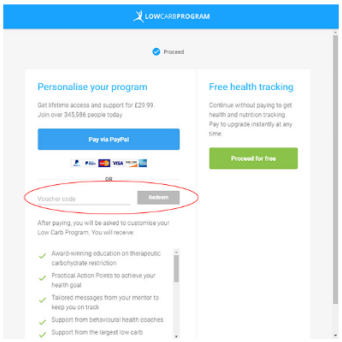
Secondly, I need to let you know the next steps! While we wait for other participants, there are two things I need you to do to get the ball rolling.

- **Step 1:** Click here to go to the first survey
- **Step 2:** Head to the program, redeem your vouchercode and settle in to the app!

Take the Survey

Once you've taken the survey, head to the register page of the health app and enter voucher code RESEARCH52.

After you add your name and email address, you'll see a text field that will let you enter your voucher code and redeem it, as shown in the screenshot below.



This will sign you up for the Premium version of the program. Once you've filled out the signup details, which will personalise the app to you can start on the first module, presented by my friend Louise, and track your food, sleep, mood and all sorts of other health markers!

Register and get started

Thank you for taking part in this important research. Together we can make big changes,

Erin - Lead Researcher
In association with University of East London

University of East London

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Appendix G9 - T2 Healthy Control Group Final Survey Email

Changing the future of healthcare · Email looking funny? View online

Diabetes.co.uk
the global diabetes community

It's time for your upgrade

The study is drawing to a close, there's only one more survey for you to fill out, and then you can access all the unlocked features of the Low Carb Program.

Take the final survey

Once you've filled it out, that's it, done!

I'll keep you up to date on any future developments with my research, and you'll receive a voucher code that you can use to access all aspects of the Low Carb Program.

Once you've redeemed your voucher, the first place you want to go is to Louise's first lesson, accessible from the Dashboard.

Thanks again for all your help, and best of luck in your health journey,
Erin - part of the Diabetes.co.uk Research Team

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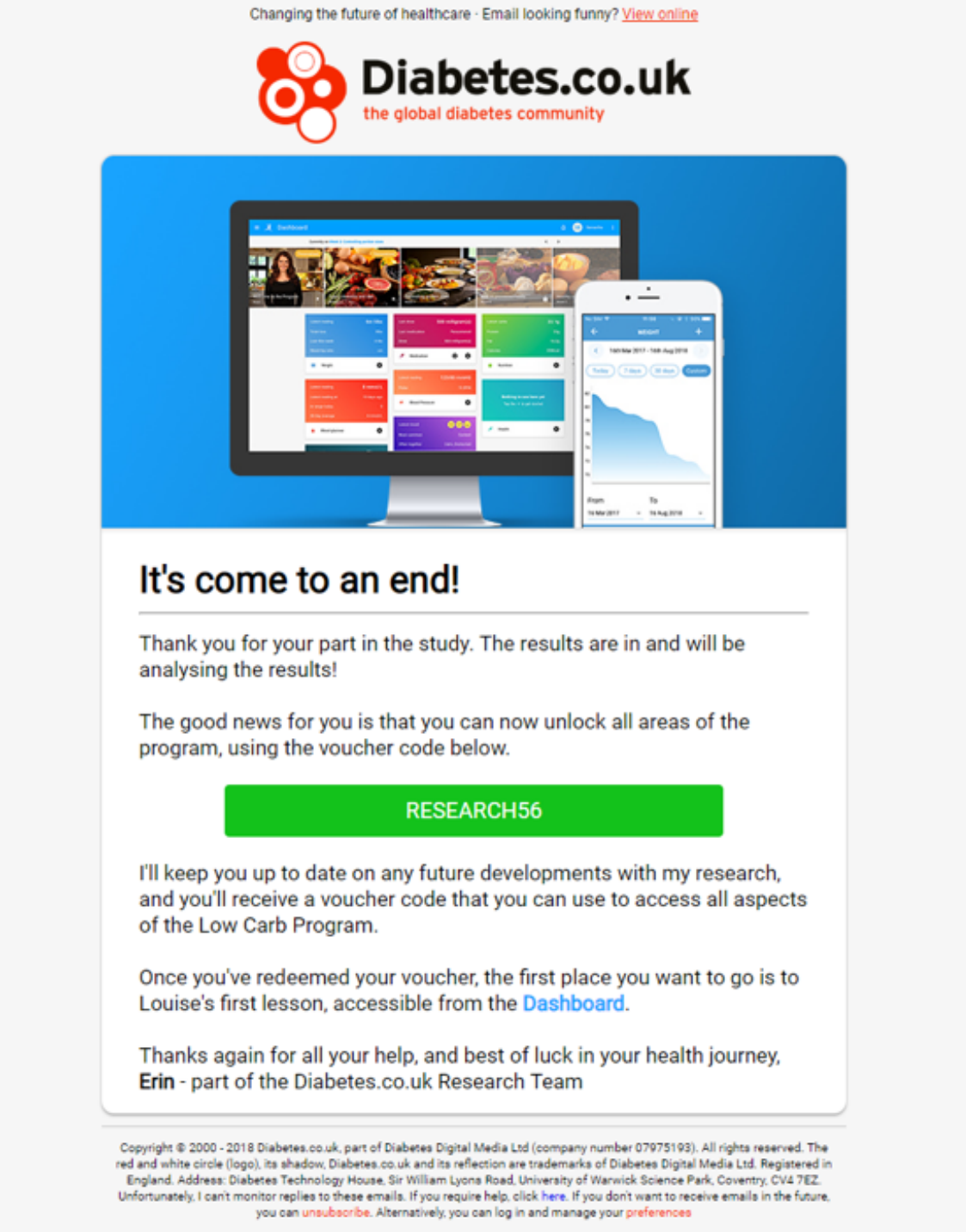
Appendix G10 - T2 Depressive Symptoms Control Group Final Survey Email



Appendix G11 - T2 Healthy LCD Group Next Survey Email

Changing the future of healthcare · Email looking funny? View online

Diabetes.co.uk
the global diabetes community

Here's your next part

I hope you've been enjoying your access to the program and making use of it's features.

It's now time for the next stage in the study.

Take the next survey

They surveys are bringing in some really interesting results and I'm excited to see how it develops!

The program has attracted so many interesting people from all walks of life, and you can see it reflected in the wide number of ways in which people interact with the program and make use of it.

Together, we're improving knowledge and understanding, and creating the future of healthcare.

Thank you for your continued help,
Erin - part of the Diabetes.co.uk Research Team

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Appendix H - Study 1 – Letter to GP

YOUR NAME AND ADDRESS

LOW CARB PROGRAM

YOUR DOCTOR'S NAME AND ADDRESS

Dear Doctor

I plan to start a reduced carbohydrate diet on DATE. This involves cutting out 'added sugar' and a gradual reduction in starchy carbohydrates such as bread and potatoes whilst eating more green vegetables. Also I will be eliminating 'trans-fats' often found in processed food and snacks. There will be a greater emphasis on home-cooked meals, portion size control and the healthier fats found in olive oil, nuts, eggs and butter.

The diet is not a high protein nor a crash diet. There will be no fasting and it is not a very low calorie diet.

I will be following guidelines on www.diabetes.co.uk/lowcarb over 10 weeks. You can find more medical details in the accompanying Information Sheet for Healthcare Professionals.

Please ask if you need to know any more and advise me whether you think I need to take any precautions before starting, or during the diet?

Thank you for taking the time to read this. I hope you agree with this plan to help me take better care of my health, and look forward to sharing my positive results in due course.

Yours sincerely,

Information Sheet for Healthcare Professionals

What is a low carb diet?

Of course there is no single 'low-carb diet', there are as many individual diets as there are people. The idea is that higher glycaemic sources of carbohydrate like bread, potatoes, pasta, cereals or rice are broken down by digestion into surprisingly large amounts of glucose.

An example would be a small slice of wholemeal bread, two hours after ingestion this has the same impact on blood glucose as three teaspoons of table sugar. So it can be seen it may be better for people with type 2 diabetes to avoid not only table sugar but all high glycaemic-index foods like bread, potatoes, rice, cereals and pasta. These starchy foods produce large amounts of glucose and therefore put a strain on the struggling pancreas to produce even more insulin.

Of course, any diet has to fit in with personal tastes, budget and family life!

Over 5,000 people have completed our evaluation survey and after 6 months, report:

- **Average weight loss of 10kg** (15% mean decrease)
- **Average HbA1c reduction at 6 months of 1.1% or 12mmol/mol** (13% mean decrease)
- **Average waist size reduction of 4.45inches or 11.3cm** (11% mean decrease)
-

On behalf of your patient thank you so much for your time.

Questions? Contact Charlotte Summers, Director of Education at charlotte@diabetes.co.uk.

CARBS Study

Information Sheet

Summary of the study

The aim of this study is to look at how different diets may affect your mental well-being.

If you agree to take part you will be asked to track your food using a food diary online and we will also ask you to track other things like weight and mood for 12 weeks. You will be asked to fill in a questionnaire online at the beginning of the study, at week six and week 12. Six months after starting the diet we will follow up with you and ask you to fill in a final questionnaire and ask you about your experience with the option to having a further discussion over the telephone at a later date. Before consenting, please check with your GP that you are well enough to participate.

The diet – What is it?

You will be asked to follow a set amount of fat, protein and carbohydrates each day. You will be asked to track your intake online using an easy to use food diary. As long as you follow the set amount you will be able to eat freely until you are full.

Possible benefits

- Lose weight
- Reduce food cravings
- Reduce hunger and increase feeling full after meals
- Increase energy levels
- Reduce risk of heart disease and other physical illnesses
- Improved memory

Possible side effects

This diet has been shown to be safe, however, as with all dietary changes, you may experience some side effects. These side effects should disappear within

the first few weeks with increased water and salt intake. Possible side effects may include:

- Flu like symptoms (Headache, Lethargy)
- Changes in bowel habits
- Leg cramps
- Bad breath
- Loss of energy

Contact details of external helplines and support groups will be provided throughout the study and participants will be encouraged to engage with the Diabetes.co.uk community forum. If you have any other issues or if your side effects persist please contact your GP.

To take part you will need to be:

- UK based
- 19-65 years old
- Non Diabetic
- No diagnosed physical health condition
- Not pregnant and not planning of becoming pregnant
- Not have lost a significant amount of weight in the past year (more than two stone)
- Not followed a low carbohydrate diet before
- If on antidepressants must have a minimum of three weeks adherence
- Have a BMI over 18.5
- No diagnosed mental health condition apart from depression
- Not currently participating in any other trial focusing on diet or exercise

Confidentiality of the Data

This study will be in collaboration with Diabetes.co.uk who receive no funding from any external bodies. This study will be self-funded by the researcher.

Where possible, participants' confidentiality will be maintained unless a disclosure is made that indicates that the participant or someone else is at serious risk of harm.

All the data will be securely stored by Diabetes.co.uk and Qualtrics Survey Software and will only be accessed securely by the researcher. It will not be possible to identify individuals as all data will be looked at together as a large group.

The data will be collected, analysed and kept for a period of up to ten years before it is securely disposed of by the researcher. This is in keeping with the data protection terms and conditions of Diabetes.co.uk. All data generated in the course of the research will be retained in accordance with the University of East London's Data Protection Policy.

Online data protection

The online version of these questionnaires have been constructed as an anonymous survey using Qualtrics software, meaning no emails, IP addresses and/or geolocation data will be identified in the responses. HTTPS survey links (also known as secure survey links) have been used, giving Secure Sockets Layer (SSL) Encryption while a questionnaire is being completed. During the study data collected online will be stored on a EU-based server and will be subject to EU Data Protection acts. All online data will be completely destroyed following completion of data collection.

Disclaimer

Your participation in this study is entirely voluntary, and you are free to withdraw at any time during the research. Should you choose to withdraw from the programme you may do so without disadvantage to yourself and without any obligation to give a reason. Please note that your data can be withdrawn up to two weeks after the final questionnaire is completed. If you feel unwell in any way please contact your GP.

University Research Ethics Committee

If you have any concerns regarding the conduct of the research in which you are being asked to participate, please contact: Catherine Fieulleteau, Research Integrity and Ethics Manager, Graduate School, EB 1.43. University of East London, Docklands Campus, London E16 2RD

(Telephone: 020 8223 6683, Email: researchethics@uel.ac.uk)

Appendix J - Study 1 – Consent Form

CARBS Experience Interview

Consent Form

Researchers at the University of East London: Erin Louise Bellamy (PhD Researcher) and Dr. Kirstie Soar (Director of Studies)

Please tick as appropriate:

	YES	NO
I have read the information leaflet relating to the above study of research in which I have been asked to participate and have confirmed that I have read it. The nature and purposes of the research have been explained to me, and I have had the opportunity to discuss the details and ask questions about this information. I understand what is being proposed and the procedures in which I will be involved have been explained to me. I have had the opportunity to download and print this information.		
I understand that my involvement in this study, and particular data from this research, will remain strictly confidential as far as possible. Only the researchers involved in the study will have access to the data.		
I understand that maintaining strict confidentiality is subject to the following limitation: Where possible, participants' confidentiality will be maintained unless a disclosure is made that indicates that the participant or someone else is at serious risk of harm. Such disclosures may be reported to the relevant authority.		
I understand that all of my information will be anonymized and that I will not be individually named at any point during the study, analysis or publications.		
I understand that some of my answers to questions may be quoted in the final write up and publications but that they will be fully anonymized or provided an Alias.		
Research findings will be written up in the form of publications for research journals in the field of Diabetes, Nutrition and Psychology. Findings will also be presented at conferences and written up into a final dissertation.		
I am happy to be contacted for future research studies by the researchers or by Diabetes.co.uk (If you do not wish to be contacted in this way you may still take part)		
It has been explained to me what will happen once the study has been completed.		
I understand that my participation in this study is entirely voluntary, and I am free to withdraw at any time during the research without disadvantage to myself and without being obliged to give any reason. I understand that my data can be withdrawn up to two weeks after the final questionnaire.		
I hereby freely and fully consent to participate in the study which has been fully explained to me and for the information obtained to be used in relevant research publications.		

Participant's Name (BLOCK CAPITALS - as signature) .....

Investigator's Signature and Date .....

Appendix K - Study 1 – T0 Screening Questionnaire

SCREENING QUESTIONNAIRE

Please take a few moments to fill out this screening questionnaire to determine your eligibility for the study.

Please check Yes or No to the following:

	YES	NO
Are you between the age of 19-65		
Are you UK based		
What is your BMI		
Are you Diabetic		
Do you have any physical health concerns		
Are you pregnant or do you plan to get pregnant in the next 6 months		
Have you lost a significant amount of weight in the past year (more than 2 stone)		
Have you followed a low carbohydrate diet before?		
Are you currently partaking in any other trial on diet or exercise?		
Have you received a diagnosis of depression?		
Do you any mental health issues other than depression?		
Recently have you had thoughts that you would be better off dead or of hurting yourself in some way?		
Are you taking regular medication (other than antidepressants)		
Are you on any antidepressant medication?		
If Yes, have you been on it for more than 2 weeks?		

- If Yes, please specify (check box and self-complete for "other")
- You are MALE or FEMALE or OTHER (check box)
- Age (self-complete)
- Waist Size
- Weight
- Height
- Level of Education
- Ethnicity

Please answer the following:

	Over the past two weeks, how often have you been bothered by any of the following problems?	Not at all	Several Days	More than half the days	Nearly Every Day
1	Little interest or pleasure in doing things	0	1	2	3
2	Feeling down, depressed or hopeless	0	1	2	3
3	Trouble falling asleep, staying asleep, or sleeping too much	0	1	2	3
4	Feeling tired or having little energy	0	1	2	3
5	Poor appetite or overeating	0	1	2	3
6	Feeling bad about yourself – or that you're a failure or have let yourself or your family down	0	1	2	3
7	Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8	Moving or speaking so slowly that other people could have noticed. Or, the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9	Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
		Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
10	If you checked off any problems, how difficult have those problems made it for you to do your work, take care of things at home, or get along with other people?	0	1	2	3

Appendix L - Study 1 – T1 Questionnaire

This survey will assess how you have been feeling generally over the last few weeks and month and will cover topics such as body satisfaction and well-being. At the end of each survey there will be an open text box where you can expand on your responses if you have experienced any extenuating circumstances e.g., change in employment, accommodation or traumatic family event etc. If you have experienced any of these it is important to include these here. This survey should take about 10-15 minutes to complete. If you have any issues or concerns about the study please use the contact details below.

(PSS)

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate by circling how often you felt or thought a certain way.

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

		0	1	2	3	4
1	In the last month, how often have you been upset because of something that happened unexpectedly?					
2	In the last month, how often have you felt that you were unable to control the important things in your life?					
3	In the last month, how often have you felt nervous and "stressed"?					
4	In the last month, how often have you felt confident about your ability to handle your personal problems?					
5	In the last month, how often have you felt that things					

	were going your way?					
6	In the last month, how often have you found that you could not cope with all the things that you had to do?					
7	In the last month, how often have you been able to control irritations in your life?					
8	In the last month, how often have you felt that you were on top of things?					
9	In the last month, how often have you been angered because of things that were outside of your control?					
10	In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?					

(PANAS)

Indicate the extent you have felt this way **over the past week**

1= Very slightly or not at all, 2= A little, 3=Moderately, 4= Quite a bit, 5=Extremely

		1	2	3	4	5
1	Interested					
2	Distressed					
3	Excited					
4	Upset					
5	Strong					
6	Guilty					
7	Scared					
8	Hostile					
9	Enthusiastic					
10	Proud					

11	Irritable					
12	Alert					
13	Ashamed					
14	Inspired					
15	Nervous					
16	Determined					
17	Attentive					
18	Jittery					
19	Active					
20	Afraid					

(SWEMWBS)

Below are some statements about feelings and thoughts.

Please tick the box that best describes your experience of

each **over the last 2 weeks**

1= None of the time, 2= Rarely, 3= Some of the time, 4= Often, 5= All of the time

Statements	**None of the time**	**Rarely**	**Some of the time**	**Often**	**All of the time**
I've been feeling optimistic about the future	1	2	3	4	5
I've been feeling useful	1	2	3	4	5
I've been feeling relaxed	1	2	3	4	5
I've been dealing with problems well	1	2	3	4	5
I've been thinking clearly	1	2	3	4	5
I've been feeling close to other people	1	2	3	4	5
I've been able to make up my own mind about things	1	2	3	4	5

(GAD-7)

Over the **last 2 weeks,** how often have you been bothered by the following problems?

		Not at all	Several Days	More than half of the days	Nearly every day
1	Feeling nervous, anxious or on edge	0	1	2	3
2	Not being able to stop or control worrying	0	1	2	3
3	Worrying too much about different things	0	1	2	3
4	Trouble relaxing	0	1	2	3
5	Being so restless that it is hard to sit still	0	1	2	3
6	Becoming easily annoyed or irritable	0	1	2	3
7	Feeling afraid as if something awful might happen	0	1	2	3

(CES-D)

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you've felt this way during the **past week.** Respond to all items.

	During the past week….	Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)
1	I was bothered by things that usually don't bother me				
2	I did not feel like eating; my appetite was poor				
3	I felt that I could not shake off the blues even with help from my family				

4	I felt that I was just as good as other people				
5	I had trouble keeping my mind on what I was doing				
6	I felt depressed				
7	I felt that everything I did was an effort				
8	I felt hopeful about the future				
9	I thought my life had been a failure				
10	I felt fearful				
11	My sleep was restless				
12	I was happy				
13	I talked less than usual				
14	I felt lonely				
15	People were unfriendly				
16	I enjoyed life				
17	I had crying spells				
18	I felt sad				
19	I felt that people disliked me				
20	I could not "get going"				

(BSSS)

Please think of persons who are close to you.

		Strongly Disagree	Somewhat Disagree	Somewhat Agree	Strongly Agree
1	There are some people who truly like me	1	2	3	4
2	Whenever I am not feeling well, other people show me that they are fond of me	1	2	3	4
3	Whenever I am sad, there are people who cheer me up	1	2	3	4
4	There is always someone there for me when I need comforting	1	2	3	4
5	I know some people upon whom I can always rely	1	2	3	4
6	When I am worried, there is someone who helps me	1	2	3	4
7	There are people who offer me help when I need it	1	2	3	4
8	When everything becomes too much for me to handle, others are there to help me	1	2	3	4
9	When I am down, I need someone who boosts my spirits	1	2	3	4
10	It is important for me always to have someone who listens to me	1	2	3	4
11	Before making any important decisions, I absolutely need a second opinion	1	2	3	4
12	I get along best without any outside help	1	2	3	4
13	In critical situations, I prefer to ask others for their advice	1	2	3	4
14	Whenever I am down, I look for someone to cheer me up again	1	2	3	4
15	When I am worried, I reach out to someone to talk to	1	2	3	4
16	If I do not know how to handle a situation, I ask others what they would do	1	2	3	4
17	Whenever I need help, I ask for it	1	2	3	4

(SCS-SF)

Please indicate how often you behave in the stated manner.

		Almost Never				Almost Always
1	When I fail at something important to me I become consumed by feelings of inadequacy	1	2	3	4	5
2	I try to be understanding and patient towards those aspects of my personality I don't like	1	2	3	4	5
3	When something painful happens I try to take a balanced view of the situation	1	2	3	4	5
4	When I'm feeling down, I tend to feel like most other people are probably happier than I am	1	2	3	4	5
5	I try to see my failings as part of the human condition	1	2	3	4	5
6	When I'm going through a very hard time, I give myself the caring and tenderness I need	1	2	3	4	5
7	When something upsets me I try to keep my emotions in balance	1	2	3	4	5
8	When I fail at something that's important to me, I tend to feel alone in my failure	1	2	3	4	5
9	When I'm feeling down I tend to obsess and fixate on everything that's wrong	1	2	3	4	5
10	When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people	1	2	3	4	5
11	I'm disapproving and judgmental about my own flaws and inadequacies	1	2	3	4	5
12	I'm intolerant and impatient towards those aspects of my personality I don't like	1	2	3	4	5

Body Appreciation Scale (BAS-2)

Please indicate whether the question is true about you never, seldom, sometimes, often, or always

		Never	Seldom	Sometimes	Often	Always
1	I respect my body	1	2	3	4	5
2	I feel good about my body	1	2	3	4	5

3	I feel that my body has at least some good qualities	1	2	3	4	5
4	I take a positive attitude towards my body	1	2	3	4	5
5	I am attentive to my body's needs	1	2	3	4	5
6	I feel love for my body	1	2	3	4	5
7	I appreciate the different and unique characteristics of my body	1	2	3	4	5
8	My behaviour reveals my positive attitude toward my body; for example, I hold my head high and smile	1	2	3	4	5
9	I am comfortable in my body	1	2	3	4	5
10	I feel like I am beautiful even if I am different from media images of attractive people (e.g., models, actresses/actors)	1	2	3	4	5

Please check the following

Activity	Got much worse	Got worse	Stayed the same	Improved a little	Much improved
Since starting the program my physical activity levels have	1	2	3	4	5

Please check the following

Health	Fair	Good	Very Good	Excellent
In general, how would you say your health has been in the past month	1	2	3	4

How often do you take part in sports or activities that are mildly energetic, moderately energetic or vigorous? Please check the following

	Three times or more a week	Once or twice a week	About once to three times a month	Never/hardly ever
Mildly energetic *(e.g. walking, weeding, hoeing, bicycle repair, woodwork, general housework)*				
Moderately energetic *(e.g. cycling, dancing, scrubbing, golf, decorating, lawn mowing, leisurely swimming)*				
Vigorous *(e.g. running, hard swimming, tennis, squash, digging, cycle racing)*				

Please expand on your responses or add any change in circumstance if you wish	

Thank you for completing this questionnaire. If you feel that you have been effected in any way by the questions asked please do not hesitate to contact the people below or speak to your GP. Alternatively, participants are encouraged to utilise the Diabetes.co.uk forum specifically made for the research study which you will find through your personal account.

Alternatively for enquiries about the research please contact Charlotte at Charlotte@diabetes.co.uk.

Mind.org.uk

Mind provide advice and support to empower anyone experiencing a mental health problem: 0300 123 3393

Rethink.org

Rethink Mental Illness help more than 48,000 people every year through their services, support groups and helplines that are open 24/7. Different helpline number are available for different areas of the UK: 0300 5000 927

Samaritans.org

Samaritans offer a safe and confidential place to talk. They can be contacted 24/7 on 116 123.

Appendix M - Study 1 - T2 Questionnaire

This survey will assess how you have been feeling generally over the last few weeks and month and will cover topics such as body satisfaction and psychological well-being. At the end of each survey there will be an open text box where you can expand on your responses if you have experienced any extenuating circumstances i.e. change in employment, accommodation or traumatic family event etc. This survey should take about 10-15 minutes to complete. If you have an issues or concerns about the study please use the contact details below.

(PSS)

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate by circling how often you felt or thought a certain way.

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

		0	1	2	3	4
1	In the last month, how often have you been upset because of something that happened unexpectedly?					
2	In the last month, how often have you felt that you were unable to control the important things in your life?					
3	In the last month, how often have you felt nervous and "stressed"?					
4	In the last month, how often have you felt confident about your ability to handle your personal problems?					
5	In the last month, how often have you felt that things were going your way?					
6	In the last month, how often have you found that you could not cope with all the things that you had to do?					
7	In the last month, how often have you been able to control irritations in your life?					

8	In the last month, how often have you felt that you were on top of things?					
9	In the last month, how often have you been angered because of things that were outside of your control?					
10	In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?					

(PANAS)

Indicate the extent you have felt this way **over the past week**

1= Very slightly or not at all, 2= A little, 3=Moderately, 4= Quite a bit, 5=Extremely

		1	2	3	4	5
1	Interested					
2	Distressed					
3	Excited					
4	Upset					
5	Strong					
6	Guilty					
7	Scared					
8	Hostile					
9	Enthusiastic					
10	Proud					
11	Irritable					
12	Alert					
13	Ashamed					
14	Inspired					
15	Nervous					
16						

	Determined					
17	Attentive					
18	Jittery					
19	Active					
20	Afraid					

(SWEMWBS)

Below are some statements about feelings and thoughts.

Please tick the box that best describes your experience of

each **over the last 2 weeks**

1= None of the time, 2= Rarely, 3= Some of the time, 4= Often, 5= All of the time

Statements	**None of the time**	**Rarely**	**Some of the time**	**Often**	**All of the time**
I've been feeling optimistic about the future	1	2	3	4	5
I've been feeling useful	1	2	3	4	5
I've been feeling relaxed	1	2	3	4	5
I've been dealing with problems well	1	2	3	4	5
I've been thinking clearly	1	2	3	4	5
I've been feeling close to other people	1	2	3	4	5
I've been able to make up my own mind about things	1	2	3	4	5

(CES-D)

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you've felt this way during the **past week.** Respond to all items.

	During the past week….	Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)
1	I was bothered by things that usually don't bother me				
2	I did not feel like eating; my appetite was poor				
3	I felt that I could not shake off the blues even with help from my family				
4	I felt that I was just as good as other people				
5	I had trouble keeping my mind on what I was doing				
6	I felt depressed				
7	I felt that everything I did was an effort				
8	I felt hopeful about the future				
9	I thought my life had been a failure				
10	I felt fearful				
11	My sleep was restless				
12	I was happy				
13	I talked less than usual				
14	I felt lonely				
15	People were unfriendly				
16	I enjoyed life				
17					

	I had crying spells				
18	I felt sad				
19	I felt that people disliked me				
20	I could not "get going"				

(GAD-7)

Over the **last 2 weeks,** how often have you been bothered by the following problems?

		Not at all	Several Days	More than half of the days	Nearly every day
1	Feeling nervous, anxious or on edge	0	1	2	3
2	Not being able to stop or control worrying	0	1	2	3
3	Worrying too much about different things	0	1	2	3
4	Trouble relaxing	0	1	2	3
5	Being so restless that it is hard to sit still	0	1	2	3
6	Becoming easily annoyed or irritable	0	1	2	3
7	Feeling afraid as if something awful might happen	0	1	2	3

Please check the following

Activity	Got much worse	Got worse	Stayed the same	Improved a little	Much improved
Since starting the program my physical activity levels have	1	2	3	4	5

Please check the following

Health	Fair	Good	Very Good	Excellent
In general, how would you say your health has been in the past month				

(SCS-SF)

Please indicate how often you behave in the stated manner.

		Almost Never				Almost Always
1	When I fail at something important to me I become consumed by feelings of inadequacy	1	2	3	4	5
2	I try to be understanding and patient towards those aspects of my personality I don't like	1	2	3	4	5
3	When something painful happens I try to take a balanced view of the situation	1	2	3	4	5
4	When I'm feeling down, I tend to feel like most other people are probably happier than I am	1	2	3	4	5
5	I try to see my failings as part of the human condition	1	2	3	4	5
6	When I'm going through a very hard time, I give myself the caring and tenderness I need	1	2	3	4	5
7	When something upsets me I try to keep my emotions in balance	1	2	3	4	5
8	When I fail at something that's important to me, I tend to feel alone in my failure	1	2	3	4	5
9	When I'm feeling down I tend to obsess and fixate on everything that's wrong	1	2	3	4	5
10	When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people	1	2	3	4	5
11	I'm disapproving and judgmental about my own flaws and inadequacies	1	2	3	4	5
12	I'm intolerant and impatient towards those aspects of my personality I don't like	1	2	3	4	5

Please expand on your responses or add any change in circumstance	

- Are you happy to be contacted in the near future for a discussion on your experience? Yes/No

Thank you for completing this questionnaire. If you feel that you have been effected in any way by the questions asked please do not hesitate to contact the people below or speak to your GP. Alternatively, participants are encouraged to utilise the Diabetes.co.uk forum specifically made for the research study which you will find through your personal account. Alternatively for enquiries about the research please contact Charlotte at Charlotte@diabetes.co.uk.

Mind.org.uk

Mind provide advice and support to empower anyone experiencing a mental health problem: 0300 123 3393

Rethink.org

Rethink Mental Illness help more than 48,000 people every year through their services, support groups and helplines that are open 24/7. Different helpline number are available for different areas of the UK: 0300 5000 927

Samaritans.org

Samaritans offer a safe and confidential place to talk. They can be contacted 24/7 on 116 123.

Appendix N - Study 1 – T3 Questionnaire

This survey will assess how you have been feeling generally over the last few weeks and month and will cover topics such as body satisfaction and psychological well-being. At the end of each survey there will be an open text box where you can expand on your responses if you have experienced any extenuating circumstances i.e. change in employment, accommodation or traumatic family event etc. This survey should take about 10-15 minutes to complete. If you have an issues or concerns about the study please use the contact details below.

(PSS)

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate by circling how often you felt or thought a certain way.

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

		0	1	2	3	4
1	In the last month, how often have you been upset because of something that happened unexpectedly?					
2	In the last month, how often have you felt that you were unable to control the important things in your life?					
3	In the last month, how often have you felt nervous and "stressed"?					
4	In the last month, how often have you felt confident about your ability to handle your personal problems?					
5	In the last month, how often have you felt that things were going your way?					
6	In the last month, how often have you found that you could not cope with all the things that you had to do?					

7	In the last month, how often have you been able to control irritations in your life?					
8	In the last month, how often have you felt that you were on top of things?					
9	In the last month, how often have you been angered because of things that were outside of your control?					
10	In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?					

(PANAS)

Indicate the extent you have felt this way **over the past week**

1= Very slightly or not at all, 2= A little, 3=Moderately, 4= Quite a bit, 5=Extremely

		1	2	3	4	5
1	Interested					
2	Distressed					
3	Excited					
4	Upset					
5	Strong					
6	Guilty					
7	Scared					
8	Hostile					
9	Enthusiastic					
10	Proud					
11	Irritable					
12	Alert					
13	Ashamed					
14	Inspired					
15						

	Nervous					
16	Determined					
17	Attentive					
18	Jittery					
19	Active					
20	Afraid					

(SWEMWBS)

Below are some statements about feelings and thoughts.

Please tick the box that best describes your experience of

each **over the last 2 weeks**

1= None of the time, 2= Rarely, 3= Some of the time, 4= Often, 5= All of the time

Statements	None of the time	Rarely	Some of the time	Often	All of the time
I've been feeling optimistic about the future	1	2	3	4	5
I've been feeling useful	1	2	3	4	5
I've been feeling relaxed	1	2	3	4	5
I've been dealing with problems well	1	2	3	4	5
I've been thinking clearly	1	2	3	4	5
	1	2	3	4	5

I've been feeling close to other people					
I've been able to make up my own mind about things	1	2	3	4	5

(CES-D)

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you've felt this way during the **past week.** Respond to all items.

	During the past week….	Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)
1	I was bothered by things that usually don't bother me				
2	I did not feel like eating; my appetite was poor				
3	I felt that I could not shake off the blues even with help from my family				
4	I felt that I was just as good as other people				
5	I had trouble keeping my mind on what I was doing				
6	I felt depressed				
7	I felt that everything I did was an effort				
8	I felt hopeful about the future				
9	I thought my life had been a failure				
10	I felt fearful				

11	My sleep was restless				
12	I was happy				
13	I talked less than usual				
14	I felt lonely				
15	People were unfriendly				
16	I enjoyed life				
17	I had crying spells				
18	I felt sad				
19	I felt that people disliked me				
20	I could not "get going"				

(GAD-7)

Over the **last 2 weeks,** how often have you been bothered by the following problems?

		Not at all	Several Days	More than half of the days	Nearly every day
1	Feeling nervous, anxious or on edge	0	1	2	3
2	Not being able to stop or control worrying	0	1	2	3
3	Worrying too much about different things	0	1	2	3
4	Trouble relaxing	0	1	2	3
5	Being so restless that it is hard to sit still	0	1	2	3
6	Becoming easily annoyed or irritable	0	1	2	3
7	Feeling afraid as if something awful might happen	0	1	2	3

Please check the following

Health	Fair	Good	Very Good	Excellent
In general, how would you say your health has been in the past month				

(SCS-SF)

Please indicate how often you behave in the stated manner.

		Almost Never				Almost Always
1	When I fail at something important to me I become consumed by feelings of inadequacy	1	2	3	4	5
2	I try to be understanding and patient towards those aspects of my personality I don't like	1	2	3	4	5
3	When something painful happens I try to take a balanced view of the situation	1	2	3	4	5
4	When I'm feeling down, I tend to feel like most other people are probably happier than I am	1	2	3	4	5
5	I try to see my failings as part of the human condition	1	2	3	4	5
6	When I'm going through a very hard time, I give myself the caring and tenderness I need	1	2	3	4	5
7	When something upsets me I try to keep my emotions in balance	1	2	3	4	5

8	When I fail at something that's important to me, I tend to feel alone in my failure	1	2	3	4	5
9	When I'm feeling down I tend to obsess and fixate on everything that's wrong	1	2	3	4	5
10	When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people	1	2	3	4	5
11	I'm disapproving and judgmental about my own flaws and inadequacies	1	2	3	4	5
12	I'm intolerant and impatient towards those aspects of my personality I don't like	1	2	3	4	5

	None of the time	Rarely	Some of the time	Often	All of the time
I have cheated or felt the need to cheat on this program	1	2	3	4	5

	Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
Following this way of eating for me has been	1	2	3	4

	Not at all	A little	Somewhat	A fair amount	A lot

I like how I feel with this way of eating	1	2	3	4	5

	None of the time	Rarely	Some of the time	Often	All of the time
I feel hungry with this way of eating	1	2	3	4	5

	Highly Unlikely	Unlikely	Maybe	Likely	Highly Likely
I will continue this way of eating	1	2	3	4	5

	Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
Sourcing the food for this way of eating is	1	2	3	4

Please check the following

Activity	Got much worse	Got worse	Stayed the same	Improved a little	Much improved
Since starting the program my physical activity levels have	1	2	3	4	5

Please expand on your responses or add any change in circumstance	

Please answer the following questions in as much detail as possible.

Q1. How have you found this way of eating?
Q2. Would you recommend this way of eating to others?
Q3. What do you like about this way of eating?
Q4. What do you dislike about this way of eating?
Q5. How would you improve the online program?
Q6. Is there anything that you would like to feedback to the researchers?

Thank you for completing this questionnaire. If you feel that you have been effected in any way by the questions asked please do not hesitate to contact the people below or speak to your GP. Alternatively, participants are encouraged to utilise the Diabetes.co.uk forum specifically made for the research study which you will find through your personal account. Alternatively for enquiries about the research please contact Charlotte at Charlotte@diabetes.co.uk.

Mind.org.uk

Mind provide advice and support to empower anyone experiencing a mental health problem: 0300 123 3393

Rethink.org

Rethink Mental Illness help more than 48,000 people every year through their services, support groups and helplines that are open 24/7. Different helpline number are available for different areas of the UK: 0300 5000 927

Samaritans.org

Samaritans offer a safe and confidential place to talk. They can be contacted 24/7 on 116 123.

Appendix O - Study 1 – T4 Questionnaire

This survey will assess how you have been feeling generally over the last few weeks and month and will cover topics such as body satisfaction and psychological well-being. At the end of each survey there will be an open text box where you can expand on your responses if you have experienced any extenuating circumstances i.e. change in employment, accommodation or traumatic family event etc. This survey should take about 10-15 minutes to complete. If you have an issues or concerns about the study please use the contact details below.

(PSS)

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate by circling how often you felt or thought a certain way.

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

		0	1	2	3	4
1	In the last month, how often have you been upset because of something that happened unexpectedly?					
2	In the last month, how often have you felt that you were unable to control the important things in your life?					
3	In the last month, how often have you felt nervous and "stressed"?					
4	In the last month, how often have you felt confident about your ability to handle your personal problems?					
5	In the last month, how often have you felt that things were going your way?					
6	In the last month, how often have you found that you could not cope with all the things that you had to do?					
7	In the last month, how often have you been able to control irritations in your life?					

8	In the last month, how often have you felt that you were on top of things?					
9	In the last month, how often have you been angered because of things that were outside of your control?					
10	In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?					

(PANAS)

Indicate the extent you have felt this way **over the past week**

1= Very slightly or not at all, 2= A little, 3=Moderately, 4= Quite a bit, 5=Extremely

		1	2	3	4	5
1	Interested					
2	Distressed					
3	Excited					
4	Upset					
5	Strong					
6	Guilty					
7	Scared					
8	Hostile					
9	Enthusiastic					
10	Proud					
11	Irritable					
12	Alert					
13	Ashamed					
14	Inspired					
15	Nervous					
16	Determined					
17						

	Attentive					
18	Jittery					
19	Active					
20	Afraid					

(SWEMWBS)

Below are some statements about feelings and thoughts.

Please tick the box that best describes your experience of

each **over the last 2 weeks**

1= None of the time, 2= Rarely, 3= Some of the time, 4= Often, 5= All of the time

Statements	None of the time	Rarely	Some of the time	Often	All of the time
I've been feeling optimistic about the future	1	2	3	4	5
I've been feeling useful	1	2	3	4	5
I've been feeling relaxed	1	2	3	4	5
I've been dealing with problems well	1	2	3	4	5
I've been thinking clearly	1	2	3	4	5
I've been feeling close to other people	1	2	3	4	5
I've been able to make up my own	1	2	3	4	5

mind about things					

(CES-D)

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you've felt this way during the **past week.** Respond to all items.

	During the past week….	Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)
1	I was bothered by things that usually don't bother me				
2	I did not feel like eating; my appetite was poor				
3	I felt that I could not shake off the blues even with help from my family				
4	I felt that I was just as good as other people				
5	I had trouble keeping my mind on what I was doing				
6	I felt depressed				
7	I felt that everything I did was an effort				
8	I felt hopeful about the future				
9	I thought my life had been a failure				
10	I felt fearful				
11	My sleep was restless				
12	I was happy				
13	I talked less than usual				
14					

	I felt lonely				
15	People were unfriendly				
16	I enjoyed life				
17	I had crying spells				
18	I felt sad				
19	I felt that people disliked me				
20	I could not "get going"				

(GAD-7)

Over the **last 2 weeks,** how often have you been bothered by the following problems?

		Not at all	Several Days	More than half of the days	Nearly every day
1	Feeling nervous, anxious or on edge	0	1	2	3
2	Not being able to stop or control worrying	0	1	2	3
3	Worrying too much about different things	0	1	2	3
4	Trouble relaxing	0	1	2	3
5	Being so restless that it is hard to sit still	0	1	2	3
6	Becoming easily annoyed or irritable	0	1	2	3
7	Feeling afraid as if something awful might happen	0	1	2	3

Please check the following

Health	Fair	Good	Very Good	Excellent
In general, how would you say your health has been in the past month				

(SCS-SF)

Please indicate how often you behave in the stated manner.

		Almost Never				Almost Always
1	When I fail at something important to me I become consumed by feelings of inadequacy	1	2	3	4	5
2	I try to be understanding and patient towards those aspects of my personality I don't like	1	2	3	4	5
3	When something painful happens I try to take a balanced view of the situation	1	2	3	4	5
4	When I'm feeling down, I tend to feel like most other people are probably happier than I am	1	2	3	4	5
5	I try to see my failings as part of the human condition	1	2	3	4	5
6	When I'm going through a very hard time, I give myself the caring and tenderness I need	1	2	3	4	5
7	When something upsets me I try to keep my emotions in balance	1	2	3	4	5

8	When I fail at something that's important to me, I tend to feel alone in my failure	1	2	3	4	5
9	When I'm feeling down I tend to obsess and fixate on everything that's wrong	1	2	3	4	5
10	When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people	1	2	3	4	5
11	I'm disapproving and judgmental about my own flaws and inadequacies	1	2	3	4	5
12	I'm intolerant and impatient towards those aspects of my personality I don't like	1	2	3	4	5

I have continued with this way of eating	YES	NO

If no, please state why	

Please expand on your responses or add any change in circumstance	

Please check the following

Activity	Got much worse	Got worse	Stayed the same	Improved a little	Much improved
Since starting the program my physical activity levels have	1	2	3	4	5

Please answer the following questions in as much detail as possible.

Q1. How have you found this way of eating since finishing the online program?
Q2. Is there anything that you would like to add?

Thank you for completing this questionnaire. If you feel that you have been effected in any way by the questions asked please do not hesitate to contact the people below or speak to your GP. Alternatively, participants are encouraged to utilise the Diabetes.co.uk forum specifically made for the research study which you will find through your personal account. Alternatively for enquiries about the research please contact Charlotte at Charlotte@diabetes.co.uk.

Mind.org.uk

Mind provide advice and support to empower anyone experiencing a mental health problem: 0300 123 3393

Rethink.org

Rethink Mental Illness help more than 48,000 people every year through their services, support groups and helplines that are open 24/7. Different helpline number are available for different areas of the UK: 0300 5000 927

Samaritans.org

Samaritans offer a safe and confidential place to talk. They can be contacted 24/7 on 116 123.

Appendix P - Study 1 - Debrief Information

Debrief Sheet

Thank you for taking part in this study. You may have found the study challenging at times but we hope that you may perhaps feel better with your health and mood.

What did we do?

In this study, all participants were randomly allocated to one of three groups. One group was asked to follow the Low Carbohydrate Program, the second group was asked to follow the Ketogenic Program and the third group was asked to continue their current way of eating as they were told they had been placed on a waiting list. The waiting list group became our comparison group.

We hoped to find out whether either of the diet programs had a positive effect on mental well-being but we are aware that this might not have been the case for everyone. We are hoping that you might have found improvements in your levels of stress, energy, anxiety, or depressive symptoms. Perhaps you might have even noticed changes in your sleep, how you care for yourself and your levels of self-compassion (how kind and caring you are to yourself when faced with challenges). Overall we hope you experienced some physical benefits as well as benefits to your overall health and outlook on life.

Other aims of the study were to see which diet showed the most improvements, (the Low Carbohydrate diet or the Ketogenic diet) and how easy they were to follow using the online system.

Why did we do this study?

There are a few previous studies which suggested that following a Low Carbohydrate or Ketogenic diet may be beneficial for both your physical and mental health. If the CARBS study shows significant improvements in mental well-being after following a diet lower in carbohydrates, it may be possible to use alterations in diet as a therapy for mental health issues alongside regular current treatments in the future.

A Ketogenic diet is a high fat, adequate protein, low carbohydrate diet. Due to the low amount of carbohydrates in the diet the body is made to break down stored fat and fat that is eaten to produce energy. Fat in the body is used as energy for most bodily functions and some fat is converted into "ketone bodies" which provide energy to the brain. This switches the body from a "sugar burner" to a "fat burner" and this usually occurs when people consume less than 50 grams of carbohydrates a day. A Low Carbohydrate diet is a high fat, adequate protein diet which is low in carbohydrates but not low enough to produce ketone bodies. A Low Carbohydrate diet is usually less than 150 grams of carbohydrates a day.

Current research into the influence of ketones suggest that they may protect the brain and may help alleviate the symptoms of depression and other illnesses, either physical or mental. Now that you have come to the end of the study we would like to thank you again for taking part and we will be in touch shortly with any updates and findings that we feel may benefit you. If you would like more information on these diets or would like some further reading please have a look at the links below:

https://www.amazon.co.uk/Keto-Clarity-Jimmy-Moore/dp/1628600071

https://www.dietdoctor.com/

Appendix Q - Study 1 - Questionnaire Quantitative Questions

For time point 1 (T1) the following quantitative questions were included.

1. In general, how would you say your health has been in the past month? (1=fair; 2=good; 3=very good; 4=excellent).

2. How often do you take part in sports or activities that are mildly energetic? (1=three times or more a week; 2=once or twice a week; 3=about once to three times a month; 4-never/hardly ever)

3. How often do you take part in sports or activities that are moderately energetic? (1=three times or more a week; 2=once or twice a week; 3=about once to three times a month; 4-never/hardly ever)

4. How often do you take part in sports or activities that are vigorous? (1=three times or more a week; 2=once or twice a week; 3=about once to three times a month; 4-never/hardly ever)

For time point 2 (T2) the following quantitative questions were included.

1. In general, how would you say your health has been in the past month? (1=fair; 2=good; 3=very good; 4=excellent)

2. Since starting the program, my physical activity levels have: (1=got much worse; 2=got worse; 3=stayed the same; 4=improved a little; 5=much improved)

3. I have cheated or felt the need to cheat on this program (1=none of the time; 2=rarely; 3=some of the time; 4=often; 5=all of the time)

4. Following this way of eating for me has been: (1=not difficult at all; 2=somewhat difficult; 3=very difficult; 4=extremely difficult)

5. I like how I feel with this way of eating (1=not at all; 2=a little; 3=somewhat; 4=a fair amount; 5=a lot)

6. I feel hungry with this way of eating (1=none of the time; 2=rarely; 3=some of the time; 4=often; 5=all of the time)

7. Sourcing the food for this way of eating is: (1=not difficult at all; 2=somewhat difficult; 3=very difficult; 4=extremely difficult)

8. How have you found this way of eating?

(1=very easy; 2=easy; 3=a bit difficult; 4=very difficult)

9. Would you recommend this way of eating to others?

(1=absolutely; 2=maybe; 3=not at all)

For time point 3 (T3) the questions from T2 were repeated with the inclusion of the following quantitative question to mark the end of the online intervention.

1. I will continue this way of eating

(1=high unlikely; 2=unlikely; 3=maybe; 4=likely; 5=high likely)

For time point 4 (T4) the following quantitative questions were included to mark the end of the research study.

1. Since starting the program my physical activity levels have:

(1=got much worse; 2=got worse; 3=stayed the same; 4=improved a little; 5=much improved)

2. In general, how would you say your health has been in the past month?

(1=fair; 2=good; 3=very good; 4=excellent)

3. I have continued with this way of eating

(0=no; 1=yes)

4. How have you found this way of eating since finishing the online program?

(1=very difficult; 2=difficult; 3=neither; 4=easy; 5=very easy)

Appendix R - Study 1 - Questionnaire Qualitative Questions

The qualitative questions added to each questionnaire are stated below.

For time point 2 (T2) end of wait list control the following open questions were included.

1. Is there anything that you would like to feedback to the researchers?
2. Please use the space below to expand on any of your previous responses, or add any changes in circumstances you think would be relevant (e.g., change in eating habits or changes to health status)

For time point 2 (T2) for intervention groups, the following open questions were included.

1. What do you like about this way of eating?
2. What do you dislike about this way of eating?
3. Please use the space below to expand on any of your previous responses or add any changes in circumstances you think would be relevant.

For time point 3 (T3) the following open questions were included.

1. What do you like about this way of eating?
2. What do you dislike about this way of eating?
3. How would you improve the online program?
4. Is there anything that you would like to feedback to the researchers?
5. Please use the space below to expand on any of your previous responses or add any changes in circumstances you think would be relevant.
6. Would you be happy to be contacted for a discussion on your experience of the program?

For time point 4 (T4) the following open questions were included.

1. Is there anything that you would like to add?
2. Please use the space below to expand on any of your previous responses or add any changes in circumstances you think would be relevant.

If participants stated that they have not continued this way of eating, the following question was asked:

1. Please state why you have not continued with this way of eating

Appendix S - Study 2 – Information Sheet

CARBS Study

Information Sheet

Researchers at the University of East London:
Erin Louise Bellamy (PhD Researcher – E.L.Bellamy@uel.ac.uk)
Dr. Kirstie Soar (Director of Studies)

Summary

Thank you so much for your help so far in the research on the impact of diet on mental health. One of the most important parts of the research is this final step of assessing why people drop out of dietary interventions, such as the one you signed up for last year. The following very brief questions (which take only 2 minutes to complete) will look at reasons why people dropped out of the dietary intervention that you started.

Your answers, along with answers to questions you provided in the initial stages of the dietary intervention research programme will help us to learn even better ways to carry out this research in the future. I understand that sticking to new diets and filling out questionnaires can be time consuming and that sometimes life gets in the way. Therefore, I would really appreciate your honest answers to these quick questions.

Confidentiality of the Data

Participants' confidentiality will be maintained unless a disclosure is made that indicates that the participant or someone else is at serious risk of harm.

All the questionnaire answers and data will taken from the surveys for analysis by the researcher. Once the study has finished, all data will be deleted from the Qualtrics

Survey Software. It will not be possible to identify individuals as all data will be looked at together as a large group.

All data generated in the course of the research will be retained and shared only where necessary in accordance with the University of East London's Data Protection Policy which can be found here: https://repository.uel.ac.uk/item/8448w. This will support associated research publications from the project. All data collected will be fully anonymised and no individual named data will be identifiable at any point.

Online data protection

The online version of these questionnaires has been constructed using Qualtrics software. All questionnaire responses will be email matched to previously completed baseline questionnaire data. Survey links (also known as secure survey links) have been used, giving Secure Sockets Layer (SSL) Encryption while a questionnaire is being completed. During the study data collected online will be stored on an EU-based server and will be subject to EU Data Protection acts. All online data will be completely destroyed following completion of data collection.

Disclaimer

Your participation in this study is entirely voluntary, and you are free to withdraw at any time during the research. Should you choose to withdraw from the programme you may do so without disadvantage to yourself and without any obligation to give a reason. Please note that your data can be withdrawn up to two weeks after the questionnaire is completed.

Questions

If you have questions about the research, please contact the researcher at E.L.Bellamy@uel.ac.uk

Appendix T - Study 2 – Consent Form

CARBS Study

Consent Form

Researchers at the University of East London:

Erin Louise Bellamy (PhD Researcher – E.L.Bellamy@uel.ac.uk)

Dr. Kirstie Soar (Director of Studies)

- I have read the information leaflet relating to the above study of research in which I have been asked to participate and have confirmed that I have read. The nature and purposes of the research have been explained to me, and I have had the opportunity to discuss the details and ask questions about this information.
- I understand what is being proposed and the procedures in which I will be involved have been explained to me. I have had the opportunity to download and print this information.
- I understand that my involvement in this study, and data from this research, will remain strictly confidential as far as possible. Only the researchers involved in the study will have access to the data.
- I understand that maintaining strict confidentiality is subject to the following limitation: Where possible, participants' confidentiality will be maintained unless a disclosure is made that indicates that the participant or someone else is at serious risk of harm. Such disclosures may be reported to the relevant authority.
- I understand that all of my information will be anonymized and that I will not be individually named at any point during the study, analysis or publications.
- I understand that some of my answers to questions may be stated in the final write up and publications but that they will be fully anonymized.

- Research findings will be written up in the form of publications for research journals in the field of Diabetes, Nutrition and Psychology. Findings will also be presented at conferences and written up into a final dissertation.
- It has been explained to me what will happen once the study has been completed. I understand that my participation in this study is entirely voluntary, and I am free to withdraw at any time during the research without disadvantage to myself and without being obliged to give any reason.
- I understand that my data can be withdrawn up to two weeks after the completion of this questionnaire.
- I understand that my data will support associated research publications from the project and that all data collected will be fully anonymised and my individual named data will not be identifiable at any point.
- If I still have questions about the way the research is conducted after speaking with the researcher at E.L.Bellamy@uel.ac.uk, I know I can contact the Research Integrity and Ethics Manager, Catherine Hitchens at researchethics@uel.ac.uk. Graduate School, EB 1.43. University of East London, Docklands campus, London, E16 2RD.
- I hereby freely and fully consent to participate in the study which has been fully explained to me and for the information obtained to be used in relevant research publications.

Appendix U - Study 2 – Email: Your Experience – My Research Study

Good morning,

Thank you for signing up to take part in my research study last year through Diabetes.co.uk.

I have one final request. Please could you answer some quick questions that will conclude my research?

Click Here: https://uelpsych.eu.qualtrics.com/jfe/form/SV_7TEtTzBqlb2LhVH

This brief questionnaire will cover reasons for dropping out of the research study. These questions will take approximately two minutes to complete.

The answers to this questionnaire will help to inform future research studies using these online dietary interventions.

Thanks in advance for your time and I wish you all the best.

Any questions, just let me know.

Appendix V - Study 2 – Email: Follow Up: Your Experience of My Research Study

Good morning,

Thank you for signing up to take part in my research study last year through Diabetes.co.uk.

I'm just following up on the email I sent a few weeks back. Please could you answer some quick questions that will conclude my research?

Click Here: https://uelpsych.eu.qualtrics.com/jfe/form/SV_7TEtTzBqlb2LhVH

This brief questionnaire will cover reasons for dropping out of the research study. These questions will take approximately two minutes to complete.

The answers to this questionnaire will help to inform future research studies using these online dietary interventions.

Thanks in advance for your time and I wish you all the best.

Any questions, just let me know.

Appendix W - Study 2 – Follow Up Questionnaire

Questionnaire

1. Consent form and Information Sheet
    a. I agree
    b. I do not agree (Skip to Q14)
2. Please enter the email address that you used for the CARBS study.
3. Did you complete the first questionnaire when you got access to your profile? (This is different to the screening questionnaire).
    a. Yes
    b. No
4. Did you complete the second questionnaire 6 weeks after starting?
    a. Yes
    b. No
5. How long did you follow your allocated diet for?
    a. I didn't start the allocated diet
    b. Less than a week
    c. 1-2 weeks
    d. 2-4 weeks
    e. 4-8 weeks
    f. 8-12 weeks
    g. 12 weeks or more
    h. I'm still following the diet / a version of the diet
6. Did you watch the educational videos on the platform?
    a. Yes – All of them
    b. Yes – Some of them
    c. No – None of them
7. Did you find these videos useful / helpful?
    a. Yes
    b. No
8. Did you track your food?
    a. Yes – I tracked my food for less than 4 weeks
    b. Yes – I tracked my food for more than 4 weeks
    c. No – I did not track my food
9. Which app if any did you use to track your food?

a. Diabetes.co.uk Profile
b. MyFitnessPal
c. Carbs and Cals
d. Cronometer
e. Fitbit Health
f. Other App (Add here)
g. I did not track my food on an app

10. What is the MAIN reason why you dropped out of the study?
    a. I found the diet difficult to stick to
    b. I didn't find the platform helpful
    c. I experienced side effects
    d. My circumstances changed (pregnancy, sickness etc.)
    e. I didn't feel good following the diet
    f. I continued the diet but not the study
    g. I found it expensive
    h. I didn't know what to eat
    i. I found social events difficult
    j. I worried about eating higher levels of fat
    k. Other (Add here)
11. What other reasons stopped you from continuing the study? (You can choose more than one answer)
    a. I found the diet difficult to stick to
    b. I didn't find the platform helpful
    c. I experienced side effects
    d. My circumstances changed (pregnancy, sickness etc.)
    e. I didn't feel good following the diet
    f. I continued the diet but not the study
    g. I found it expensive
    h. I didn't know what to eat
    i. I found social events difficult
    j. I worried about eating higher levels of fat
    k. Other (Add here)
    l. No other reason
12. Would you like to restart the study?
    a. Yes – I would like to restart the study
    b. No – I would not like to restart the study

13. Is there anything else you would like to share with the researcher?

End of Survey Message

Thank you - Your responses have been submitted

If you feel that you have been affected in any way by the questions asked please do not hesitate to contact the people below or speak to your GP.

Mind.org.uk
Mind provide advice and support to empower anyone experiencing a mental health problem: 0300 123 3393

Rethink.org
Rethink Mental Illness help more than 48,000 people every year through their services, support groups and helplines that are open 24/7. Different helpline number are available for different areas of the UK: 0300 5000 927

Samaritans.org
Samaritans offer a safe and confidential place to talk. They can be contacted 24/7 on 116 123.

Appendix X - Study 3 – Email: Your Experience of My Research

Dear X,

I hope this email finds you well.

A huge thank you for completing my diet study through Diabetes.co.uk last year. Your participation and feedback will help to push the nutrition science forward!

You agreed you would be happy to be contacted in the future to discuss your experience - can we arrange this - it won't take long - just a quick chat.

It would be great to chat about what you found tricky on the diet and your experience overall with the low hunger levels you mentioned.

This is important to me because your feedback on using the program will help me to improve it for people in the future.

Please have a look at the attached information sheet and let me know if you would be happy to have a chat with me!

I am happy to work around your schedule, evenings / weekends etc.

Just hit reply to this email and let me know.

Really looking forward to hearing from you.

University of East London

Consent to Participate in a Research Study
The purpose of this letter is to provide you with the information that you need to consider in deciding whether to participate in this study.

Diabetes Digital Media ltd. (Diabetes.co.uk)
Technology House
Sir William Lyons Road
University of Warwick Science Park
Coventry
CV4 7EZ

Research Integrity
The University adheres to its responsibility to promote and support the highest standard of rigour and integrity in all aspects of research; observing the appropriate ethical, legal and professional frameworks.
The University is committed to preserving your dignity, rights, safety and wellbeing. Formal ethical approval for this study has been sought and granted by the University Research Ethics Committee.

The study is part of a PhD project by researcher, Erin Louise Bellamy (E.L.Bellamy@uel.ac.uk) under the supervision of Director of Studies, Dr Kirstie Soar (K.Soar@uel.ac.uk) through the University of East London, Stratford Campus, Water Lane, E15 4LZ. The study is in collaboration with Diabetes.co.uk.

CARBS Experience Interview

Information Sheet

Summary of the interview

This interview will be no longer than 20 minutes long and its purpose is to understand how you felt during the study and since its completion. It will provide a safe space to discuss both the effects of participating in the program as well as the program itself. These interviews will take place over Zoom to encourage discussion and sharing of experiences with the researcher. The information provided during this interview will add evidence in support or refute of the diet and online programs. It will explore how programs could be adapted to fit the needs and experiences of those who complete it. This may encourage further take up of the diet and may help the researcher to develop tools and supportive activities to improve completion rates for future participants.

Possible side effects

When expressing their emotions and experiences in this interview, you may experience mood changes when sharing your experience. This depends on the type of experience that you had during the study and the extent to which you found it easy or difficult to adhere to. If you do have ongoing concerns, then please don't hesitate to contact one of the services related to these listed below:

Contact details of external helplines

- Mind.org.uk – 0300 123 3393

Mind provide advice and support to empower anyone experiencing a mental health problem.

- Sane.org.uk – 0300 304 7000

Providing specialist mental health emotional support daily 4.30pm-10.30pm.

- Samaritans.org – 116 123

Samaritans offer a safe and confidential place to talk. They can be contacted 24/7.

To take part you will need to have:

- Completed 24 weeks of the CARBS study
- Have access to a computer or phone with internet
- Be happy to share your experience and take part in a discussion with the researcher

Confidentiality of the Data

This study will be in collaboration with Diabetes.co.uk who receive no funding from any external bodies. This study will be self-funded by the researcher.

Participants' confidentiality will be maintained, and pseudonyms will be used where necessary to provide anonymity to all participants.

All interviews will be audio recorded and transcribed within the University of East London. All audio recordings will be deleted once transcribed.

All the data will be securely stored in an encrypted format by the researchers and will only be accessible by the researchers. Individual quotes from the interview may be used in the reporting, but they will be anonymised, and all identifiable information will be removed.

The data will be collected, analysed and kept for a period of up to ten years before it is securely disposed of by the researcher. This is in keeping with the data protection terms and conditions of Diabetes.co.uk. All data generated in the course of the research will be retained in accordance with the University of East London's Data Protection Policy.

Disclaimer

Your participation in this study is entirely voluntary, and you are free to withdraw at any time during the research. Should you choose to withdraw from the program you may do so without disadvantage to yourself and without any obligation to give a reason. Please note that your interview data can be withdrawn up to two weeks after the group interview has taken place.

University Research Ethics Committee

If you have any concerns regarding the conduct of the research in which you are being asked to participate, please contact: Catherine Fieulleteau, Research Integrity and Ethics Manager, Graduate School, EB 1.43. University of East London, Docklands Campus, London E16 2RD

(Telephone: 020 8223 6683, Email: researchethics@uel.ac.uk)

CARBS Experience Interview

Consent Form

Researchers at the University of East London: Erin Louise Bellamy (PhD Researcher) and Dr. Kirstie Soar (Director of Studies)

Please tick as appropriate:

	YES	NO
I have read the information leaflet relating to the above study of research in which I have been asked to participate and have confirmed that I have read it. The nature and purposes of the research have been explained to me, and I have had the opportunity to discuss the details and ask questions about this information. I understand what is being proposed and the procedures in which I will be involved have been explained to me. I have had the opportunity to download and print this information.		
I understand that my involvement in this study, and particular data from this research, will remain strictly confidential as far as possible. Only the researchers involved in the study will have access to the data.		
I understand that maintaining strict confidentiality is subject to the following limitation: Where possible, participants' confidentiality will be maintained unless a disclosure is made that indicates that the participant or someone else is at serious risk of harm. Such disclosures may be reported to the relevant authority.		
I understand that all of my information will be anonymized and that I will not be individually named at any point during the study, analysis or publications.		
I understand that some of my answers to questions may be quoted in the final write up and publications but that they will be fully anonymized or provided an Alias.		
Research findings will be written up in the form of publications for research journals in the field of Diabetes, Nutrition and Psychology. Findings will also be presented at conferences and written up into a final dissertation.		
I am happy to be contacted for future research studies by the researchers or by Diabetes.co.uk (If you do not wish to be contacted in this way you may still take part)		
It has been explained to me what will happen once the study has been completed.		
I understand that my participation in this study is entirely voluntary, and I am free to withdraw at any time during the research without disadvantage to myself and without being obliged to give any reason. I understand that my data can be withdrawn up to two weeks after the final questionnaire.		
I hereby freely and fully consent to participate in the study which has been fully explained to me and for the information obtained to be used in relevant research publications.		

Participant's Name (BLOCK CAPITALS - as signature) .....

Investigator's Signature and Date .....

Appendix Z - Study 3 - Interview Schedule

CARBS Study: A qualitative study to explore participants experiences of the diet and online program

Interview Schedule: Group 1 or Group 2

Prompt: Any questions regarding confidentiality or anonymity etc.

Indicative Interview Questions:

To help me understand your experience, it would be helpful if you could briefly describe how you had been feeling psychologically / emotionally before starting this program

Prompts:

- What were reasons for joining the program
- How do you think diet played a part in how you felt
- What was your opinion of yourself

Please can you describe your journey on the diet

Prompts:

- How did you feel in the first few days
- What were the physical effects noted
- What were the mental/emotional effects noted
- How did these change as the weeks went on

How do you feel psychologically/emotionally since finishing the program?

Prompts:

- How do you think the diet affected your psychological well-being
- Better/Worse
- How has your mental state or mood changed

Thinking now of the online program, how did you find using it?

Prompts:

- Was it easy to use
- Was it easy to follow
- What would you change about the program or research?

Finally thinking about your overall experience of the diet change and program

Prompts:

- What was the most difficult part of this change?
- What was the most rewarding part of this change?

Participant number _____ : Demographic Questionnaire

1. Gender: Male ( ) Female ( )

2. Age: _____
3. Occupation? _____
4. Highest level of Educational achievement: _____
5. Ethnicity:
   White ( ) Black or Black British ( )

   Mixed ( ) Chinese ( )

   Asian ( ) Other (please specify)_____

Appendix AA - Study 3 - Debrief Information

Debrief Sheet

Thank you for taking part in this study. You may have found the study challenging at times, but we hope that you may perhaps feel better with your health and mood.

What did we do?

In this study, participants who had completed either the Low Carbohydrate Diet Program or the Ketogenic Diet Program were invited for a one on one interview with the researcher to discuss their experience.

We hoped to find out whether either of the diet programs had a positive effect on psychological well-being, but we are aware that this might not have been the case for everyone. We are hoping that you might have found improvements in your levels of stress, energy, anxiety, or depressive symptoms. Perhaps you might have even noticed changes in your sleep, how you care for yourself and your levels of self-compassion (how kind and caring you are to yourself when faced with challenges). Overall, we hope you experienced some physical benefits as well as benefits to your overall health and outlook on life.

Other aims of the study were to see which diet showed the most improvements, (the Low Carbohydrate diet or the Ketogenic diet) and how easy they were to follow using the online system.

Why did we do this interview?

There are a few previous studies which suggested that following a Low Carbohydrate or Ketogenic diet may be beneficial for both your physical and mental health. If the CARBS study shows significant improvements in mental well-being after following a diet lower in carbohydrates, it may be possible to use alterations in diet as a therapy for mental health issues alongside regular current treatments in the future.

Current research into the influence of ketones suggest that they may protect the brain and may help alleviate the symptoms of depression and other illnesses, either physical or mental.

This interview took place to understand how you felt during the study and since its completion. It provided a safe space to discuss common issues and share your experience with other participants and the researcher. The information provided during this interview will add anecdotal evidence in support or refute of the diet and online program.