“Watch and Wait” - Examining the potential impact of uncertainty in illness on the mental health of individuals with Chronic Lymphocytic Leukemia and Low Grade Lymphomas

S.N. O’Byrne

A thesis submitted for the degree of Doctorate in Clinical Psychology (D Clin Psych)

Department of Health and Social Care

University of Essex

April, 2018

Acknowledgements

It is a great pleasure to have the opportunity to thank all of the individuals who made this work possible, as this research project was truly a cumulative effort.

I would first like to thank both of my research supervisors, Dr. Susan McPherson and Dr. Frances Blumenfeld. Thank you for all of the time that you spent reading drafts and providing feedback and recommendations. Your insights were extremely helpful, and I have learned so much through the feedback process.

Secondly, I would like to extend my gratitude to Dr. Michael Hamblin and to all of the research nurses who work in the Hematology Unit at Colchester General Hospital. Dr. Hamblin, thank you for your support and for ensuring that this study got off the ground! To the research nurses, thank you for all of your work on my behalf, especially with regards to recruitment and administering the outcome measures. I would also like to thank the nursing staff for keeping me company while I inputted data, for offering me a cup of coffee, and for all of your kind words.

To my family and friends, whose constant support in all areas made the past three years truly special for me. I would particularly like to acknowledge my parents, Paul and Irene, and my wife, Chalice, whose love and encouragement provide me with a degree of confidence that is always invaluable. To my daughter, Alice, one day I hope you will come to realize that you not only inspired me, but motivated me to work harder and longer and to push myself when I felt I had no more energy to work, in hopes that one day this venture will afford you some of the remarkable opportunities that I have been given.

Finally, and most importantly, I would like to thank, Tina Hickey. Without your initial idea this venture would not have been possible. The initial concept for this research was yours alone and it was your tireless work and determination that allowed us to undertake this project. You were the driving force behind this research, and I will be eternally grateful to you for all of the work you did and the support you have provided me with over the past 3-years.

Table of Contents

4.0 Results Chapter

List of Tables

1.0 Abstract

Chronic lymphocytic leukemia (CLL) and non-localised low grade or indolent lymphomas (LGL) are two of the common cancers that individuals are diagnosed with in the UK. Both of these chronic illnesses are considered slow growing and these individuals are often diagnosed when one is not exhibiting any symptoms from the cancer. For a high proportion of individuals who are diagnosed with these forms of cancer, they are subject to a form of care known as "watch and wait". As conventional chemotherapy treatments do not cure the disease nor prolong survival, a policy of watch and wait is utilized until the patients become symptomatic from the disease. For those patients who have been given a diagnosis of CLL, the watch and wait approach will include periodic medical examinations and laboratory analysis to determine whether the disease is stable or beginning to progress. The goal is of course to maintain QOL by not administering unnecessary treatment rather than 'least invasive treatment'. Such an approach is due to the fact that the research has not evidenced a medical benefit for early intervention. Since being given a diagnosis of cancer and being told that there would be no immediate intervention may be contrasting to how an individual would conceptualize cancer, the researchers questioned the impact that such a diagnosis and form of care can have on the individual's well-being. Participants with a diagnosis of CLL or LGL were recruited to complete psychological questionnaires (uncertainty in illness, anxiety, depression posttraumatic stress). These questionnaires were administered 4 times over a 12-month period to determine the impact of the diagnosis and what being placed on watch and wait has on their psychological well-being. Results indicated that a high proportion of participants were above clinical cut-off at time-1, but that there was also not much group or individual change over the 6-month time period. Results also

highlighted that posttraumatic stress at time-1 was the strongest predictor of psychological distress at 6-months, and a number of strong relationships between the psychological variables were also found at time-1, following the participants' initial diagnosis. Although preliminary, the findings were not in keeping with initial hypotheses that psychological distress would decrease over time-1, as participants developed greater understanding and had less uncertainty about their illness as well as watch and wait as a form of care. The findings suggest that the there is an impact that such a diagnosis and form of care can have on an individual psychologically, and more research needs to be undertaken to understand this effect and how to better support these individuals with their diagnosis of cancer.

2.0 Introduction Chapter

2.1 Introduction Overview

The introduction chapter of this thesis provides important definitions, a systematic review of the literature, and the various aims and hypotheses of the research. Specifically, the introduction will attempt to provide the reader with an understanding of chronic lymphocytic leukemia (CLL) and low grade lymphoma (LGL) in terms of prevalence, incidence, causes, and different forms of intervention, including watch and wait. In addition, definitions of chronic illness and psychological constructs have been covered, specifically psychological constructs such as anxiety, depression, and trauma as they relate to those individuals who have a diagnosis of cancer. The chapter has also defined Mishel's theory of uncertainty in illness and considers how her theory has been applied to cancer research. Following the broader definition of terms, the chapter contains an analysis of the current literature in terms of uncertainty in illness, anxiety, depression and trauma and considers how these constructs have been investigated in people with CLL and LGL. The analysis also includes how Mishel's uncertainty in illness theory has been researched in individuals with other forms of cancer, as there were no papers from the literature that dealt with uncertainty in illness in individuals with CLL or LGL. A synthesized discussion of the current literature is provided as well as a methodological critique and, finally, the gaps in the current literature have been highlighted which provides a rationale as to why this research project has been undertaken

2.2 Chronic Lymphocytic Leukemia: Prevalence, Incidence, and Morbidity

Chronic Lymphocytic Leukemia (CLL) is the most common Leukemia in the western world and it accounts for a third of all leukemia diagnoses in the UK, with an overall prevalence estimated to be upwards of 20,000 (Else et al., 2012; Cancer Research UK, 2009). CLL occurs more frequently in men than in women; 90% of the individuals who are affected with CLL are over 50 years of age and the average age of initial diagnosis is approximately 65 years (Zent, Kyasa, Evans & Schichman, 2001; Holzner et al., 2004; Bhayat, Das-Gupta, Smith, McKeever & Hubbard, 2000). The cause of CLL is unknown and there has been no established links of a diagnosis of CLL to previous chemotherapy or radiation exposure, as can be seen with other forms of acute leukemia. There are also no clear connections to viral infection, nicotine use, or diet (Elphee, 2008). CLL is identified by an accumulation of lymphocytes within the peripheral blood, bone marrow, lymph nodes or tissue, and spleen, and these cells continue to grow and accumulate as they have "escaped" programmed cell death (Harris et al., 1990; Dighiero, 2003; Dighiero, 2005). Specifically, CLL begins in a type of lymphocyte called a B cell. In CLL, these B cells escape the body's mechanisms that control how long cells live and how they are able to multiply, which can result in the cells not working correctly and multiplying uncontrollably. These B cells that multiply in an uncontrolled manner are referred to as 'malignant B cells' and, over time, these malignant B cells can accumulate and disrupt the production of normal blood cells as they build up in the bloodstream, bone marrow, and lymph nodes (Else et al., 2012). Approximately 75% of patients are diagnosed with CLL following a routine blood count and, at the time of diagnosis, they may not have any symptoms that are commonly related to the diagnosis (Matutes et al., 1994; Kaufman, Rubin & Rai, 2009).

Throughout the course of this chronic illness, one-third of those diagnosed with CLL will never require any form of treatment; one third will require an intervention during the time they have the disease; and the final third, who present with symptoms, will require an immediate intervention at the time of diagnosis (Dighiero & Binet, 2000; Dighiero, 2003). However, for those individuals who will eventually require an intervention, symptoms tend to develop slowly and initial symptoms may include weight loss, swollen lymph nodes, fever and night sweats, excessive bruising, fatigue, weakness, shortness of breath or more frequent infections (Cheson et al., 1996; Cancer Research UK, 2009). Aside from CLL, the study will also be recruiting individuals who have a diagnosis of low grade lymphoma and who have also been placed on the watch and wait pathway.

2.3 Low Grade Lymphomas: Prevalence Incidence and Morbidity

Lymphomas are solid tumors of the immune system. Hodgkin's lymphoma accounts for about 10% of all lymphomas and the remaining 90% are referred to as non-Hodgkin lymphoma. Non-Hodgkin lymphomas have a wide range of clinical features at presentation and the course of lymphoma can vary based on the rate of growth. Non-Hodgkin’s low grade lymphomas or indolent low grade - Lymphomas (LGL) tend to progress slowly and much like CLL, patients are often not symptomatic early in the course of the disease (Cheson et al., 2007; Cancer Research UK, 2008). For the purposes of this research, only individuals who have a diagnosis of non-localized indolent non Hodgkins lymphoma will be under study. The primary difference between those patients with a diagnosis of CLL and LGL is that the malignant B cell will typically proliferate preferentially in the lymph nodes rather than blood (Cheson et al., 2007).

Two-thirds of the patients who are initially diagnosed with the disease are over the age of 60; the disease occurs equally in both men and women. Unlike CLL, there are more established risk factors for the onset of non-Hodgkin lymphoma and the most common risk factor is immune-suppression. (Horning & Rosenberg, 1984; Shakland, Armitage & Hancock, 2012). Also, whilst lymphoma can be seen in immune suppressed patients the vast majority of low grade lymphoma cases are idiopathic.

2.4 Watch and Wait - Chronic Lymphocytic Leukemia (CLL) or Low Grade Lymphoma (LGL)

As outlined above, after receiving a diagnosis of CLL or LGL, approximately one-third of patients will receive some form of direct intervention to deal with the illness (generally immunochemotherapy but radiotherapy for some localized LGLs). However, the remaining two-thirds of patients who do not require an immediate intervention are given the initial diagnosis of CLL and then are subject to an approach of "watch and wait". It has been determined that, as conventional chemotherapy treatments do not cure the disease, a policy of watch and wait is utilized until the patients become symptomatic from the disease (Spaner et al., 2005; Binet et al., 2006).

For those patients who have been given a diagnosis of CLL, the watch and wait approach will include periodic assessment to determine whether the disease is stable or beginning to progress. Features that would suggest progression of the disease include rapid increase in the number of lymphocytes in the blood, a decrease in the overall number of platelets, an increase in the size of the spleen or lymph nodes, worsening anemia, and other symptoms, such as weight loss, fatigue, fever, etc. (Spaner et al., 2005; Spaner et al., 2007). The watch and wait approach is based on research that suggests immediate or

early treatment of patients with a ‘low or intermediate level’ of the disease does not prolong the life of the patient (Dighiero et al., 1998; Tam et al., 2014). CLL is an extremely heterogeneous disease and some patients can live for decades without any need for intervention; therefore, the goal of therapy for these patients is to maintain the highest quality of life (QoL) and avoid unnecessary treatment (Gribben, 2010). For clinicians to deviate from this watch and wait approach, the research would need to demonstrate either the benefits of earlier medical intervention (Hallek & German, 2005; Dighiero & Binet, 2010).

Similarly, to CLL, many of the patients who are diagnosed with LGL are asymptomatic at the time of diagnosis and again similar to CLL, these patients are normally subject to the approach of watch and wait (Ardeshna et al., 2003; Armitage & Longo, 2016). In the past, different approaches have been used to treat these individuals who have been given the diagnosis of non-localized LGL; to date, none of these initial interventions have proven to result in a ‘long-term disease free’ outcome (Linch, 2001). The inability of either chemotherapy, even if combined with radiotherapy, to achieve a lasting cure has led researchers to question whether there is a need to immediately treat patients with LGL using such an aggressive intervention especially if there are no “distressing symptoms or life-threatening organ impairment” (Ardeshna et al., 2003; El-Galaly et al., 2015). Much like CLL, the research does not indicate an overwhelming positive impact for immediate treatment; the patient’s QoL needs to be considered and it is deemed more prudent to place the patients on watch and wait until they become symptomatic from the disease (Horning & Rosenberg, 1994; Horning, 2000). Although it may seem perplexing to these individuals who are given the diagnosis of CLL or LGL, the main benefit for

these patients on watch and wait is that they are not exposed to a serious form of treatment before it is deemed necessary. Such an approach may seem counterintuitive to individuals in westernized cultures and to those who have just received a diagnoses of CLL or LGL in that the western approach to illnesses is to deal with it before the disease becomes too aggressive. Since the majority of individuals who have just received a diagnosis of CLL or LGL will not have any understanding of the research, and why early intervention may not result in an improved outcome for them, watch and wait can possibly lead to a degree of confusion, distress and uncertainty.

2.5 Chronic Illness

Both CLL and LGL are considered to be 'chronic illnesses' in that they are both an illness that an individual may have for a prolonged period of time and one does not spontaneously remit; and they are rarely cured completely (Centers for Disease Control and Prevention, 2003). As stated in the above definition, such chronic conditions such as CLL and most LGLs are incurable and the goal of any form of medical treatment is to avoid unnecessary treatment but when treatment does become necessary the aims are to induce durable remissions prolong survival and reduce the level of suffering. The World Health Organization (WHO) has stated that the burden of chronic diseases will be one of the greatest challenges that will face health care systems globally (WHO, 2005; Lupkin & Karsen, 2006). Increasing life expectancies, "modernization of lifestyle", with an increasing exposure to different chronic disease risk factors, and the ever-improving ability of medical interventions to treat individuals who would have historically died, have all combined to change the burden of disease that are currently having a great impact on health-care systems (Wagner, Austin, Davis, Hindmarsh, Schaefer & Bonomi,

2001; Nolte & McKee 2008). Many of these chronic conditions (stroke, HIV, cancer, asthma, etc.) will require a "complex response" over an extended period of time which will most likely require involvement from a number of different health professionals (Wagner, Austin, Von Korff, 1996; Bodenheimer, Wagner & Grumbach, 2002; Unwin, Jordan & Bonita, 2004).

As the prevalence and incidence of chronic diseases have been increasing globally, due to the aforementioned factors, research has also increased into the concept of QoL, for those individuals suffering with a chronic disease. The WHO defines QoL for an individual as:

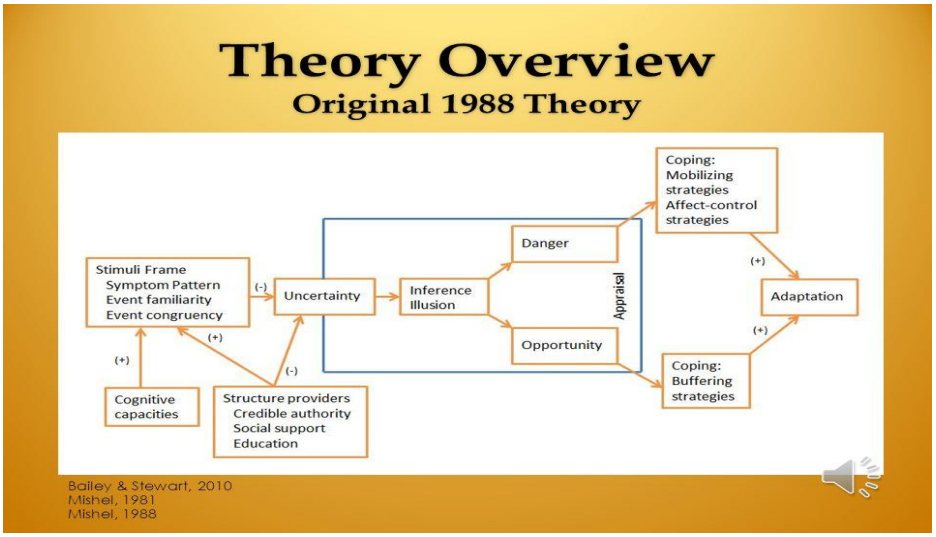
> Perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns QoL is the feeling of overall life satisfaction, as determined by the mentally alert individual whose life is being evaluated" (WHO, 1996).

A common factor that would impact on an individual's QoL could be the level of uncertainty with regards to the illness. Such a degree of uncertainty can be understood in terms of the individual's future health and the prognosis of their illness, what the symptoms may mean when a diagnosis cannot readily be made, and the speed of how quickly the illness may progress (Mishel, 1999).

2.6 Uncertainty in Illness

Mishel's 1988 paper *Finding Meaning: Antecedents of Uncertainty in Illness,* put forth a theory about how an individual interprets an illness-related event. Mishel's theory postulates that uncertainty in illness is defined as a cognitive state resulting from insufficient cues or knowledge; specifically, an individual is unable to form meaning to

the illness or illness-related event. The theory (1988) proposed that the ability of the individual to tolerate or cope with uncertainty could allow the individual to remain hopeful and decrease their level of anxiety or, conversely, the inability for an individual to manage uncertainty as it related to their illness can lead to an increase in an individual's level of anxiety and lower one's mood (Mishel & Braden, 1988). Mishel's uncertainty in illness theory was initially influenced by cognitive psychologists (Bower, 1978; Shalit, 1977) who conceptualized the construct of uncertainty as being a cognitive stressor for an individual and by (Budner, 1962) who described "ambiguous, novel, or complex stimuli" as being sources of uncertainty (Smith, 2013). In addition, the original uncertainty in illness model comprised four distinct, yet connected forms: firstly, a level of ambiguity concerning the state of the illness; secondly, the degree of complexity regarding the treatment of the illness and the overall system of care that one finds oneself in; thirdly, a lack of information regarding the diagnosis or seriousness of the illness; and finally, the unpredictability with regards to the course of the disease or the initial prognosis (Mishel, Hottstetter, King & Graham, 1984).



Within the theory, there are two appraisal processes that the individual makes in regards to the above four different forms and the significance that is placed on the uncertainty: inference and illusion. Inference relates to the evaluation of uncertainty based on the examples the individual can draw upon from similar situations. Similarly, to what was highlighted previously, if the inferences are seen as positive, the uncertainty may be appraised as an opportunity. If the inferences are viewed to be 'threatening', then the uncertainty will be understood as being a danger. Secondly, illusion refers to the construction of beliefs that have an overall positive outlook. Due to the vague and nebulous nature of uncertainty, the illness-related events could be formed into an illusion that would indicate a positive outcome. Illusion is only used when the illness has a negative outlook or downward trajectory; wherein, any uncertainty the individual encounters may be understood and translated into a positive (Mishel, 1984; Mishel & Braden, 1988; Mishel, 1990; Mishel, Braden, Grant & Sorenson, 1991).

Mishel's initial research in regards to her uncertainty in illness construct and the theoretical underpinnings that she developed primarily focused on those individuals who were dealing with the acute phase of illness, or when their health was on a clear downward trajectory (Mishel, 1984; Mishel & Clayton, 2008). The initial focus of her theory did not address the experience of those people who were living with continuing, constant uncertainty as a result of having a chronic disease. The original theory postulates that the appraisal of uncertainty as an opportunity would only occur when there is a clear negative outcome. Essentially, the theory is highlighting something that is logical: when the outcome is certainly a negative then uncertainty would be a more 'preferable state' (Mishel, 1990). However, there were conflicting findings (King &

Mishel, 1986; Mishel & Murdaugh, 1987; Mishel, 1988b), which led Mishel to re-conceptualize the theory in one specific area: that is when an individual is suffering from a chronic illness with a long-term downward trajectory. The re-conceptualized theory highlighted that if one is dealing with a chronic illness with a downward trajectory, the individual may shift from the initial uncertainty experienced following diagnosis to a point where uncertainty becomes the "foundation within which the person's sense of order is constructed". Therefore, when it is thought that the chronic illness will have a negative outcome, the individual may reformulate their thinking and use uncertainty as a protective factor, hoping for a more positive outcome in relation to their chronic illness (Mishel, 1990, McCorkmick, 2002; Neville, 2003). Although not a major departure from the original theory, it is an important addition nonetheless, as it considers those patients who are dealing with a chronic condition.

Since Mishel's seminal work, research has been conducted using her theory in an attempt to understand how individuals are able to manage and interpret diseases such as cancer, where the outcome of the disease may be uncertain for the patient (Mishel & Sorenson, 1991; Clayton, Mishel & Belyea, 2006; Bailey, Wallace & Mishel, 2008; Suzuki, 2012). Specifically, research has been conducted in various cancer related illnesses to examine the relationship of how an individual's uncertainty in relation to their illness can have an impact on the individual's psychological well-being (Nelson, 1996; Mishel et al., 2002; Bailey, Mishel, Beylea, Stewart & Mohler, 2004; Wellam & Degnar, 2007).

2.7 Psychological Constructs and Cancer

2.7.1 Anxiety and Depression

There has been much research undertaken to attempt to understand the impact of cancer on an individual's mental health. Specifically, research has examined the level of anxiety and depression that an individual experiences following a diagnosis of cancer, as well as a large number of intervention type studies to support the individual with mental health difficulties that may be associated with a cancer diagnosis (Sheard & Maguire, 1999; Osborne, Demoncada & Fuererstein, 2006). Recent estimates give the prevalence to be between 15 – 40% of patients who have been diagnosed with cancer will have symptoms of anxiety and low mood, which will have an impact on their overall functioning (Massie & Holland, 1990; Parle et al, 1996). The research also indicates that even for those individuals who have been "ostensibly cured" of cancer, the rates of anxiety and depression are higher than those individuals in the general population (Linden et al., 2012). It is also important to note that research on anxiety and depression in relation to cancer has highlighted that individuals suffering from mental health difficulties as a result of the cancer diagnosis tend to have longer hospitalization, higher mortality, and a decreased level of overall emotional well-being (Prieto et al., 2002; Pinquart & Duberstein, 2010; Reich, Lesur, & Perdrizet- Chevallier, 2008). There has also been research done to understand the mechanisms or thinking behind the distress associated with such a medical diagnosis. For instance, the perception of cancer as a threat is an important aspect in understanding anxiety and low mood; as the disease progresses, the threat as related to the illness becomes more serious and more debilitating and therefore and the individual's level of anxiety and low mood will decrease (Harrison & Maguire, 1994; Stark & House, 2000). Aside from perception of cancer as threat, the treatment for

cancer that one undergoes can be understood as being a serious contributor to emotional distress. Traditional treatments for cancer offer both negatives and positives and there can of course be a high degree of physical pain from the process of treatment (Loge, Abrahamsen, Ekeberg, Hannisdal & Kaasa, 1997; Stark & House, 2000). However, although the aforementioned factors are important in understanding the role cancer can play in relation to one's mental health, it is a disease that has a tremendous impact on the individual and the distress that it can cause a patient is related to the meaning that the individual associates with his or her diagnosis. Again, as there is an individual element in regards to the type of cancer, course of the disease, how the cancer is controlled or treated, overall consequences, and how one identifies with the illness, the diagnosis of cancer is truly related to the meaning the individual prescribes to the disease (Lazarus, 1993).

2.7.2 Trauma and Older Adult Mental Health Estimates

As a diagnosis, cancer can be understood as a traumatic event. Although, in comparison to psychological constructs such as anxiety and depression, there is not as much research on the psychological concept of traumatic stress as it relates to receiving a diagnosis of cancer. Systematic reviews have placed the estimated incidence rate of cancer related post-traumatic stress to be between 3 – 22%, wherein individual's rate the cancer diagnosis and the subsequent treatment as being the major traumatic stressor that is impacting on their mental health (Alter et al., 1996; Andrykowski, Cordova, Studts, & Miller,1998; Smith, Redd, Peyser & Vogl, 1999; Abbey, Thompson, Hickish & Heathcote, 2014). There have been a number of studies that have attempted to determine the factors that mediate an individual's vulnerability to cancer related post-traumatic

stress. A number of the factors that have been identified as playing a role are as follows: "lower social economic status, educational and intelligence level, gender, social support, and prior individual or familial psychological difficulties" (Thomson, Ecclestone & Hickish, 2001; Kangas et al., 2002; Girgis, Lambert, Johnson, Waller & Currow, 2012). There is also research to support the idea that a number of the aspects that lead to a level of vulnerability for developing cancer related post-traumatic stress also predispose individuals to receiving a diagnosis of cancer. For instance, lower socioeconomic status, excessive smoking, or alcohol use, may increase the likelihood of an individual developing cancer and also may predispose them to be more vulnerable to post-traumatic stress (Hoffman & Saski, 1997; Akechi et al., 2004). A framework that has been posited in relation to one developing post-traumatic stress following a diagnosis of cancer suggests that an individual diagnosed with cancer may be at risk of developing severe stress reactions because the individual has had to deal with a serious stressor for an extended period of time. Specifically, a diagnosis of cancer may disrupt one's pre-existing ideas, as they related to personal well-being and, if the course of the cancer is uncertain, one may not be able to develop thoughts of safety that would possibly be helpful in counteracting negative cognitions associated with one's physical well-being and safety (Kangas et al., 2002; Mehnert, Berg, Henrich & Herschbach, 2009; Whitaker, Watson & Brewin, 2009). In addition to threats to one's pre-existing ideas about safety, research has highlighted an avoidance or denial that is common in those who receive a diagnosis of cancer, which may impact on the "emotional processing" of the traumatic event (Wool, 1998; Amir & Ramati, 2002). As avoidance is known to be a tenant of post-traumatic stress, the avoidance in relation to coming to terms with a diagnosis of cancer may limit "activation of aversive memories" associated with diagnosis, which may also

lead to difficulty with acceptance and facing the memories associated with the diagnosis and the treatment (Brewin et al., 1996; Cordova, Studts, Hann, Jacobsen & Andrykowski, 2000; Kangas et al., 2002). In summary, a diagnosis of cancer can have a traumatic impact on the individual. It is therefore important to conduct research that betters our understanding around cancer related traumatic stress in order to provide those diagnosed with cancer a greater level of informed support.

It is important to also provide context in regards to mental health difficulties for those older adults who may also receive a diagnosis of cancer. A recent systemic review attempted to determine the prevalence of anxiety difficulties in a population of older adults (> 60 years old). The review found that the prevalence of older adults who suffer from mental health difficulties related to anxiety (diagnosis of anxiety disorder) in community samples ranged from 1.2% to 15%. In clinical settings, the range of anxiety related difficulties was higher, as one would expect 2% - 28% (Bryant, Jackson & Ames, 2007). Another review examined the rates for individuals who would have a diagnosis of major depression in older adult populations (65 – 100 years old). The results from the study found that individuals who would meet criteria for such a diagnosis was approximately 4% in women and 2.5% in men. In addition, it was also found that the rates of other mental health illnesses related to depression were surprisingly low, and the combined point prevalence of both men and women was found to be 1.6% (Steffens et al., 2000). Finally, as it relates to trauma, the data is not as strong or has not been a widely studied. One study examined PTSD diagnosis and difficulties associated with PTSD in older adults (> 60 years old). The study cites the difficulty in finding prevalence estimates, as often PTSD is “not recognized or misdiagnosed”. However, the current

study found prevalence estimates to be 1% for those older adults with a diagnosis of PTSD and "sub threshold PTSD" at 13% (van Zelst et al., 2003).

2.8 Literature Review Search

A review was conducted to determine whether a relationship exists between uncertainty in illness and psychological well-being (anxiety, depression, and trauma) in individuals with a diagnosis of CLL or LGL.

2.9 Method of Search

Searches were carried out using the major psychological and medical research databases which included: Psych Articles, Psych Info, Medline, CINHAL, E-Journals. In addition, the majority of the reference lists from many of the initial relevant articles identified were searched in order to find additional articles in the area of interest.

Table 1 highlights the search terms employed and the number of articles identified for the research papers that explored the relationship between uncertainty in illness in individuals with a diagnosis CLL or LGL. Table 2 highlights the search terms employed and the number of articles identified for the research papers that examined psychological constructs associated with mental health in individuals with CLL or LGL.

2.10 Data Extraction

Figure 1 illustrates how many studies were removed at each stage of the process. In terms of critical appraisal tools, parts of the Downs and Black (1998) tool were used to assist in determining the methodological quality of the studies that were identified.

2.11 Results

Overall, 16 studies met the inclusion criteria for more detailed examination. The studies that were selected for further review were completed in a number of different countries and included a number of different cancer diagnosis in relation to uncertainty in illness. Of the 16 studies selected, 4 of the studies were of longitudinal design and 12 were of cross-sectional design, with outcome measures being completed at one single time point. It is also important to note that while completing the above search, there were no studies that directly examine Mishel's theory of uncertainty in illness with patients who have a diagnosis of CLL or LGL. Therefore, it was important to expand the search as it relates to uncertainty in illness to other forms of cancer, in order get a better understanding of how uncertainty in illness has been researched in other cancer-related diseases to inform the current study. All of the studies that met the inclusion criteria can be reviewed in Table 3.

2.12 Systematic Search: The Impact of a Diagnosis of Chronic Lymphocytic Leukemia or Low Grade Lymphoma on an Individual's Mental Health

Table 1: *Uncertainty in Illness and Chronic Lymphocytic Leukemia or Low Grade Lymphoma*

Search Number	Search Term	CINHAL Complete	Psych Info	Psych Article	MEDLINE
1	"Uncertainty in illness" AND "Chronic Lymphocytic Leukemia"	1	0	0	12
2	"Uncertainty in illness" AND "CLL"	1	0	0	16
3	"Uncertainty in illness" AND "Low Grade Lymphoma"	0	0	0	0
4	"Uncertainty in illness" AND "Indolent Lymphoma"	1	0	0	0
5	Uncertainty in illness" AND "Cancer"	209	176	86	1
6	"Mishel" AND Cancer	128	99	0	85
7	"Mishel" and "CLL"	0	0	0	0
8	"Mishel" and "Indolent Lymphoma"	1	0	0	0

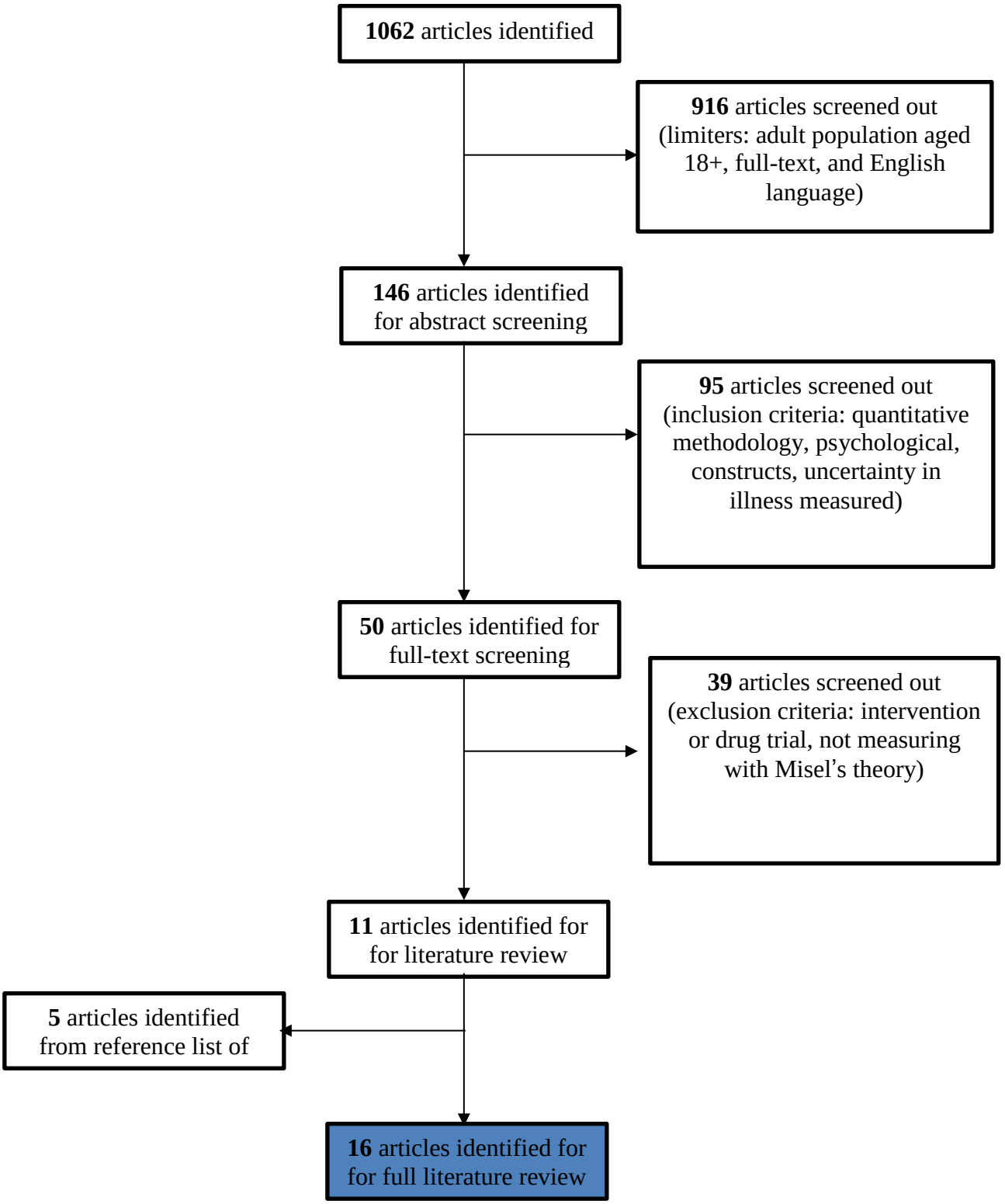
Table 2: *Anxiety, Depression and Trauma in Chronic Lymphocytic Leukemia or Low Grade Lymphoma*

Search Number	Search Term	CINHAL Complete	Psych Info	Psych Article	MEDLINE
1	"CLL" AND "Anx*" and "Depre"	7	5	0	9
2	"Indolent Lymphoma" AND "Anx*" AND "Depre"	2	0	0	0
3	"Low Grade Lymphoma" AND "ANX" AND "Depre"	10	7	0	26
4	"CLL" AND "Trau*"	3	3	0	18
5	"Low grade lymphoma" AND "Trau*"	1	0	0	10
6	"CLL" AND "PTSD" OR "POST TRAUMATIC STRESS DISORDER"	0	0	0	2
7	""Low Grade Lymphoma" AND "PTSD" OR "POST TRAUMATIC STRESS DISORDER"	0	0	0	1

Combined results (duplicates removed) = 1,062

Search Limiters and Expanders	Justification
English Language	Translation unavailable
Journal articles	Accessible empirical evidence wanted
Search within full-text	Identify full range of available research
Inclusion Criteria	**Justification**
Quantitative methodology	Methods used in current research
Psychological constructs (uncertainty in illness, anxiety, depression and trauma)	Constructs measuring in current research
Mishel's uncertainty in illness	Not general uncertainty but related to having a disease (cancer)
Exclusion Criteria	**Justification**
Studies measuring impact of psychological Intervention studies	Do not want intervention interfere with psychological constructs
Studies measuring impact of drug trials or surgical intervention	Drugs interfering or surgery with measuring of psychological constructs
Individuals with aggressive lymphoma as opposed to indolent or low grade lymphoma	Different form of LGL, required treatment and more physically debilitating.

2.13 Figure 1:
Search Diagram



2.14 Table 3*: Studies Investigating Relationships Between Cancer, Uncertainty in Illness; Psychological Well-Being; and Watch and Wait*

Study	Design	Sample	Outcome Measures	Statistical Analysis	Results
1.Geffen, Blaustein, Amir & Cohen	Case Control Study	*N* = 36 LGL *N* = 44 controls who had diagnosis of PTSD	PTSD Inventory SF – 36 HRQOL	Chi-square analysis Pearson correlation MANCOVA	Both groups correlated with lower QoL Significant increase in hyper arousal scale in the LGL group LGL group had significant lower physical health than LGL group, as measured by QoL scale
2. Hall, Mishel & Germino, 2014	Cross - Sectional Questionnaire study	*N* = 313 breast cancer survivors 2 – 4 Years Post Treatment Mean age 66	MIUS, PANAS, ISI	Hierarchical regression analyses controlled for relevant sociodemographic variables.	Cancer-related uncertainty was significantly associated with more self-reported fatigue, insomnia, negative affect, and less positive affect.
3. Holtzer – Goor et al., 2015	Longitudinal	Patients with diagnosis of CLL receiving treatment and on watch an wait General Population	EORTC QLQ-C30, EQ-5D	Not clearly specified	Patients with CLL worse than general population in fatigue and role function Active treatment worse HRQOL than those on watch and wait.
4. Kazer et al., 2012	Longitudinal Follow-up Design Following treatment of cancer 48, 60 and 72 months after	*N* = 338 men following treatment for prostate cancer	MUIS, SCA, FLAS	Relationships among measures were characterized by Spearman rank correlation coefficients (r).	Lower level of education related to greater level of uncertainty. Greater level of uncertainty was associated with a greater perception of danger. High uncertainty and perceived danger correlated

	treatment				with less satisfaction of treatment outcome. Younger patients experienced less uncertainty, but reported higher levels of perceived danger.
5. Kurita et al., 2014	Cross - Sectional Questionnaire study	*N = 49* Diagnosed with lung cancer at least 6-months Mean age = 64 71 % female	MIUS, PSS,	Regression analyses, adjusted for neuroticism.	Higher levels of stress and poorer emotional well being were associated with higher levels of intolerance of uncertainty and higher perceived illness-related. Depressive symptoms were associated with higher levels of intolerance of uncertainty. Avoidance mediated intolerance of uncertainty with depressive symptoms and emotional well-being only.
6. Levin et al., 2007	Cross - Sectional Questionnaire Study	*N* = 105 diagnosed with CLL on watch and wait or active treatment Mean age = 58	BAI, BDI, PHQ-9, SF-36	Repeated measures Anova T- tests	No significant difference between patients on watch and wait and active treatment. Younger patients had had levels of distress than older patients.
7. Liao et al., 2008	Longitudinal study 3 time points - Before biopsy After biopsy After	*N* = 127 women diagnosed with breast cancer or diagnosed with benign tumors. Mean age = 48	MIUS, SAI	Chi-square test used to see differences in demographic attributes Repeated-measures analysis of variance	The results showed that uncertainty and anxiety levels were significantly higher before than after diagnosis. At the 3 data collection

	diagnosis of breast cancer Questionnaire study			was used to examine changes in uncertainty and anxiety. Simple linear regressions and simultaneous multiple regressions were used to analyze predictive factors for uncertainty.	times, uncertainty and anxiety were significantly lower for participants diagnosed with benign tumors than for those with malignant diagnoses. Uncertainty and anxiety were positively correlated.
8. Lin Lin et al., 2013	Cross sectional Questionnaire Study	*N* = 186 men and women with primary brain tumor at different stages of illness trajectory	MIUS, PMS-SF, KPS	Structural equation modeling was used to explore correlations among variables	Results indicate those individuals earlier in the illness trajectory and who indicated lower functional status was associated with greater levels of uncertainty. Higher uncertainty and lower mood were associated with symptom severity related to the primary brain tumor.
9. Mast, 1998	Cross-sectional Questionnaire Descriptive Correlational	*N* = 109 women 1 – 6 years post treatment for breast cancer	MIUS, FRQ, GTUS, POMS	Descriptive, Correlational, Regression, ANOVA	Uncertainty in illness positively related to emotional distress. Uncertainty explained over half of the variance in regards to emotional distress.
10.Montgomery, Pocock, Titley & Llyod	Cross-sectional questionnaire study	*N* = 51 patients with CLL	HADS, MACS	Regression analysis	Individuals with higher levels of distress were deemed to have a more negative coping style. Associations were found between higher levels of anxiety and depression and

					level of satisfaction in regards to information the patient received.
11.Morrison et al., 2016	Cross - sectional questionnaire study	*N* = 112 patients on watch and wait for CLL	GAD, IES-R, CES-D	Multiple regression and moderation analysis.	Linear regression highlighted that greater symptom burden covaried with anxiety, depression and stress. Low social support, lower relationship satisfaction reported greater symptoms of burden and psychological difficulties.
12. Pashos et al., 2013	Cross-sectional Questionnaire Study	*N* = 1140 Diagnosis of CLL beginning of treatment Mean age = 69	BFI, FACT –LEU, EQ – 5D	ANOVA	Women reported greater fatigue than men.
13. Sammarco, 2001	Cross-sectional Questionnaire Study	*N* = 101 Diagnosis of breast cancer Under age 50	MIUS, SSQ, FPQoL – Cancer	Pearson product-moment correlation and stepwise multiple regression	Significant negative correlations were found between perceived social support and uncertainty, as well as time since diagnosis and treatment, Perceived social support and uncertainty accounted for a significant amount (27.2%) of variance of QoL,
14. Sammarco & Konecny, 2008	Cross – Sectional Descriptive correlational	*N* = 82 breast cancer survivors	SSQ, MIUS, FPQOL-Cancer III	Pearson product moment correlation and multiple regression.	Significant positive correlation was found between perceived social support and total QOL.

	Questionnaire Study			Post hoc data analysis analysis of variance (ANOVA) and an independent sample t test	A significant negative correlation was found between uncertainty and QOL. Social support predicted 15.1% of QOL variance, and uncertainty predicted 10.4% of additional QOL variance.
15.. Sammarco & Konecny, 2010	Cross - Sectional Descriptive correlational Questionnaire Study	*N* = 280 (182 Caucasian, 98 Latina)	MIUS, FPQOL-Cancer III, SSQ	Chi – square analysis Independent sample t test	Caucasian women reported higher levels of QoL, perceived social support and lower levels of uncertainty. Mental health difficulties and lower level of education were noted as contributing factors in QoL.
16. Suzuki, 2012	Longitudinal Questionnaire Study 2 Time points – pre treatment and 6 weeks after treatment	*N* = 52 adults newly diagnosed with head and neck cancer pre treatment	MIUS, FACT-H/N, PICS	Multivariate analyses Regression Analysis	Post-treatment QOL was lower than pretreatment. QOL was associated with uncertainty at Time 1 and Time 2. Uncertainty and QOL at the time of pretreatment were predictors of post-treatment QOL.

MUIS, Mishel Uncertainty in Illness Scale; PANAS, Positive and Negative Affect Scale; ISI, Insomnia Severity Index; PSS, Perceived Stress Scale; IES, Impact of Event Scale; IUS, Intolerance of Uncertainty Scale; EPQ – R, Eysenck Personality Questionnaire – Revised; SAI, State Anxiety Inventory; CWS, Cancer Worry Scale; HADS, Hospital Anxiety and Depression Scale; SSQ, Social Support Questionnaire; FPQOL – Cancer III, Fearran & Power QoL Questionnaire – Cancer III; SCA, Service Satisfaction Questionnaire; FLAS, Folkman & Lazarus Appraisal Scale; EORTC QLQ-C30, European Oranization of Reseach and Treatment of Cancer QoL; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; SF-36, Standard Form Health Survey; PHQ-9, Patient Health Questionnaire – 9; BFI, Brief Fatigue Inventory; EQ-5D, General Health Related

QoL; FACT – Leu, Functional Assessment of Cancer Thereapy – Leukemia; STAI, State Trait Anxiety Index; QLI, QoL Inventory; FORS, Fear of Reoccurrence Scale; MOCFS, Medical Outcomes Cognitive Functioning Scale; GTUS, Growth Through Uncertainty Scale; POM – SF, Profile of Mood State Short-Form; FP, Karnofsky Performance Status Scale; MACS, Mental Adjustment to Cancer Scale; SF-36; Health Related QoL; PTSD Inventory, Post-Traumatic Stress Inventory; PTSD-C, Post Traumatic Stress Checklist; MOS-SSS, Medical Outcome Study Social Support Survey

2.15 Overview of Studies and Methodological Considerations

The following will provide an overview of the studies that met inclusion criteria from the literature review search. Initially, an overview of the studies will be provided, highlighting what each study attempted to explore, the results, and an overall assessment of the methodological quality.

It is important to note that within many of the following studies, QoL is used as an umbrella term, in that, the researchers tend to refer to QoL as being synonymous with psychological well-being, physical functioning, social relationships, and level of independence. As noted in the inclusion criteria, studies that were included in this review were ones that examined psychological well-being under the umbrella term of QoL.

2.16 Cross Sectional Studies

Relationship between Uncertainty in Illness and Psychological Well – Being in Cancer Patients: Pre – Intervention

Kurita and colleagues (2014) studied the relationship between uncertainty and psychological adjustment in patients who had been newly diagnosed with lung cancer (less than 6-months). The researchers of this study hypothesized that poorer psychological adjustment (greater feelings of low mood, higher perception of stress, and poorer emotional well - being) following diagnosis would be associated with higher levels of uncertainty and higher perceived ambiguity in relation to one's illness. The findings supported the initial hypotheses, in that, those individuals who had higher levels of stress and reported greater feelings of low mood also had higher levels of uncertainty in illness. The study had a relatively small sample size (N = 49) and had a cross-sectional design, which raises questions about the results from the multiple regressions. The study

also did not indicate statistical power needed and whether it was achieved. Additionally, the study collected data from women who were mainly of a higher socioeconomic status in the United States, which leads to better care and outcomes, and may not be representative of those who do not have access to the same care. However, the study used reliable and validated measures, and conducted the research in an understudied group of individuals. Overall, the study was of satisfactory methodological quality.

Relationship between Uncertainty in Illness and Psychological Well-Being in Cancer Patients: Post - Intervention

One of the first studies to explore uncertainty in illness and the relationship between psychological well-being was conducted by Merle Maste in 1998. The overall objective of the study was to explore the relationship between different variables such as uncertainty in illness and emotional distress for breast cancer survivors (Mast, 1998). Two of the major findings of the study were that: uncertainty in illness was positively related to emotional distress, and that an individual's level of uncertainty in regards to illness explained over half of the variance (51%) in regards to the individual's emotional distress. Two of the main limitations to this study were a lack of diversity in the sample as, out of the 109 participants, only 2 were non-white and there were essentially no women of low income. Also, for two of the measures that were used (FRQ, GTUS), there was limited data in regards to the measures psychometric value (reliability and validity). Maste's study was one of the first quantitative studies to examine uncertainty in illness and emotional distress in cancer, and confirmed reports from previous qualitative research that related uncertainty to physical symptoms and fear of recurrence. Overall, due to the questionnaires used and the homogenous sample, methodologically, the study

was one of the weaker studies reviewed.

Hall, Mishel and Germino (2014) conducted a study in breast cancer survivors 2-4 years following treatment. The goal of the research was to determine whether cancer related uncertainty had an impact on physical well-being (fatigue, insomnia), as well on an individual's mood. Results from the study outlined that cancer related uncertainty in illness was associated with greater fatigue, insomnia, negative affect, and lower positive affect. One of the largest samples sizes of the reviewed studies (N = 344), and a relatively heterogeneous sample, where 50% of the participants were of African American and Caucasian heritage. The participants were also of varying socioeconomic and educational backgrounds. Additionally, the validity of the outcome measures were reported for each measure and the age of participants varied within the sample. Overall, the study was one of the strongest studies in terms of methodological quality, in comparison to the others that were reviewed.

Dr Angela Sammarco has completed a number of studies that investigated the relationship between uncertainty in illness, social support, and psychological well-being in women who have a diagnosis of breast cancer (Sammarco, 2001). One of her first studies in this area (Sammarco, 2001) was done with young breast cancer survivors (younger than 50 years of age), and the specific goal was to examine the relationship between uncertainty in illness, social support, and psychological well-being. The study hypothesized that there would be a positive correlation between perceived social support and psychological well-being. It was also hypothesized that uncertainty in illness and social support would explain most of the variance in terms of QoL and psychological well-being in comparison to each variable taken together. The results from the study

confirmed all three of the above hypotheses, as well as negative correlations between network size and uncertainty in illness, and time since diagnosis and uncertainty. It is also important to note that uncertainty in illness and social support were two variables that explained 27% of the variance in the regression model, which highlights that there is a 'large amount' of variance that remains unexplained. In terms of methodological limitation, the sample was predominately white (90%) which suggests a degree of sampling bias, as well as a high educational level for most of the sample, which can have an impact on level of uncertainty in relation to one's illness (Mishel, 1997). Overall, the study used validated and reliable measures, collected a degree of demographic data, which the researchers used in the statistical analyses, and had a relatively large sample (N = 109), which met the power calculation reported in the paper. The study was of good methodological quality, and was one of the stronger papers in terms of the review.

Sammarco and Konecny (2008) also conducted research on women who had a diagnosis of breast cancer, post treatment. The goal of the research was to examine the relationship between perceived social support, uncertainty in illness, and the individual and combined effects on QoL including psychological well-being among Latina breast cancer survivors. Results indicated that both perceived social support and level of uncertainty in relation to one's illness had a significant impact on an individual's QoL. In terms of methodological quality, the sample was rather homogenous, only dealing with Latina women of high socioeconomic and educational background and most were married. In addition, although the reliability and validity co-efficient were outlined in the paper, the socioeconomic subscale of the QLI-CV demonstrated questionable reliability. Yet, it was one of the few papers that clearly highlighted that power calculations were completed a priori and these

were met with 89 participants. Overall, the paper is of moderate methodological quality, but one of the stronger papers in terms of the other papers included in this review.

In 2010, Sammarco and Konecny completed a follow-up study that included both Latina and Caucasian women who had survived breast cancer. The results from the study illustrated that Caucasian women reported higher levels of QoL as well as psychological well-being, perceived social support, and lower levels of uncertainty in illness. Also, the study highlighted that mental health difficulties and lower level of education were noted as contributing factors in individuals who reported lower QoL. Similar to the initial research study (2008), Sammarco and Konecny highlighted power calculations, effect sizes for comparisons, and the participants needed in both groups to meet these power calculations, which were met. Again, much like the previous study, this study used reliable and validated measures and indicated the alpha values in the paper and, overall, the article is of moderate methodological quality, but one of the stronger papers in terms of the other papers included in this review.

Relationship between Uncertainty in Illness and Psychological Well-Being in Cancer Patients: Pre Treatment or Engaged in Treatment

Lin Lin and colleagues (2013) completed a study examining the relationship between uncertainty related to one's illness, mood state, and illness trajectory and symptom severity in individuals with a diagnosis of a primary brain tumor (PBT). A total of 186 participants engaged in the research study, who were at different stages of the illness trajectory and who had varying symptom severity and different functional abilities as a result of the PBT. The results from the study indicated that lower functional ability and those individuals who were at an earlier point in the illness trajectory had higher levels of

uncertainty in relation to their illness and reported lower levels of mood. With regard to studies limitations, the sample was rather homogenous (white, high level of education and married) and the nature of the study was a secondary data analysis with a self-selected sample. Secondary data analysis suggests a primary researcher collected the data and therefore the data may have been used for a different objective or to answer another research question, which could mean that the data may not be appropriate to answer a the above research questions (Denscombe, 2010).

Psychological Well-Being in Patients with Chronic Lymphocytic Leukemia or Low Grade Lymphoma

One of the first studies that examined psychological well-being and QoL in patients who have a diagnosis of CLL was conducted by Levin and colleagues (2007). Specifically, this study examined whether there were differences in QoL and psychological well-being (levels of anxiety and mood) in patients diagnosed with CLL who were either on watch and wait or engaged in active treatment. The researchers hypothesized that those patients who were in active treatment for CLL would have greater levels of psychological distress and worse QoL than those patients who were on watch and wait and this hypothesis is imbedded in the fact that those patients who were receiving a direct form of treatment have a more serious manifestation of the illness. However, the results indicated that there was no statistical significant difference in terms of psychological well-being and QoL in those patients who were on watch and wait or receiving treatment. Although a cross-sectional study with a large sample, the study did not achieve statistical power and therefore any results need to be interpreted with a degree of caution. Overall, the study was of moderate methodological quality in comparison to the other studies reviewed.

A recent cross-sectional design study done by Morrison and colleagues (2016) examined the impact of physical burden in response to psychological difficulties which included anxiety, depression, and stress. The second aim of the study was to determine if individual differences (social support, relationship satisfaction) exist that could have an impact on the level of psychological distress for an individual diagnosed with CLL on watch and wait. In contrast to the Levin study (2007), the Morrison study (2016) found that higher physical symptom burden associated with the individual's CLL had a greater impact on the level of psychological distress that the individual experienced. Additionally, it was found that those participants with less social support and less satisfaction in regards to relationships had higher levels of psychological distress following the diagnosis of CLL. A real strength of the study is that it was the first to look at elements of social support, psychiatric history, and psychological constructs of anxiety and depression in patients in CLL on watch and wait. The study indicated power calculations, used validated measures, and again was one of the first studies to consider traumatic stress as measured by the IES-R in the understudied group of individuals with CLL on watch and wait. Overall, the study was one of the strongest in terms of methodological quality

A 2003 paper published by Montgomery and colleagues explored the relationship between coping style, QoL, and psychological well-being (anxiety and depression) for patients who had been diagnosed with CLL and LGL at various points of disease progression (watch and wait and active treatment). The results from the study highlighted that those individuals who had greater difficulty adjusting to the diagnosis of cancer also had significantly higher scores with regards to psychological well-being. The study

suffered from a number of methodological limitations, such as low power for the regression models as well as being cross sectional in design. The cross-sectional design is particularly limited in this study as it engaged people at different times of the disease process and the research indicates that those individuals with more severe forms of cancer, or who are further along in terms of illness progression, will have greater levels of psychological distress and lower QoL. Although this study is important as it is one of the few studies that has examined psychological well-being in patients with CLL and LGL it would still be considered to be one of the weakest in regards to methodological quality

Pashos and colleagues (2013) completed a study that investigated whether there were differences in terms of gender, QoL, and psychological well-being in patients who had a diagnosis of CLL. The results from this study were varied, in that, women reported higher levels of anxiety and depression, worse global fatigue, and higher pain or discomfort; whereas, men reported lower family and social functioning, and lower engagement in activities. The sample for the study was large (N = 1,142), participants were recruited from 162 different centers, and the data was collected in a standardized fashion directly from American clinical centers. In addition, the data that was presented highlighted statistical significance as well as the overall effect size of the aforementioned differences between the different variables and gender. A particular limitation to the research was that, while the sample was large, it was rather homogenous, as 81% of the participants were white of higher socioeconomic and educational background. Another limitation to the study was the lack of information about whether patients were currently engaged in treatment or whether they were on watch and wait. Overall, this study was of

strong methodological quality, due to the strength of the reported data and the rigorous data collection.

Post-Traumatic Stress in Patients with Low Grade Lymphoma

The research conducted by Geffen and colleagues (2003) was one of the few studies that examined the construct of post-traumatic stress in individuals following a diagnosis of LGL. Specifically, the study examined those individuals with a diagnosis of LGL and those individuals who had experienced a traumatic event and who may have potential difficulties associated with post-traumatic stress, in order to compare the level and severity of the symptoms experienced by both groups. The study found that there were a higher proportion of individuals with a diagnosis of LGL, who would be classified as having post-traumatic stress in comparison to those who experienced a discrete traumatic event, although the differences between the two groups were not statistically significant. The results also indicated that those individuals with a diagnosis of LGL suffered higher levels of distress associated with intrusion and avoidance in comparison to those who experienced a singular traumatic event. Another important result of the research highlighted that the younger the individual the higher the experience of distress as it related to post-traumatic stress in both groups. A major limitation as cited by the authors was that the control group (discrete or singular traumatic eventmay not be an appropriate comparative group in comparison to those individuals who had LGL. Overall, the study is of particular importance as it attempts to understand post-traumatic stress; it relates to LGL and was of good methodological quality

2.17 Longitudinal Studies

Uncertainty in Illness in Cancer Patients – Post Treatment

Suzuki (2012) examined the relationship between uncertainty in illness, QoL, psychological well-being, and decision making in patients with head and neck cancer in pre and post treatment periods. Participants were recruited and data collection was completed during the initial consultation about treatment. Data was then collected 6-weeks following treatment. The outcomes from the study were that post-treatment QoL, including psychological well-being were lower than pre-treatment; level of uncertainty in regard to the illness and QoL were both significant predictors of QoL and psychological well-being post-treatment, after the researchers controlled for variables such as 'unemployment, treatment used, and physician'. Finally, the participants' perception of involvement in the decision making process was not significantly associated with uncertainty in illness or QoL. Specific limitations to the research were the small sample size and the number of dropouts that did not complete the study. Initially, 52 participants were recruited, but 35 participants completed questionnaires both pre and post treatment, which could have biased the results for those completers. Additionally, due to the varying nature of treatment, the time differed greatly for those participants involved in the study and, if there was a longer follow-up, these different time periods could have been better controlled. Strengths of the study were that the sample was rather heterogeneous in terms of cultural background and educationsince participants were recruited from 6 different hospital sites. The outcome measures were all tools that have been used in previous studies of uncertainty; QoL and cancer research and alpha values for each measure were highlighted within the paper. However, due to a relatively small

sample, and the high rate of drop-outs, the study would be considered one of the weaker studies in comparison to the other longitudinal studies that were reviewed.

Kazer and colleagues (2012) completed another longitudinal study that examined uncertainty in illness, QoL, and psychological well-being in cancer patients. Specifically, the aims of this study were to determine what variables may be contributing to uncertainty in illness, QoL and psychological well-being, and to also investigate uncertainty and perception of danger following treatment of prostate cancer. The results were varied, in that, younger people reported less uncertainty in illness but greater perception of danger in regards to the treated prostate cancer. In addition, education was one of the more prominent variables, as there was a significant relationship between lower levels of education that was associated with greater uncertainty in illness. Another important finding was that there was a moderate association between all of the outcomes: greater uncertainty was associated with greater perception of danger and, as uncertainty and perception of danger increased, there was a noted decrease in satisfaction with treatment outcome. Limitations of the study were that there was no time-1 data collected at diagnosis or prior to treatment and the sample was not heterogeneous, as out of the 338 participants, 300 were white. However, there are a number of methodological strengths: out of the 338 participants, 328 completed outcomes measures over the 3 time points following treatment (48 months, 60 months, and 72 months). What is of the utmost importance and a real strength in regards to the study is the length of follow-up, as other studies have focused on the period immediately after treatment. Overall, this study is one of the strongest longitudinal studies reviewed due to the large sample, the lengthy period of follow-up, and the amount of individuals who completed the study.

Uncertainty in Illness and Psychological Well-Being in Cancer Patients: Diagnostic Period

Liao and colleagues (2008) investigated the level of uncertainty and psychological well-being for women who had a suspected diagnosis of breast cancer over three time points: during the diagnostic phase (upon notice of breast biopsy), before biopsy, and after diagnosis. Findings from the study are as follows: levels of uncertainty in illness and anxiety were significantly higher before than after diagnosis (important for CLL); over the three time points uncertainty was much higher for those diagnosed with benign tumors than malignant diagnosis; uncertainty and anxiety were moderately correlated, and uncertainty was predicted by "age, marital status, education level, religious status, family history of benign breast tumour, regular breast self-examination, self-perceived probability of receiving a breast cancer diagnosis, and biopsy result". A real strength of this study was that it was one of the only studies that investigated uncertainty in illness and psychological well-being during the diagnostic period, a that one would presume would be extremely anxiety-provoking and fraught with uncertainty. However, there are number of methodological limitations; the average time between times 1 to 3 was 8-days which is not much of a time period and one must wonder how much one's emotional or psychological state will vary over such a short time period. Finally, 20% of the 117 participants did not complete the questionnaires and the researchers query whether that led to underestimating the level of anxiety and uncertainty, and therefore the study is one of the weaker studies in terms of the longitudinal studies that were reviewed.

Psychological Well-Being in Patients with Chronic Lymphocytic Leukemia

Another longitudinal study that dealt specifically with CLL and QoL was a study that was completed in the Netherlands by Holtze-Goor and colleagues (2015). The specific aims of the Holtzer-Goor study were to examine both HRQoL (fatigue, nausea, pain) and QoL (social functioning, emotional functioning, global QoL) in patients who were engaged in treatment and those who were not in treatment and compare the results with age-matched norms. The results indicated that overall both HRQoL and QoL were significantly lower in patients with CLL in comparison to the norms. The paper also reports that those patients who had a diagnosis and who were not in treatment (watch and wait) had reduced QoL in comparison to those individuals who were engaged in treatment (drug treatment). The study had a number of methodological limitations: the sample was not large enough in order to make statistically significant comparisons between groups, no power calculations were highlighted, the data collection or different time points was not clearly reported, nor was there any data reported in terms of the make-up of the sample. It is also important to note that although the study claims to be of longitudinal design, it was unclear whether the participants were given the same measures at different time-points or whether the participants were enrolled in the study and given the outcome measures at one time-point, which would suggest it was not longitudinal and therefore, the study is considered to be the weakest of the longitudinal studies that have been discussed.

2.18 Methodological Considerations

In addition to a general overview of the studies, the following section will provide specific methodological limitations that were consistent across a number of studies in the review.

2.18.1 Samples

The majority of the cross-sectional studies that were reviewed had large samples which would suggest that the relationships that were detected between the different variables were accurate. However, there were a number of studies which had small sample sizes and also did not indicate whether or not the desired power was achieved. Kurita and colleagues is a cross-sectional study where the small sample was a major limitation to the generalizability of the results and the study's authors did not indicate what power was required for the different statistical tests used. Similar to the Kurita (2014) study, the Suzuki (2012) study had N = 52, but the authors did indicate that they did not achieve power in regards to the varying statistical techniques used. Overall, the longitudinal studies that were reviewed had relatively large samples sizes and most seemed to achieve statistical power. The only study that had a small sample and did not provide detail in regards to the sample was Holtzer-Gooer and colleagues (2004), as it was unclear whether they had enough participants to be confident in the results, which did highlight a difference between groups (treatment versus watch and wait).

Another important methodological factor in relation to the various samples in the studies reviewed was a lack of diversity in the subject populations of a number of the studies. Pathos and colleagues (2013) was a study whose sample was 81% Caucasian and the majority of that group were of higher economic status, with higher levels of education.

Out of the 109 participants in Maste's (1998) study, only 2 participants were non-white, and there were essentially no women of lower economic status. Sammarco and Konecny's (2008) first study was completely homogenous but, by design, as they were attempting to gain insight into uncertainty, social support, and QoL in Latina patients with breast cancer; a group that has not been well represented in the literature (Sammarco & Konecny, 2008; Sammarco & Konecny, 2010).

Although a number of the above studies had difficulty with recruitment and had a lack of diversity in regards to the samples, it must be noted that attempting to recruit a vulnerable population of cancer patients into studies that are psychologically oriented, where there is essentially no immediate or direct benefit to the research participants, can prove difficult. A diagnosis of cancer can be a traumatic experience for any individual and following a new diagnosis, these individuals are most likely going to feel overwhelmed in attempting to understand the diagnosis, understanding the care that they will undergo, and of course, dealing with a number of individual and relationship factors which would also lead to a degree of stress (Moyer et al, 2009). Therefore, even those studies that attempt to provide psychological interventions to support individuals with cancer treatments have much difficulty in terms of recruitment, retention and research such as the above studies that offer no clear benefit or support are obviously going to struggle in recruiting such a vulnerable population (Moyer et al. 2010).

2.18.2 Outcome Measures

Overall, most of the studies used reliable and valid measures, which are common in cancer, uncertainty, and psychological well-being research. However, in a number of the studies, measures were used that were not as common in the literature and the researchers

did not provide Cronbach's alpha values to highlight the validity and reliability of these measures. Specifically, Holtzer-Goor and colleagues (2015); Pashos and colleagues (2013); and Morrison and colleagues (2007) did not indicate the alpha values for the measures used and therefore one must question whether the measures are consistent in evaluating the constructs that they are expected to measure. As the studies under review are either cross-sectional or longitudinal, the measurement of certain variables is of specific significance and, therefore, the validity and reliability of the measures is of importance.

As a number of the studies were completed in different countries, outcome measures had to be translated from the original language to a different language so the participants could answer the specific items. The first goal of translating an outcome measure is to produce a new version, in a new language, that is conceptually equivalent and maintains similar content-validity as the original. Another goal when translating an outcome measure to a different language is to ensure that the new outcome measure is 'relevant in the new target culture'; essentially, ensuring the new outcome measure has the same construct validity for the new target population (Goggin et al., 2010). A number of reviews (Grove et al., 2005; Acquadro et al., 2008) recommended the following in terms of translating outcome measures: translation of the original outcome measure to the new target language by two separate and independent translators and "reconciliation into one version (forward step)"; translating the reconciled version back into the original version (backward step); review the reconciled version of the instrument with the original developer; to test the new outcome measure on a number of participants in the target country (cognitive interview step); have the new measure reviewed by a number of

experts; and finalize the new translated instrument into an outcome measure (Acquadro, Bayles & Juniper, 2014).

In terms of the studies that have been reviewed, two different studies had to translate outcome measures into a new target language. One study that took place in the Netherlands used outcome measures that had to be translated from English into Dutch, but provided no information on the methods used to translate the measure, or whether the measure had been translated by another study (Holtzer – Gooer et al. 2004). In contrast to the above study, the study conducted by Liao and colleagues (2008), which was carried out in Taiwan highlighted the paper that initially translated the Mishel Intolerance of Uncertainty Scale (MIUS) into Mandarin, from the original English. Although the Liao paper does not specifically indicate the steps that were taken to translate the MIUS in the original study, the paper, which the authors cite, was a psychometric study that tested the validity of the MIUS in Mandarin (Sheu & Hwang, 2006). When using measures that have been translated into a new language from the original language it is an important methodological consideration that the original studies be transparent about the process or the research used to ensure that the translated version had content validity as well as being reliable in the new language.

2.19 Conclusions

As noted previously, the studies that have been appraised in the literature review section of this introduction vary in quality and a number of the studies would be considered to be of low to moderate methodological quality. However, from the studies that were reviewed, there were specific patterns that emerged in regards to uncertainty, psychological distress, watch and wait, time, and cancer.

An initial pattern that emerged from this literature is that a number of studies reported no significant differences in terms of psychological well-being in patients with CLL or LGL who were either engaged in treatment or placed on watch and wait (Holzter – Goor et al., 2015 & Levin et al., 2007). The Levin (2007) study dealt specifically with individuals who had a diagnosis of CLL, and again highlighted no significant differences between those participants in treatment and on watch and wait. Although difficult to generalize from two studies, it is nevertheless surprising that those engaged in an active treatment and who would therefore have a more threatening form of cancer would not have higher levels of distress and worse psychological well-being. The lack of difference between watch and wait and a direct form of intervention may highlight the powerful impact of a diagnosis of cancer and watch and wait as a form of care, regardless of the perceived level of severity.

Another important pattern that was determined from the studies that were reviewed was the impact of uncertainty in relation to an individual's diagnosis of cancer and psychological well-being. Higher levels of stress, negative affect, and poorer emotional well-being were correlated with higher levels of illness uncertainty in relation to cancer (Hall, Mishel & Germino, 2013; Kurita et al., 2014; Liao et al. 2008; Lin et al., 2013; Maste, 1998; Sammarco & Konecny, 2008)

Finally, in regards to the impact of time, a number of the longitudinal studies were able to indicate the impact of uncertainty in illness and psychological well-being at diagnosis and how these variables may have changed over time. Suzuki (2012) and Kazer and colleagues (2012) highlighted the higher levels of uncertainty and psychological well-

being following a diagnosis were predictive of post-treatment psychological well-being and treatment satisfaction. Furthermore, the study conducted by Liao (2008) indicated that level of uncertainty in relation to one's cancer and anxiety were higher following diagnosis, over time.

2.20 Rationale for Current Study

From reviewing the literature, there is a dearth of quantitative research in the area of CLL or LGL, uncertainty in illness, psychology well-being, the impact of the diagnosis, and watch and wait. Moreover, there does not seem to be any quantitative, longitudinal studies that focus on CLL or LGL and the construct of uncertainty in relation to one's illness.

The lack of studies is relatively surprising as CLL and LGL are two of the most common forms of cancer and the gold standard for those individuals who are not symptomatic at the time of diagnosis is watch and wait, which means a high proportion of patients with CLL or LGL will not be receiving any form of direct intervention. As highlighted previously, receiving a diagnosis of cancer and being told that one will not be receiving treatment is in contrast to a westernized medical model, and most likely to an individual's understanding of how cancer is normally treated. Therefore, one would hypothesize that being put on watch and wait could potentially lead to a degree of uncertainty and confusion following the initial diagnosis.

Based on the above rationale, and due to a lack of research, it was deemed important to conduct a study that examined the psychological impact on those individuals with CLL or LGL who have been placed on watch and wait to determine the associations between

uncertainty in illness and psychological well-being, and whether or not these psychological constructs increase or decrease over time, following an initial diagnosis of CLL or LGL.

2.21 Overall Aims

Aim 1

The first aim of the study is to identify levels of anxiety, depression, and trauma following a diagnosis (time-1) of CLL or LGL.

Aim 2

The second aim of the study was to determine whether relationships existed between initial levels of uncertainty in illness and levels of anxiety, depression, and trauma following an initial diagnosis of CLL or LGL.

Aim 3

The third aim was to determine whether psychological variables such as uncertainty in illness, anxiety, depression, and posttraumatic stress at time-1 were predictive of the same psychological variables at 6-months following the initial diagnosis of CLL or LGL.

Aim 4

The final aim of the study was to determine whether change occurred over time (following diagnosis to 6-months) in relation to the psychological variables under study (uncertainty in illness, anxiety, depression, and posttraumatic stress). The goal for this aim was to determine if the mean group values, as well as individual values, significantly increased or decreased over time.

3.0 Methods Chapter

3.1 Methods Overview

The following methods chapter will include the research design (longitudinal cohort study), the methodology (quantitative), and the epistemological position (positivist) of the thesis. In addition, specifics have been outlined in regards to the procedure for collecting data, how participants were recruited, and how informed consent was obtained from the participants. As the thesis was a quantitative study, the measures that were selected and used are highlighted and the psychometric properties of each measure are outlined. The chapter also provides an overview of how the data were analyzed, what considerations were made in regards to the ethics of the research process, and how the results will be disseminated to the participants and the wider public. Finally, the chapter will conclude with information in relation to the overall participant sample (age, gender, diagnoses, ethnicity, employment, education, relationship status).

3.2 Longitudinal Research

Similarly, to a cross-sectional research design, a longitudinal design can be observational, in that, the researchers do not interfere or place any particular conditions on the participants. However, in contrast to cross-sectional research where data is collected at one-time point, in longitudinal research, data is collected from the participant over time and employs continuous or repeated measures to follow a single participant or group of people (Taris & Kompier, 2014; Caruana, Roman, Hernadez-Sanchez & Solli, 2015). Because the data is collected for predefined groups of participants or an individual, suitable statistical techniques can be used in order to understand change over time for a particular group or for an individual participant (Montero & Leon, 2007;

Caruana et al., 2015). There can be advantages to conducting longitudinal research in contrast to cross-sectional research. For instance, when one uses the cross-sectional research design, data for one or more variables are collected at one specific time point; whereas, for longitudinal research, the data are collected for one or more variables at two or more distinct time periods, and therefore, the analysis of the data involves comparison between time periods (Menard, 2002; Menard, 2007). A longitudinal research design can provide insight into the causes of distinct phenomena, or attempt to determine specific antecedents and consequences. As such, the temporal ordering of events is quite often the closest that researchers can get to causality. In addition, longitudinal designs can also provide better insight into the causal relationships that may exist between data sets that have been collected in a specific study (Pettigrew, 1997; Ruspini, 2002).

3.3 Cohort Design Studies

Although scientifically rigorous, controlled trials (RCTs) are not always a viable option to evaluate clinical and behavioural outcomes (Mann, 2003; Grossman & Mackenzie, 2005; Scriven, 2008; Guest & Namey, 2015). In a cohort study, the researchers chose a group of individuals to participate who have a common 'exposure' that the investigators wished to study and, by definition, the cohort are those who share that common characteristic (ie. diagnosis CLL or LGL) (Hadorn, Baker & Hodges, 1996; Warner & Dee, 2015).

There are two common types of cohort studies: prospective and retrospective, and one type which is far less common-'ambidirectional'. These different types of studies are defined by the time-point at which the follow-up begins. The prospective cohort study, often referred to as a longitudinal cohort study, attempts to observe and gather data on

individuals following identification of the specific characteristic(s) that define the cohort. The retrospective cohort study, often referred to as a historical cohort study, attempts to collect data and make interpretation on the participants prior to the participants attaining the specific characteristic related to the makeup of the cohort. Lastly, the 'ambidirectional' cohort study makes observations and collects the data using both a prospective and retrospective approach (Glenn, 2005; Warner & Dee, 2015).

3.4 Current Study

The current research study utilized a longitudinal cohort design. The use of a longitudinal cohort design was chosen because it allowed the analysis of changes in different variables. Initial time-1 data were planned to be collected following the participant being told that they have a diagnosis of CLL or LGL and placed on the 'watch and wait' standard pathway. The importance of this initial data collection time-point was to obtain time-1 data as close to the date that the participant was told of their diagnosis. The subsequent time points (3-months post diagnosis, 6-months post diagnosis, 12-months post diagnosis) were determined in order to collect data when patients visit the Hematology Clinic for their clinical reviews. These time points not only allowed one to determine change over time, but were also deemed to be the least taxing form of data collection for patients (they complete the questionnaires whilst in clinic) and the most efficient means of data collection for the clinical research nurses who assisted in the data collection process.

Longitudinal research designs can be associated with a number of disadvantages. For example, there can be a high level of drop-out from the original sample (Rogosa, 1995; Ruspini, 2000; Taris & Kompier, 2003); specifically, those with a diagnosis of CLL or

LGL may become too unwell and require a more direct intervention and no longer meet eligibility criteria, or may become too unwell to participate in the research. The participants may also move to a different area, or may, over time, lose interest in the research and no longer wish to participate. Research indicates that the longer the study goes on, the higher the potential for dropout (Schmidt & Teti 2001; Taris & Kompier, 2003), and due to all the aforementioned factors, it can be difficult to determine the rate of attrition that may occur over the 12-month time-period. In addition, longitudinal research designs can be more expensive and time-consuming than other methodologies. The current research study utilized a staggered recruitment process, due to practicality, and this resulted in data collection that was extended over a 15-month period. Another important potential disadvantage that must be highlighted is that of 'panel conditioning', which is when an individual's response is influenced due to previous questionnaires or interviews (Ruspini, 1999; Lavrakas, 2008; Warren & Halpern – Manners, 2012). The a priori assumption for this type of longitudinal research is that "attitudes, behaviors, and statuses of respondents to longitudinal surveys are not altered by the act of measuring them". Yet, the theory of 'panel conditioning' is that the participant may be influenced by their response to the previous set of questionnaires or surveys and this can lead to bias, and assigning causal relationships where one may not exist (Warren & Halpen-Manners, 2012). In this specific longitudinal cohort study, the research is attempting to generalize the findings to other cohorts with a diagnosis of CLL or LGL; however, the particular cohort may be unique (geographical location, age, other forms of illness) and it therefore may be difficult to generalize the findings from this one specific research study (Farrington, 1991).

Quantitative Research

3.5 Empirical: Deductive Theory

Longitudinal quantitative research designs are associated with the idea of empirical research and deductive theory. Empirical research is based on experimentation or observation in order to test a particular hypothesis, or to answer a specific question. In deductive theory, the research begins with abstract concepts or a specific theoretical proposition that could outline a 'logical connection between concepts'. Therefore, when utilizing deductive theory, one would evaluate different concepts and propositions utilizing concrete evidence – moving in a linear fashion from the initial idea, to the hypotheses, towards observable empirical evidence, and finally, the conclusions that are developed (Hayes, 2000; Gelo, Braakmann, & Benetka, 2008; Neuman, 2014). Within a deductive theory framework, the hypotheses that are being tested will contain variables such as: behaviours, thoughts, and specific characteristics that may be displayed by a cohort and then the researcher will attempt to determine if a relationship exists between these variables. Once the data is gathered from the cohort, and it is analyzed, the results will either provide confirmation of the initial hypothesis or evidence that refutes it (Crowley, 2008).

3.6 Ontological Position: Objectivism

The quantitative research and the longitudinal design utilized in this study are associated with the ontological position (how one views reality) of objectivism. Objectivism can be defined as: 'an ontological position that implies social phenomena confront us as external facts that are beyond our reach or influence', where the phenomena and the specific 'categories' that are discussed in daily discourse exist independently or separately from

the actors (Healy & Perry, 2000; Krauss, 2005; Bryman, 2015). From an individual perspective, as one develops and matures over time, so does their understanding of the differences between thoughts and the external reality of the surrounding world. In his work: *Contemporary Philosophy of Social Science,* Brian Fay states that as one ages and grows an 'epistemic maturation' occurs; wherein, one not only learns to make distinctions between the reality of the external world and one's own thoughts, but one comes to seek and value truth, in opposition to what he Fay states is a 'sea of illusion' (Fay, 1996; Johnson & Onwuegbuzie, 2004). The objectivist position posits that an objective external reality already exists, that there are 'pre-existing structures' of this external reality, and an individual needs to accumulate more information to have a more complete understanding of these structures. In order to accumulate more information about the objective external reality, it is necessary to generate hypotheses and test these hypotheses while attempting to remain objective, and by remaining objective, one does not allow subjective interpretations to impact on this process (Krauss, 2005; Clark et al., 2014).

3.7 Epistemology: Positivism

Positivism is the epistemology (the nature of knowledge) of this quantitative research, and it is an epistemology that is associated with the ontological position of objectivism. The positivist paradigm postulates that social observations that occur should be examined in the same manner that physical or natural scientists treat physical or natural phenomena (Ponterotto, 2005; Mackenzie & Knipe, 2006; Muijs, 2010). Positivism evolved from a nineteenth-century philosophical approach which identified with the idea that the purpose of conducting research is 'scientific explanation'. Positivists approach the social sciences

as a method for linking deductive logic with experimental observations of human behavior in order to verify a pre-existing set of 'probabilistic causal laws', which can then be used to predict and generalize certain patterns of human activity (Michell, 2003; Ryan, 2006; Morgan, 2007). As previously outlined with regards to objectivism, positivism attempts to add to the understanding that all patterns of social reality are understood to be constant, and all novel discoveries via experimentation are added to the knowledge of these social constants (Winter, 2000; Sale, Lohfeld, & Brazil, 2002; Neuman, 2003; Tuli, 2010).

Attempts have been made to capture the specific tenets of positivism and the following can be considered general characteristics of the research paradigm. The characteristic of *phenomenalism* emphasizes that what one is to 'count as knowledge' can only be determined by what the researcher can perceive by his or her senses. The rule of *nominalism* asserts that abstract concepts that one may use when attempting to make scientific explanations must be derived from observation and one's experience. The notion of *general laws* states that scientific theories can be understood as a: 'set of highly general, law like statements', and therefore, the goal of science is to form a set of *general laws. Atomism* is a characteristic of positivism that highlights that the entities of observation should be regarded as distinct and independent events that make up the central foundations of the world. The characteristic of *value judgments and normative statements* suggests that the researcher must make a distinction between facts and individual values and that values cannot be considered knowledge. Specifically, values have no empirical content, as the validity of values cannot be tested through direct observation. An extremely important characteristic of the positivist paradigm is

verification. *Verification* is how 'truth and falsity' of scientific investigations can be determined, in that, generalizations are made from the initial observation and further confirmed by more and more evidence. The greater the amount of evidence that can be accumulated, the more weight is given to the researchers conclusions. Lastly, *causation,* which is another central characteristic of positivism, stipulates that there are only 'predictabilities' and the idea that specific 'events' will always be followed by a specific event of another kind – one event will follow another (Blaikie, 2007). These concepts illustrate how those who approach research from a positivist perspective embrace the idea that knowledge is determined via empiricism and that what they deem to be logical, and therefore, one's knowledge is guided by the natural sciences and the logical by mathematics and logic.

3.8 Limitations of the Positivist Research Paradigm

The positivist approach to research used as a means to understand human behaviour has been much debated and criticized. Philosophical thinkers from different backgrounds contest the tenants of positivism and, in many ways, destabilized the notion of absolute truth, provable hypotheses, and unbiased, value-free researchers (Giddings & Grant, 2007). In their work *Comparing Paradigms in Qualitative Research,* Guba and Lincoln outline the primary limitations to positivist quantitative research, and a number of these limitations will be highlighted in this section. Guba and Lincoln address the idea of *context stripping*, in that, positivist tend to focus on a particular subset of variables, and in doing so possibly remove other variables that would provide more context and a degree of generalizability to the research (Guba & Lincoln). Another limitation is the idea of *the exclusion of meaning and purpose*, arguing that human behaviour cannot be

understood unless one understands the motivations behind the individual actors conducting the research. A central limitation to positivist methodology is the proposition of the *inapplicability of general data to individual cases* - that although the generalizations of the research data may prove to be statistically significant, it does not mean that it will be applicable to each individual case. *The critique of 'value-ladenness of facts'* proposes that as theory and facts are not independent, neither are values and facts. The separation of values and facts is a central characteristic of positivist research, but it is suggested that theories in themselves are value statements, and therefore, it is illogical to state that facts and values can be completely independent. A final, and possibly the most important limitation of the positivist research approach, is the proposed *interactive nature of the inquirer and inquired into dyad.* The goal of positivist research is to be a 'silent observer' of natural phenomena and record it objectively and when positivist research is done correctly the researcher does not influence the phenomena, or vice versa. However, critics highlight that it is a near impossibility that the researcher not influence what is being observed or what is being observed influences the researcher and the idea of complete objectivity has been disproved in natural sciences (Heisenberg uncertainty principle). Therefore, in the social sciences, when one is observing people, it is much more difficult to achieve that level of 'complete objectivity'. The counter-argument to this final limitation is that research findings are not only discovered through objective observation, but also, and maybe more importantly, through the social interaction of the observer and the phenomena (Guba & Lincoln, 1994; Van Ness, Fried & Gill, 2011).

A longitudinal cohort research study is able to provide one with insight into social phenomena and additionally it is a methodology that can improve one's understanding of causal inferences over time. In contrast to cross-sectional designs, which are often limited due to problems of 'ambiguity' with regards to the direction and the power of the causal interpretations made from the data. Although longitudinal research does not account entirely for the problem of ambiguity when attempting to make causal inferences, the methodology does allow the researcher to identify independent variables at 'time-point one', and because of this one may be able to infer effects at 'time-point two' (Bryman, 2007). As outlined above, there are a number of limitations to longitudinal research and the conclusions that one can derive from using such a methodology can be imperfect; however, empirical research conducted in traditional epistemology of positivism allows the research to test specific hypotheses, which may provide greater insight into the pre-existing structure that this type of research attempts to expound. It is accepted that longitudinal research is useful when the researcher is attempting to delineate causal findings on individual behaviour. The aforementioned acceptance is associated with the understanding that longitudinal research studies can highlight the "nature of growth, trace patterns of change, and possibly give a true picture of cause and effect over time" (Rajulton, 2001). Social processes have become increasingly complex and if one would like to grasp this complexity, one needs longitudinal data for establishing temporal order, measuring change, and making stronger causal interpretations

3.9 Design

The research design was a longitudinal cohort study that used quantitative methodology for collecting and analyzing the data.

3.10 Procedures

Role of Participant

1. Time-1 (Visit 1) – **Participant Inclusion and Exclusion Criteria**

a. Inclusion Criteria: Watch and Wait

i. Patients were 18 years of age.

ii. Patients had a confirmed diagnosis of chronic lymphocytic leukemia or low grade lymphoma who were on "watch and wait" pathway. i.e. not requiring active treatment of their disease.

iii. Were literate in English.

iv. Had capacity to give informed written consent to participate.

v. Patients diagnosed with CLL or LGL within the last 3 months.

vi. Patients who were willing to attend possible additional meeting with researcher to complete questionnaire.

b. Exclusion Criteria

i. Patients who were too unwell, symptomatic, or distressed to participate- as judged by clinical team (Consultant Hematologist and Clinical Nurses).

ii. Patients who did not speak English or are not able to read English.

iii. Any patient who had received prior treatment for chronic lymphocytic leukemia or low grade lymphoma.

iv. Any patient who was unwilling to provide informed written consent.

v. Any patient who was unwilling to complete research assessment tools ie Questionnaires.

vi. Any patient who had severe, concurrent diseases or mental health difficulties that could interfere with their ability to participate in study.

2. Time point 1: Time-1
    a. Following initial diagnosis
    b. Approached for Consent to participate and given participation information sheets.
    c. If they gave consent, questionnaires were administered.
3. Time point 2: (3-months). Questionnaires were administered following the initial 3-month medical follow-up or next visit to clinic with the consultant or clinical nurse.
4. Time point 3: (6-months). Questionnaires were administered following the 6-month review. If disease remains stable and no evidence for intervention the patient will continue on trial.
5. Time point 4: (12-month) Questionnaires were administered following 12- months review as long as patient did not required treatment during the period prior to 12-month review. However, for the purpose of this study only 6-month data was used for the group analysis and 12-month data was used for reliable and clinical significant change analysis.
6. Clinical research nurses attempted to gather data as close to the time points as possible.

3.11 Identification and consent:

1. Participants were approached during the standard visit for management of their disease. They were screened in the first instance by a member of their clinical team against the inclusion and exclusion criteria of study. If they were screened as appropriate and eligible by the clinical team, the potential participants were invited to join the study and given an information sheet by clinician or researcher. This information included rationale, design, and personal implications of the trial. Potential participants had the opportunity for further discussion with the clinical trial nurse outside the clinic and sufficient time to ask questions.
2. It was clearly stated on the information sheet (Appendices - B) that participation is completely voluntary and that potential participants could withdraw consent at any time, without providing any reason. If they chose to withdraw, participation in the research project ended immediately and no further information was collected. Participants will continue on the watch and wait pathway and there was no consequence for withdrawal from the study.
3. Following the verbal briefing, potential participants were given a copy of the information sheet and the informed consent form. They were offered as long as they needed to consider participation and will be encouraged to discuss the study with their family. All potential participants were given at least 24 hours to consider their decision.
4. Potential participants were followed up by a telephone call from clinical trials nurse (at least 24 hours later). If they expressed interest in participating in study, they were invited back to the hospital to provide informed written consent. Informed written consent was taken by the hematology consultant or clinical trials nurse. This visit

would be additional to routine care and participants will not receive any payment to cover costs.

5. If participants had any questions about the collection and use of information, or any general questions in regards to the research, participants were able to contact the primary investigators of the study.

3.12 Documentation of Study Participation:

All participants who gave written consent to participate were given a copy of the information sheet to retain and keep and they were also offered a copy of their signed consent form to keep. A copy of the signed consent form was filled out in their medical notes. The research team also retained the original signed consent form in site file. All site files were kept in the locked office of research team.

3.13 Collection of Demographic Data

Participants who gave written informed consent had demographic data collected. This included age, gender, ethnicity, religion, occupation, previous education, and marital status. This information was collected directly from participants and through extraction from clinical records. A unique study identification number was on the demographic form including date of recruitment and interview setting ie. clinic or ward or day unit.

3.14 Outcome Measures (Appendices - A)

The following outcome measures were administered at the 4 time points in order to determine the participant's levels of anxiety, depression, and trauma.

Anxiety and Depression

1. ***Hospital Anxiety and Depression Scale (HADS)***: The HADS (Zigmond & Snaith, 1983) is a quantitative measure used to detect states of anxiety and depression in patients who are being treated for a number of physical health problems in different hospital settings. The measure was initially developed by its authors in order to isolate 'caseness' among patients who would not be in a psychiatric hospital setting. The full outcome measure consists of 14 items total, which is further divided into 2 subscales that assess anxiety and depression and each subscale consists of 7-items. The items are based on the relative frequency of symptoms over the past week, using a 4-point Likert scale ranging from 0 (not at all) to 4 (very often indeed). Overall the measure can be distributed into 3 different scores: a depression subscale score between 0 and 21, an anxiety subscale score between 0 and 21, and finally, a total score combining the two subscales between 0 and 42. Again, the authors of the original study, ZIgmond and Snaith (1983) recommended specific cut-off points when one uses the outcome measure: a score of 7 – 8 on either scale would possibly indicate mild anxiety or depression, a score of 10 – 14 would indicate moderate levels of anxiety and depression, and a score of 14 – 21 would indicate more severe levels of anxiety and depression. Similar to the other questionnaires, the HADS is easy for the investigators to administer and for the participants to complete. Those individuals who developed the HADS did not include "physical or biological indicators of emotional distress", such as experiencing weigh loss. The rationale for this was that it may be that the physical symptom could lead to "false positive scores", and this is important to consider when attempted to discern psychological difficulties in a population of individuals who have a physical illness such as cancer (Crowley, 2008; Hermann, 1997). In terms of reliability the internal consistency of the anxiety subscale is

excellent, (Cronbach's α = 0.85), and internal consistency on the Depression subscale is in the adequate to excellent range (Cronbach's α = (0.79-0.81) (Berry & Kennedy, 2003; Woolrich et al., 2006).

Another literature review conducted by Bjelland and colleagues (2002) examined the significant psychometric information of the HADS. Initially identifying 747 studies that used the HADS, and finally focusing on 71 specific studies in order to examine the psychometric properties of the measure. The review determined that the sensitivity and the specificity of both the anxiety and depression subscales were 0. and the authors also highlighted that, as a screening tool, the HADS optimal balance between sensitivity and specificity when the caseness was defined by a score of 8 or above on both the anxiety and depression subscales (Bjelland et al., 2002).

2. ***Mishel's Uncertainty in Illness Questionnaire – Short Form (MUIS - SF):*** The original MUIS (Mishel, 1983) is a 30-item self-report questionnaire, each item using a 5-point Likert scale that was developed in an attempt to measure the individual's uncertainty in symptomatology, diagnosis, treatment, relationship with caregivers, and planning for the future for patients with cancer. Scale development was based on theoretical framework of cognitive appraisal model and perceived uncertainty in illness model, as well as interviews with patients. The internal consistency of the MUIS is excellent and it has been determined to have a Cronbach's α that ranges from 0.89-0.91. However, for the purpose of the current study, and attempting to remain cognizant of the participants' time, the Mishel Uncertainty in Illness Short Form (MUIS-SF) was used in order to determine level of uncertainty in regards to the participants' illness. The MUIS –SF is a 5-item questionnaire that was developed in 2013, taken from the original Mishel

questionnaire in an attempt to provide a less invasive tool in measuring the ambiguity concerning the state of the individual's illness and the complexity regarding the treatment and system of care (Mishel, 2012). The 5-items represent: "ambiguity; concerning the state of the illness, and complexity; regarding treatment and system of care, the controllability of the illness" (Hagen 2009).

A recent study conducted by Hagen and colleagues (2009), assessed the psychometric properties of the MUIS-SF on a sample of 209 breast cancer patients. Face validity of the SF-MUIS appeared "satisfactory both from the "experts" and patients' point of view". The SF-MUIS correlated significantly with scores on anxiety (r = 0.35), depression (r = 0.28), social support (r = 0.27), emotional well-being (r = 0.30). Additionally, the SF-MUIS discriminated significantly in regards to those breast cancer patients who had anxiety (n = 36) (HADS-A > 8) reported more illness uncertainty than those (n =173) without anxiety (HADS-A < 8), (mean and 95% confidence interval) 13.5 (12.4 -14.5) and 11.4 (10.9 -11.8) respectively, $p < 0.0001$. In terms of reliability, the ordinal coefficient alpha for the SF-MUIS was 0.70. One would consider the scale to be reasonably consistent if its alpha is in the range of 0.65 and 0.90 (Streiner, 2003). Overall, the results indicate that the 5 items SF-MUIS for assessment of illness uncertainty performed acceptably in patients who have a diagnosis of breast cancer. Ordinal alpha was deemed to be satisfactory and the scale correlated significantly with "anxiety and depression, quality of information, emotional well-being and social support; factors that are well known to interact with uncertainty in illness" (Hagen et al., 2009).

3. ***Impact of Event Scale – Revised (IES-R):*** The IES-R (Weiss & Marmar, 1997) assesses the frequency of avoidance, intrusive thoughts, and hyperarousal to stressful life events.

Scale scores are formed for the three subscales, which reflect intrusion (8 items), avoidance (8 items), and hyperarousal (6 items). IES-R is made up of 22 items, an increase of 7-items from the original IES, as the original did not measure symptoms of arousal (Weiss & Marmar, 1997). The IES – R measures symptoms of: 'intrusion (dreams about the event), avoidance and numbing (effort to avoid reminders of the event), and hyperarousal (feeling watchful and on guard) with respect to a particular life-threatening event' (Brunet, St-Hilaire, Jehel, & King, 2003) and the subjects rate each item on a 5-point Likert scale (0-4), the amount the items apply to their experience (Weiss & Marmar, 1997). Not a diagnostic tool, the IES-R highlights greater degree of distress for individuals who have possibly experienced a traumatic event. Therefore, higher scores indicate greater levels of distress. It is recommended that mean scores be used for the subscales, with higher scores indicating greater distress, and an overall score ranges from (0-88). Cut-offs have been recommended for the overall scores: a score >24 may have potential symptoms of distress in relation to their trauma experience. Scores >33 could possibly represent potential symptoms of trauma that are in keeping with an individual who has posttraumatic stress disorder (PTSD) (Hutchins, & Devilly, 2005).

The IES-R has a high degree of intercorrelation (*rs* = .52 to .87). High levels of internal consistency have been previously reported (Intrusion: Cronbach's alpha = .87 – .94, Avoidance: Cronbach's alpha = .84 – .87, Hyperarousal: Cronbach's alpha = .79 – .91, (Creamer et al., 2003; Weiss & Marmar, 1997).

3.15 Aims and Analyses

Analyses and Power Calculation

Aim 1

Identify time-1 (following diagnosis) levels of anxiety, depression, posttraumatic stress, and uncertainty in illness following a diagnosis of CLL or LGL.

Analyses

Descriptive statistics analyses were used to determine initial levels of anxiety, depression, posttraumatic stress, and uncertainty in illness following diagnosis and being placed on watch and wait.

Aim 2

Examine if any relationships exist between psychological variables at time-1, following an initial diagnosis of CLL or LGL to determine the strength and the shape of the relationships.

Analysis

Correlation analyses were used to determine the strength and the shape of any detected relationships.

Power Calculation

Based on previous research (Sammarco, 2001; Sammarco & Konecny, 2008; Morrison et. al., 2016), power was set at 0.80 with a medium effect size of 0.30, and significance criterion set at 0.05, the minimum sample needed for the analysis was 82 participants.

Aim 3

Multiple regressions were run to determine if any of the psychological variables at time-1 are predictive of a specific psychological variable at 6-months following a diagnosis of CLL or LGL.

Power Calculation

An a priori sample size calculation was calculated for the multiple regression analyses using the G*Power software 3.1. A medium to large effect size of 0.45 (based on Cohen, 1988) which was take from research of Kurita and colleagues that highlighted a moderate effect in terms of uncertainty and psychological distress. Using three predictors, a total of 43 participants were needed to detect a medium effect size $f = .45$, and power set at 95%.

Aim 4

To determine both group level and individual level change of the psychological variables over time (following diagnosis, 3-months and 6-months).

Analyses

Repeated measures ANOVA was used to determine group level change and Jacobson and Truax's Reliable Change Index was used to determine if any individual level change occurred.

Power Calculation

Again, using G*Power software 3.1, another a priori sample size calculation was completed for the repeated measures analysis to determine how many participants were needed to detect significance change over time and a moderate effect. Within subjects

repeated measures ANOVA was the analyses used and a medium effect was used based on (Cohen) and longitudinal research conducted by Liao and colleagues. Over 3 different points, using the probability level of $p<0.05$, power set at 95%, and the estimated effect size $f = 0.40$, the calculation indicated that 18 participants were required to accurately determine if change occurred over time.

3.16 Ethical considerations

Ethical Considerations

Potential Risks and Benefits to Human Subjects

It was possible that participants may become distressed or difficulties may be raised for them whilst completing the questionnaires, but the researchers did assess the risk of any potential harm to be low. The proposed measures for this research study have not been reported to cause psychological or physical distress. If the participant demonstrated any signs of distress, the research team would have gained consent from the participant to discuss matters with the relevant members(s) of the clinical team, such as: treating Hematologist, Clinical Nurse Specialist, or General Practitioner. Aside from psychological distress, it was also important for the investigators to remain cognizant of physical difficulties which may have an impact on the participants. Although the individuals who were recruited to participate in the study were not at a level of acute illness to result in a more direct form of intervention for their CLL or LGL, there still could be physical symptoms that could have resulted in the participants experiencing a level of impairment or distress. Therefore, it was important for the investigators to verbally consult with the participants to ensure that the undertaking of completing the necessary questionnaires was not proving to be too physical taxing for them. Participants

were informed that they would receive no direct benefit from this study or receive any financial payment. However, participants were informed that taking part may provide insight and help those individuals seeking assistance with their potential levels of anxiety, depression, and trauma as it applies to their diagnosis of CLL or LGL whilst on the watch and wait pathway of standard care.

Ethical Approval

Ethics for the study were initially submitted to NHS East of England – Essex Research Committee (REC) in July 2016, and were reviewed by the REC in September 2016. The REC deemed that changes needed be made to the initial protocol and resubmitted for further evaluation. The principle investigator was also requested to meet before the REC to discuss the ethical implications of the study, and at this point further recommendations were made by the committee to amend certain aspects of the proposed research. Following the recommendations and subsequent amendments, the investigators received ethical approval from the REC and the Health Research Authority in October 2016, which allowed the investigators to begin recruitment and data collection. The ethics approval form can be found in the appendices; this form includes the REC reference number as well as the Integrated Research Application System (IRAS) project ID (Appendices - B).

3.17 Dissemination

Dissemination of Work

Dissemination of the research is a critical aspect of any research project and it is essential that the method of dissemination be appropriate and attuned to the audience who will be accessing the research. Therefore, the practical needs, level of knowledge, and the

language and terminology of the target audience must be considered.

Community Dissemination

Service Users and Participants

Following completion of the research, the findings and outcomes from the project should be presented to those who participated in the research study and should be accessible to those who have a diagnosis of CLL or LGL. In person dissemination should be considered a strategy, such as hosting a community event where the research is presented in a manner that is accessible to those who may not have psychological knowledge.

NHS community newsletters (online) or brochures may be another method of dissemination for those individuals who have a diagnosis of CLL or LGL. Again, the brochure or newsletter must be written and organized in a manner that is accessible and free of psychological or academic jargon in order for those community members to understand the research question, the process, and the conclusions drawn.

Academic Dissemination

Consultant Hematologists and Clinical Research Nurses

A brief research report and summary of the findings and the impact of said findings should be developed for the consultant hematologists and research nurses who work with patients with CLL or LGL.

University of Essex Post-Graduate Research Day(s)

The department of Health and Human Sciences at the University of Essex holds an annual research day where research is presented and discussed amongst the post-graduate students and University lecturers. As part of the Doctorate in Clinical Psychology

Program, it is required during year one and year two that trainees engage in a poster presentation and interact with other students who are conducting research in the department. In the final year of training, trainees are required to do a formal presentation about their specific area of research, which may include the research process, the methodology used to complete the study, and discuss any preliminary results, as well as the potential impact of the research.

Peer-Reviewed Journals and Conference Abstracts

As the research deals with the psychological difficulties (symptoms of anxiety, depression, and trauma) in those patients with CLL or LGL, the research should aim to be published in journals that have a focus on Health Psychology. Journals such as: *The Journal of Health Psychology, Health Psychology, The International Journal of Clinical Health Psychology, Psychology and Health* would be appropriate to target for publication. Conferences such as the yearly European Health Psychology Society and the International Society of Hematology provide an opportunity to present an abstract or poster to two different disciplines.

3.18 Data Collection and Participant Information

Sampling

Non-probability, purposive sampling will be used in order to recruit patients who have been newly diagnosed (<3months) with CLL or LGL, who are being followed up on standard pathway of watch and wait.

Data Collection

Participants were recruited and data was collected from patients who were attending Colchester General Hospital for treatment. Specifically, the researcher nurses from the Hematology Department conducted all of the participant recruitment, data collection, and also ensured that questionnaires were filled out correctly and collected at each given time point. For the purpose of this thesis, data was collected from October 2016 until January 2018. However, it is important to note that as the study was longitudinal in design, all of the time points had not been collected from all of the participants who had been recruited, and therefore, data was still being collected by the other members of the research team. As was outlined in the participant information sheet, participants knew that data could be withdrawn from the study, and that the participants could request that the data that they had submitted not be used for the purposes of this research project. At four separate time-points during the data collection process, the data was input on a password-protected computer and uploaded onto SPSS version 21 for preliminary analyses.

3.19 Demographic Information

In total, 33 participants were recruited to participate in the study from September 2016 until January 2018. Out of the 33 total participants, only 3 completed the questionnaires at time 4 (12-months follow-up). There were 23 participants who completed the data at time 3 (6-months), 26 participants who completed the questionnaires at time 2 (3-months), and 33 participants who completed the questionnaires at time-1 (< 3-months).

Table 4*: Participant Age*

Mean Age (Yrs) (n = 33)	Standard Deviation (S.D)
70.48	11.54

Table 5: *Gender*

Gender (n = 33)	Frequency	Percentage (%)
Male	19	57.6 %
Female	14	424 %

As illustrated in the two tables above, the average age of the participants in the study was approximately 70 years old, which is in keeping with the older population who are diagnosed with CLL or LGL. The youngest participant in the study was 50 years of age and the oldest participant in the study was 89 years of age. The average age and the frequency of men and women that were recruited into the study were close to keeping with recent CLL demographic data from the UK. Cancer Research UK reported that the largest proportion of individuals diagnosed with CLL fall within the age range of 70 – 74 and the percentage of men diagnosed was estimated to be 62% in comparison to the percentage of women diagnosed was estimated to be 38% (Cancer Research UK, 2014).

Table 6: *Diagnosis (CLL or LGL)*

Diagnosis (n = 33)	Frequency	Percentage (%)
Chronic Lymphocytic Leukemia (Watch and Wait)	25	75.8 %
Low Grade Lymphoma (Watch and Wait)	8	24.2 %

Over three-quarters of the participants in the present study had a diagnosis of CLL and were placed on watch and wait as a form of intervention.

Table 7: *Ethnic Composition of Participants*

Ethnicity	Frequency	Percentage (%)	Valid Percentage (%)
White British	28	82.4 %	96.6 %
White Irish	0	0	0
Black African	0	0	0
Black Caribbean	0	0	0
White and Black African	0	0	0
White and Black Caribbean	0	0	0
Indian	0	0	0
Pakistani	0	0	0
Bangladeshi	0	0	0
Chinese	0	0	0
Other	1	2.9 %	3.4 %
Missing	5	14.7 %	0

Essentially, the entire sample was of "White British" ethnicity and only one other individual identified as "other". In addition, 4 participants selected to not fill out the ethnicity portion of the demographic data sheet and were therefore recorded as missing data. The overall ethnic composition of the study does compare with the UK census data from 2011 of the area from which the population were drawn (Colchester), where 92% of the population identified as being "White" (UK Census Data, 2011). It is important to note that such a high proportion of "White British" individuals who participated in the study are not indicative of the wider ethnic diversity of those presenting with CLL or LGL. Although research has reported that CLL and LGL are higher in those individuals who identify as being White or Black in comparison to other ethnicities, it is not as high as reported in those study (Cancer Research UK, 2014), and is therefore a limitation in terms of the generalizability of the data.

Table 8*: Marital Status of Participants*

Marital Status (n = 33)	Frequency	Percentage (%)
Married	21	61.8 %
Single	4	11.8 %
Divorced	3	8.8 %
Widowed	5	14.7 %

The largest proportion of individuals within the current study were married and the second largest proportion of individuals were widowed.

Table 9: *Educational Level of Participants*

Educational Level (n = 33)	Frequency	Percentage (%)
Secondary	24	72.7 %
Post-Secondary	8	23.5 %
Graduate	1	2.9%

Of the total 31 participants, the largest proportion had completed secondary level education, and second largest proportion of the sample had completed post-secondary education.

Table 10: *Current Employment Status*

Current Employment Status (n = 33)	Frequency	Percentage (%)
Currently Working	10	30.3 %
Retired	22	66.7 %

Given the mean age of the sample, 71 years old, it is in keeping that two-thirds of the participants who had been recruited for this study are no longer employed and are currently retired.

Finally, the sample from which our current population was drawn from (33 total participants) was representative of those individuals who were presenting to the CGH with CLL or LGL. Specifically, throughout the recruitment process, 41 individuals were approached to participate. Out of the 41 individuals who were approached to participate, 5 individuals declined and 3 individuals were deemed ineligible to participate as their physical symptoms associated with the diagnoses were deemed to be too serious.

4.0 Results Chapter

4.1 Results Chapter Overview

This chapter will provide an overall analysis of the data that has been collected and describe the different analyses used to answer the aims that were set out in the introduction chapter. In addition, the results chapter has made interpretations of the findings and how these interpretations relate to the overall aims of the research. The results in this chapter will describe the data collected from questionnaires administered in this longitudinal research, over the 6-month period of data collection. The results chapter will initially look at the descriptive data at time-1, to determine levels of uncertainty in illness, anxiety, depression, and posttraumatic stress measures, following a diagnosis of CLL or LGL. The analyses will be presented (correlation, multiple regressions, repeated measures ANOVA) and will identify how the results from these analyses are in keeping with the overall aims of the research study. Finally, an overall summary of the results will be presented. All of the data were analyzed using Statistical Package for the Social Sciences Version 21 (SPSS v.21).

4.2 Data Input

Data were input at the Colchester General Hospital where the data were transferred from the paper copies of the questionnaires to a password protected Microsoft Word document. While the data was being input onto the personal computer of the researcher, the data were checked for missing items and incorrect scoring. At different intervals throughout the data collection process, the data were input to SPSS v.21, where again data were screened to ensure that all the correct entries had been made.

4.3 Internal Reliability of Measure

Table 11: *Internal Reliability of Scales and Subscales: Time Point 1 (following diagnosis), Time Point 2 (3-Months), and Time Point 3 (6-months)*

	Cronbach's Alpha		
Scales	Time-1 (*N* = 33)	Time-2 (*N* = 26)	Time-3 (*N* = 23)
HADS – Anxiety	.902	.935	.917
HADS – Depression	.791	.880	.810
HADS – Total	.900	.943	.918
IES-R – Intrusion	.911	.945	.961
IES-R - Avoidance	.885	.910	.831
IES-R - Hyperarousal	.888	.907	.921
IES-R – Total	.931	.960	.970
MIUS-SF	.734	.791	.869

HADS Hospital Anxiety and Depression Scale, IES Impact of Event Scale - Revised, MIUS – SF Mishel's Uncertainty in Illness Scale – Short Form

Internal reliability of all of the scales and subscales that were used in the analyses were calculated using Cronbach's alpha scores, as in the absence of reliability, it is impossible to have validity in terms of the scores of a scale (Fields, 2014). All of the subscales have Cronbach's greater than 0.7 and were therefore considered as having good internal reliability (Fields, 2013 & Gray & Kinnear, 2014).

4.4 Parametric Analysis

Normality of Variables

Prior to inspecting the descriptive data, the data were explored to determine whether it met the assumptions for parametric analyses and to determine the most accurate measure of central tendency. Data for variables at time-1 were explored (anxiety, depression, HADS total, intrusion, avoidance, hyperarousal, IES-R total, and uncertainty), and data were also explored for each variable at each time point (following diagnosis, 3-months,

6-months). To determine whether the data met assumptions, “Normality test with plots” were run, and for a variable to be normally distributed the z-scores must fall within the range of -1.96 and +1.96 (Fields, 2013). Upon inspecting the z-scores, it was clear that a number of the variables, at some time-points, fell out of the required range. Therefore, the histograms, box plots, and q-q plots were examined which also indicated a number of the variables had positively skewed distributions, as well as being heavily tailed in regards to kurtosis (Appendices – C and D).

4.5 Psychological Variables at Time-1

Aim 1

Identify levels of anxiety, depression and trauma following a diagnosis of CLL or LGL and subsequently being placed on the standard pathway of watch and wait:

Descriptive Data on Questionnaire Scales and Subscales

One of the goals, as outlined in the methods chapter, was to illustrate the descriptive data (measure of central tendency) for all of the questionnaires that were administered to participants over the different time points of the study.

Table 12: *Median for Scales and Subscales and Time Point 1 (following diagnosis) N = 33*

Scale and Subscale	Median	Clinical Cut-Off	% > Clinical Cut-Off
HADS – Anxiety	5	8	43.8%
HADS – Depression	3	8	11.7%
HADS – Total	9	-	
IES-R – Intrusion	8	-	
IES-R – Avoidance	9	-	
IES-R – Hyperarousal	3	-	
IES-R – Total	20	24	44%
MIUS-SF	11	11.7	41%

HADS Hospital Anxiety and Depression Scale, IES Impact of Event Scale-Revised, MIUS – SF Mishel's Uncertainty in Illness Scale – Short Form

Data were collected from 33 participants at time point1 and the median and clinical cut-off scores can be seen in Table 12. Scores on the HADS anxiety and depression scales between 0-7 would be considered to be in the normal range, a score between 8-10 would be considered to be mild and borderline level of anxiety or depression, scores between 11-14 would suggest moderate level of anxiety or depression, and scores between 15-21 would be considered to be a severe level of anxiety or depression (Snaith and Zigmond, 1994). The median score for time-1anxiety was 5, and the median score for time-1 depression was 3; both subscales of the HADS. Although the median score is outside of the clinical norm, 43% of the participants would have been considered to be in the clinical range at time-1for the anxiety outcome, and approximately 12% would have been in the clinical range for the depression. As 43% of the participants would be considered to be above the clinical cut-off for anxiety, one would hypothesize that the diagnosis of CLL or LGL had an impact on these individuals' level of anxiety.

In regards to the IES-R, an overall score higher than 24 would indicate symptoms that are associated with post-traumatic stress, a score of 33 and higher would identify an individual who is experiencing post-traumatic stress disorder, and a score of 37 and above would be considered to be a high level of post-traumatic stress (Weiss & Marmar, 1997). The subscale scores (avoidance, hyper-arousal, intrusion) were also recorded, but there are no clear guidelines on cut-offs in the literature, and it is suggested that clinicians use them for identifying specific clinical targets, or for using them as indicators of change over time, as is being attempted in this present study (Christianson & Marren, 2012). The median score for the participants at time-1 was 20, but 44% of participants would have been considered to be in the mild range for experiencing difficulties related to posttraumatic stress. An important percentage was that out of the 33 participants at time-1, 27% would have been in the severe range for posttraumatic stress as measured by the IES-R, which could be related to the impact that a diagnosis of CLL or LGL can have on an individual.

Research that has been undertaken using the MIUS has suggested that a score greater than 50% in relation to the total score is considered indicative of a moderate level of uncertainty in illness; however, recent research conducted by Hagan and Colleagues (2014) in individuals who have received a diagnosis of breast cancer, and that used the MIUS-SF, suggested that 47%, or a score of greater than or equal to11.7 should be considered to be a moderate level of uncertainty in illness. The median score for the MIUS-SF was 11, which is just below the clinical cut-off for moderate level of anxiety as suggested by Hagan and colleagues (2014). Yet again, and similar to the anxiety scores and IES-R total scores, the percentage of individuals who were over the recommended

clinical cut-off for uncertainty in illness was 41%, which suggests that almost half of the participants were experiencing moderate levels of uncertainty in illness following their initial diagnosis of CLL or LGL.

4.6 Associations between Uncertainty and Psychological Distress following Diagnosis (Time-1)

Aim 2

The second aim of the study was to determine if relationships existed between the psychological variables following an initial diagnosis of CLL or LGL and being placed on watch and wait.

Assumptions: Correlation Analysis

Normality of Variables

As the initial data indicated above, the time-1 data for the psychological variables were positively skewed and for the correlation analyses, the Shapiro-Wilks statistic was also taken into account, highlighting a number of significant values which confirmed that the data violated the assumption for normality. Out of the 24 possible variables, 15 had statistically significant values ($p < .05$) on the Shapiro-Wilks test for normality, and only two of the dependent variables (avoidance and uncertainty in illness) had non-significant values at each one of the three time points (Appendices - C).

Outliers - Log Transformation

Following the initial inspections, the box-blots were explored to look for outliers and it was clear a number of the dependent variables had extreme values, which could have an impact on the normality of the data. The outliers were converted to the means of the

particular dependent variable, at the particular time point. Once these outliers were identified and converted, the data remained positively skewed, violating the assumptions for normality, and again, only avoidance and uncertainty in illness had non-significant values based on the Shapiro-Wilks test at each time point.

The data were then $\log_{10}$ transformed to attempt to make the data less skewed and in the hope of meeting the assumption to run the parametric analysis (Fields, 2013; Gray & Kinnear. 2012). After log transforming the data, the data were explored using the same method described above, "normality tests with plots", and the different variables were examined to determine if they were normally distributed and met the assumptions for parametric analysis. Of the 6 log transformed dependent variables that were explored, 4 of them met the assumptions for being normally distributed, while also having non-significant values on the Shapiro-Wilks Test (Appendices - E).

Assumption: Linearity

Following transforming the data, the variables were explored to determine which variables had a linear relationship, so one could determine the strength and shape of that relationship (Fields, 2013). To determine whether a linear relationship existed between the variables, scatter plots were examined between the variables and each time point (time-1, 3-months, 6-months). Scatterplots were included for those relationships that were deemed to be linear (Appendices - F). From examining the variables at each time point it was clear relationships existed between the variables. At time-1, a number of relationships between variables met the assumption for linearity (anxiety – intrusion, anxiety-avoidance, anxiety – uncertainty in illness, HADS total – intrusion, HADS total -

IES-R total, intrusion – hyperarousal, intrusion – uncertainty in illness, avoidance – IES-R total, hyperarousal – uncertainty in illness and IES-R total – uncertainty in illness).

Table 13: *Associations between Psychological Variables at Time-1, N = 33*

	Anx*	Dep*	HADS total	Intrusion	Avoidance	Hyperarousal	IES-R Total	Uncertainty in illness
Anxiety	1	.526*	.720**	.618**	.587**	.124	.624**	.349*
Depression		1	.406*	.159	.017	.032	.160	.184
HADS total	-	-	1	.660**	.419*	.075	.562**	.339
Intrusion	-	-	-	1	.551**	.174	.907**	.513**
Avoidance	-	-	-	-	1	.073	.693**	.196
Hyperarousal	-	-	-	-	-	1	.100	.201
IES-R total	-	-	-	-	-	-	1	.311
Uncertainty in illness	-	-	-	-	-	-	-	1

**p < 0.05, ** p < 0.01*

Time 1: Following Diagnosis

Due to the fact that the hyperarousal and uncertainty in illness time-1 data were still skewed following the transformation of the data, the non-parametric equivalent, Spearman's r correlation coefficient was used to assess the relationship whenever those 2 variables were being examined. Of specific interest was the relationship between an individual's uncertainty in illness and the other psychological variables (anxiety, depression, traumatic stress).

The relationship between variables at time-1, following a diagnosis of CLL or LGL are shown in Table 13, and one can see that there are a number of strong correlations

between these variables. The participants' level of anxiety, as measured by the HADS questionnaire was strongly associated to the psychological construct of intrusion as it relates to traumatic stress, highlighting that higher levels of anxiety were associated with higher levels of intrusion. In addition to intrusion, the psychological construct of avoidance as it relates to traumatic stress was strongly associated with anxiety and therefore, as one of these indicators of distress increased, so would the other. As expected, given the relationship between anxiety and the two subscales of the IES-R (avoidance and intrusion), anxiety was also strongly related to IES-R total score. The only psychological construct associated with traumatic stress that anxiety was not associated with at time-1 was hyperarousal. Lastly, anxiety was also moderately related (r = .349) to uncertainty in illness, as measured by the MIUS-SF. Again, such a positive relationship indicates that as either of these indicators of psychological distress increase, one would expect the other to increase as well.

The HADS-total score showed a similar pattern of correlations with the IES-R and uncertainty in illness. Specifically, the HADS was strongly associated with intrusion and the IES-R total score and was also moderately associated with avoidance. Similar to anxiety, there was no statistically significant relationship that was detected between hyperarousal and the HADS total score. In regards to Mishel's theory of uncertainty in relation to one's illness and HADS total score, there was not a statistically significant association between the two variables.

As expected, time-1 scores for the subscales of avoidance and intrusion were all strongly associated with the IES-R total score. In addition, the subscales intrusion and avoidance were strongly related, but no statistically significant relationship was detected between

either intrusion or avoidance and hyperarousal. Essentially, the above associations illustrate that as the two subscales related to traumatic stress increase one would also expect the overall score for traumatic stress as measured by the IES-R to increase. It must be noted that the hyperarousal subscale was not related to the other subscales, which is not what one would initially expect. Upon reviewing the raw data, it is clear that the items that dealt with hyperarousal were detected to be much lower than the other 2 subscales. One may hypothesize that any physical discomfort experienced by the patient diagnosed with cancer may be attributed to their physical illness as opposed to experiences related to a traumatic event and therefore not rated as highly.

In regards to uncertainty in illness as measured by MIUS-SF, there was only one statistically significant association related to traumatic stress, avoidance, but no significant association was identified for hyperarousal, intrusion, and IES-R total score with uncertainty in illness.

4.7 Multiple Regression Analyses

Aim 3

The third aim of the current study was to determine which of the psychological constructs at time-1 would be predictive of psychological distress at time-3, 6-months following initial diagnosis of CLL or LGL. To complete this aim, multiple regression analyses were completed with the psychological variables of uncertainty in illness, anxiety, depression, and posttraumatic stress.

Assumptions: Multiple Regression Analyses

The assumptions for regression analyses differ in comparison to the earlier analyses completed in this study, as one is attempting to determine if a linear relationship exists between the outcome and predictor variables. One must also determine multivariate normality, whether the residuals are normally distributed. It is also important to examine whether there is multi-collinearity between the independent variables. Finally, one needs to check for homoscedasticity) and this can be done by examining a scatter plot of the residuals versus the predicted values.

Assumption: Linearity between Outcome and Predictor Variables

The data that had not been log-transformed were initially inspected to determine if linear relationships existed between the outcome and predictor variables; however, upon inspection, and in comparison to the log-transformed data, it was determined that the log-transformed data were better suited for the multiple regression analyses (Fields, 2013). Scatterplots were initially examined to see if the outcome variable had a linear relationship with the predictor variables, from the inspection, it was determined that the uncertainty in illness at 6-months was the only outcome variable in comparison to the other psychological measures of distress that did not have a linear relationship with the predictor variables (anxiety time-1, depression time-1, IES-R time-1). Therefore, 3 multiple regression models were run, where anxiety at 6-months was the outcome variable and uncertainty in illness, depression, and IES-R total score at time-1 were the predictors. A second multiple regression was completed, where IES-R total score at 6-months was the outcome variable and uncertainty in illness, depression, and anxiety at time-1 were the predictor variables. A third multiple regression where depression at 6-months was the outcome variable and uncertainty in illness, anxiety, and IES-R total

score at time-1, were the predictor variables. Also, as there were no clear theoretical guidelines, due to the fact that these specific psychological constructs of uncertainty in illness, posttraumatic stress, anxiety and depression had been used in individuals with CLL or LGL on watch and wait, forced entry was used for inputting the data into the regression models.

4.7.1 Multiple Regression 1: Trauma Outcome Variable

Assumptions: Linearity, Homoscedasticity, Normality, Multi-Collinearity

As the data met the initial assumptions for linearity and unusual cases, the initial regression was run and further assumptions were investigated to determine the suitability of the model. Visual inspection of the P-P plot and of the histogram for the outcome variable residuals (IES-R total 6-months) indicated a normal distribution (Appendices - G). The lack of a curved formation when inspecting the partial plots illustrated the linearity of the data and indicated a positive relationship between uncertainty in illness and anxiety at time-1. A *ZRESID vs *ZPRED graph was generated, which highlighted a sufficient array of scatter plots, with no data point above or below +3 or -3, providing confirmation that the assumption for homoscedasticity had been met (Appendices - G) (Fields, 2013). In regards to multicollinearity, there were no strong correlations between the predictor variables and the mean variance inflation factor (VIF) was 1.15, which does not violate the assumption of multicollinearity as set out by Fields (2013).

Independence

In order to determine independence, the Durbin-Watson test statistic was used. The Durbin-Watson test statistic tests for serial correlations between errors and the value in

output was 2.06, which falls within the recommended boundaries of >1 and <3 (Durbin & Watson, 1951; Fields, 2013).

As the assumptions were met, a multiple linear regression was calculated in order to determine if one could predict posttraumatic stress at 6-months based on time-1 levels of depression, anxiety, and uncertainty in illness. A non-significant regression equation was found (F (3,19) = 2.133, p = 1.30, with an R^2 .252. As a non-significant regression equation was found, the model was not further explored and, based on this data, one can draw the conclusion that anxiety, depression, and uncertainty in illness at time-1 is not predictive of posttraumatic stress at 6-months following diagnosis of CLL or LGL.

4.7.2 Multiple Regression 2: Anxiety Outcome Variable

Assumptions: Linearity, Homoscedasticity, Normality, Multi-Collinearity

Yet again, the data met the initial assumptions for linearity and unusual cases, the regression was run, and further assumptions were investigated to determine the suitability of the model. Visual inspection of the P-P plot and of the histogram for the outcome variable residuals (anxiety 6-months) indicated a normal distribution (Appendices - G). The lack of a curved formation when inspecting the partial plots illustrated the linearity of the data and indicated a positive relationship between uncertainty in illness and anxiety at time-1. A *ZRESID vs *ZPRED graph was generated, which highlighted a sufficient array of scatter plots, with no data point above or below +3 or -3, providing confirmation that the assumption for homoscedasticity had been met (Appendices - G) (Fields, 2013). When checking the assumption for multicollinearity, there were no strong correlations between the predictor variables and the mean variance inflation factor (VIF) was 1.2, and again, this does not violate the assumption (Fields, 2013).

Independence

The Durbin-Watson test statistic tests for serial correlations between errors and the value in output was 1.76, which once again falls within the recommended boundaries of >1 and <3 (Durbin & Watson, 1951; Fields, 2013).

Again, as the above assumptions were met, a multiple linear regression was calculated in order to determine if one could predict anxiety at 6-months based on initial levels of IESR-total score, depression, and uncertainty in illness. A significant regression equation was found and the results of the regression indicate that the three predictors, predicted 62% of the variance, (R^2 = .622, F (3,22) = 1.88, p = .00). It was found that IES-R total score at time-1 predicted anxiety at 6-months (ß = .810, p = .00). In addition to IES-R total score, it was also found that depression score at time-1 predicted anxiety at 6-months (ß = .416, p = .012).

4.7.3 Multiple Regression 3: Depression Outcome Variable

Assumptions: Linearity, Homoscedasticity, Normality, Multi-Collinearity

Visual inspection of the P-P plot and of the histogram for the outcome variable residuals (depression 6-months) indicated a normal distribution (Appendices - G). The lack of a curved formation when inspecting the partial plots illustrated the linearity of the data and indicated a positive relationship between uncertainty in illness and anxiety at time-1. A *ZRESID vs *ZPRED graph was generated, which highlighted a sufficient array of scatter plots, with no data point above or below +3 or -3, providing confirmation that the assumption for homoscedasticity had been met (Appendices - G) (Fields, 2013**.** Finally, checking for multicollinearity, there were no strong correlations between the predictor

variables and the mean variance inflation factor (VIF) was 1.41 and again, this does not violate the assumption (Fields, 2013).

Independence

The Durbin-Watson test statistic tests for serial correlations between errors and the value in output was 1.59, which once again falls within the recommended boundaries of >1 and <3 (Durbin & Watson, 1951; Fields, 2013).

The above assumptions were met; a multiple linear regression was calculated in order to determine if one could predict depression 6-months based on initial levels of IESR-total score, anxiety, and uncertainty in illness. Similar to anxiety outcome multiple regression, a significant regression equation was found and the results of the regression indicate that the three predictors predicted 33% of the variance, (R^2 = .334, F (3,22) = 4.68, p = .013). It was also found that uncertainty in illness, as measured by the MIUS-SF, significantly predicted depression at 6-months (ß = .401, p = .014).

4.7.4 Summary of Multiple Regression Results

The various regression models highlighted that for both anxiety and depression at 6-months' time there were specific psychological variables that acted as significant predictors at time-1. Specifically, uncertainty in illness, depression, and IES-R total score were all seen to be predictive of different psychological outcomes. The highest percentage of variance was for the regression model when anxiety was the outcome variable, and both depression and IES-R total score were statistically significant predictors. The variance for when depression was the outcome variable was half of what it was for anxiety at 6-months, and uncertainty in illness was a statistically significant

factor. Finally, when IES-R total at 6-months was the outcome variable, the regression model was not statically significant. Overall, it was determined that anxiety and depression at 6-months can be predicted by a number of psychological variables at time-1 within this data set.

4.8 Change over Time: Psychological Variables

Aim 4

The fourth aim of this research study was to determine if the participants' level of uncertainty in illness, anxiety, depression, and traumatic stress following a diagnosis of CLL or LGL, who have been placed on the watch and wait pathway, would increase or decrease over time.

Time Points

The initial goal of the research was to analyze if a change had occurred over a 12-month period, and data were collected at 4 different time points (time-1, 3-months, 6-months, and 12-months). However, for the purposes of this thesis, and given the specific time-constraints, the researchers collected data for as long as possible, but were unable to collect enough data for participants at 12-months that would allow for meaningful repeated measures analysis. It was therefore decided to use 6-months as the final data collection point for the repeated measures analyses; however, for the individual change analyses, 12-month data were used.

Table 14: *Change Over Time (Means and Standard Deviations)*

Psychological Variable	Mean	Standard Deviation
Anxiety Time-1	.723	.367
Anxiety 3-Months	.750	.308
Anxiety 6- Months	.744	.356
Depression Time-1	.465	.329
Depression 3-Months	.523	.349
Depression 6-Months	.516	.337
HADS Total Time-1	.957	.234
HADS Total 3-Months	.893	.402
HADS Total 6-Months	.931	.360
Intrusion Time-1	.872	.367
Intrusion 3-Months	.842	.437
Intrusion 6-Months	.821	.379
Avoidance Time-1	.912	.352
Avoidance 3-Months	.940	.343
Avoidance 6-Months	.918	.355
Hyperarousal Time-1	.737	.418
Hyperarousal 3-Months	.582	.452
Hyperarousal 6-Months	.570	.448
IES-R Time-1	1.25	.395
IES-R 3-Months	1.29	.387
IES-R 6-Months	1.22	.396
MIUS-SF Time-1	1.02	.128
MIUS-SF 3-Months	1.03	.118
MIUS-SF 6-Months	1.04	.127

Parametric Analysis:

Anxiety (Log Transformed Data) (Following Diagnosis, 3-Months, 6-Months)

A one way within-subjects repeated measures ANOVA was conducted to determine if anxiety levels of participants significantly increased or decreased over the three time points (following diagnosis, 3-months, and 6-months). Prior to determining if a statistically significant result had been found, the assumption of sphericity had to be determined. The assumption of sphericity assumes that the variation within the experimental conditions is relatively similar and that “no two conditions are any more dependent than any other two” (Fields, 2013). To ensure that the repeated measures

ANOVA met the assumption for sphericity, the Maulchy's test of sphericity statistic was checked in the SPSS output and, if the test is statistically significant (p <0.05), one can reject the null hypothesis and accept that the variance of the differences is not equal (Fields, 2013). The Maulchy's test of sphericity statistic in this current analysis was non-significant (p = 0.892), which met the assumption for sphericity. In regards to the repeated measures analysis, there was a non-significant effect of time on the level of anxiety (Wilk's Lambda = 0.986, F (2, 21) = .154, p = 0.859). As this was a non-significant result, no post-hoc analyses were conducted to determine which time point had the greatest impact on change in level of anxiety.

4.8.1 Group Change: Depression Over Time (Following Diagnosis, 3-months, 6-months) (Log Transformed Data)

A one-way repeated measure ANOVA was completed to determine if depression levels as measured by the HADS increased or decreased over the three time points. The Maulchy's test of sphericity statistic in this current repeated measures analysis was non-significant (p = 0.764), which met the assumption for sphericity. The repeated measures analysis indicated that there was a non-significant effect of time on the level of anxiety, (Wilk's Lambda = 0.952, F (2, 21) = 0.538, p = 0.595). Yet again, because the analysis demonstrated a non-significant result, no post-hoc analyses were completed.

4.8.2 Group Change: HADS-Total Over Time (Following Diagnosis, 3-Months, 6-Months) (Log Transformed Data)

Another one-way repeated measures ANOVA was done to determine if the HADS total data changes in any statistically significant way over the three time points. To confirm that the assumption of sphericity had been met, the Maulchy's test statistic was

examined, which indicated a statistically non-significant value (p = .892). Similar to the data with regards to anxiety and depression, there was a non-significant effect of time on HADS total score, (Wilk's Lambda = 0.986, F (2, 21) = 0.154, p = 0.895). Once again, no post-hoc analysis was done, as the results from the repeated measures analysis were non-significant.

4.8.3 Group Change: Avoidance over Time (Following Diagnosis, 3-Months, 6-Months)

As the data for avoidance subscale on the IES-R did not violate the assumptions for normality, it did not require that the data be log-transformed in order to run a parametric analysis, and therefore, the data were analyzed using the means from the initial data. The Maulchy's test statistic was a non-significant value (p = 0.479), meeting the assumption for sphericity. Although the data for avoidance decreased over each time point, the analysis demonstrated a non-significant result, (Wilks-Lambda = 0.942, F (2, 21) = 0.616, p = 0.058). Yet again, as no statistically significant results were demonstrated from the analysis, no post-hoc analysis was required.

4.8.4 Group Change: Intrusion Over Time (Following Diagnosis, 3-Months, 6-Months) (Log Transformed Data)

For the intrusion subscale of the IES-R another within-subjects, repeated measures ANOVA was used to determine if the participants' level of intrusion as it relates to post-traumatic stress increased or decreased over the three time-points. The data met the assumption for sphericity, as Maulchy's test statistic was non-significant (p = 0.827). Similar to the avoidance subscale, the intrusion subscale of the IES-R decreased over the three different time-points, over the 6-month period of data collection; however, this

change was not statistically significant (Wilks Lambda = 0.904, F (2, 21) = 1.104, p = 0.398).

4.8.5 Group Change: Uncertainty in Illness over Time (Following Diagnosis, 3-Months, 6-Months)

Similar to the avoidance subscale, uncertainty in illness as measured by the MIUS-SF did not require the data to be log transformed in order to meet the assumption for normality. The repeated measures analysis used the means from the initial data to determine whether any change occurred over the 6-month time period in regards to the participants' level of uncertainty in illness. The Maulchy's test statistic was a non-significant value (p = 0.479), meeting the assumption for sphericity and, as the mean scores were consistent across each of the three time points, there was no statistically significant change as a result of the independent variable over time, (Wilks Lambda = 0.996, F (2, 21) = 0.44, p = 0.957). Again, similar to the previous non-significant results, uncertainty in illness data was not further explored.

4.9 Non Parametric Analyses: Freidman's ANOVA

As the data for both hyperarousal and IES-R total score did not meet the assumption for normality both in regards to the initial data and also after the data had been log transformed, it was required that non-parametric analysis be used in order to determine if a change occurred over the three time points. Similar to the one way repeated measures ANOVA, the Friedman's ANOVA is used in testing the differences that exist between "conditions", where there are more than two conditions of the same unit, and the units have provided scores in all of the conditions. Specifically, the Freidman's ANOVA is used when the researchers wish to counteract the presence of unusual cases found in the

data and when the data has violated the other assumptions for the repeated measures ANOVA that have been listed previously in this chapter (Fields, 2013; Gray & Kinnear, 2014).

4.9.1 Group Change: Hyperarousal over Time (Following Diagnosis, 3-Months, 6-Months)

To determine if change had occurred in the participants' level of hyperarousal over the 6-month time period, a non-parametric Friedman's ANOVA of differences among repeated measures was used. Although the overall score of hyperarousal as measured by the IES-R decreased over each time point, the data rendered a Chi-Square value of 1.315, which was determined not to be a statistically significant change ($p = 0.518$). Similar to the parametric repeated measures tests that were described above, as the results were non-significant, no post-hoc analyses were required in order to determine which time point had the greatest impact on change in the participants' level of hyperarousal.

4.9.2 Group Change to IES-R Total Score over Time (Following Diagnosis, 3-Months, 6-Months)

For the total score of the IES-R the Friedman's ANOVA was the analysis used to determine if change occurred in regards to the participants' level of post-traumatic stress. The overall score on the IES-R decreased over the three time points during the 6-month data collection period, and the data demonstrated a Chi-Square value of 7.292 that was determined to be statistically significant level of change ($p = 0.019$).

4.9.3 Post-Hoc Analysis: Wilcoxon Signed-Rank Test

As the data highlighted a significant level of change over the three time-points, post-hoc

analyses were done in order to specifically determine at which time point the statistically significant change had occurred. In order to determine where the change occurred, Wilcoxon's signed-rank test was used. The Wilcoxon signed-rank test does not assume that the data is normally distributed and it is considered to be the non-parametric equivalent to the dependent t-test. Firstly, the Wilcoxon signed-rank test was used to determine if the statistically significant change occurred between time-1 IES-R total data and 3-months IES-R total data. The results from the analysis indicated that scores increased slightly from time-1 to 3-months and were not statistically significant. The test was used again to determine if a difference between the scores at time-1 and 6-months following a diagnosis of CLL or LGL were significantly different and the results demonstrated a statistically significant change ($p = 0.001$). A final Wilcoxon signed-rank test was used in order to determine if a statistically significant change occurred in IES-R total from 3-months to 6-months following diagnosis of CLL or LGL. The results from this analysis also demonstrated a statistically significant change ($p = 0.039$). When evaluating the data in a longitudinal frame, it is clear that a statistically significant decrease in participants' post-traumatic stress as measured by the IES-R occurred between 3-months post diagnosis to 6-months post diagnosis.

4.9.4 Summary of Group Change over Time Data

The above analyses indicate that there was not much group change that occurred over time in relation to the psychological constructs that were being used in this research. Specifically, out of the 8 constructs that were measured, 7 did not show any statistically significant change using both the parametric and non-parametric analysis. However, the IES-R total score that includes all of the subscales (avoidance, hyperarousal, intrusion)

demonstrated a significant change from 3-months to 6-months following the participants' diagnosis of CLL or LGL and after being placed on watch and wait pathway. Although post-traumatic stress as measured by the IES-R decreased over time, the results from the repeated measures and Freidman's ANOVA do not support the initial hypothesis that psychological distress would decrease over-time following an individual's initial diagnosis.

4.10 Individual Change over Time to Psychological Variables

Due to the relatively small sample, and that the mean data may not be indicative of change over time, the Jacobson and Truax (1991) methods for calculating clinically and reliably significant change were also used in order to determine level of change in the participants. Jacobson and Truax's (1991) reliable change index (RCI) was used in order to determine more individual change that occurred in relation to the independent variable: time. In addition to exploring individual change as opposed to mean change, this method allowed the exanimation of the data from 6-months to 12 months. Table 16 shows that reliable and clinical change outcomes can fall into one of four categories (Wise, 2004). The data were analyzed by using the Leeds Reliable Change Index Calculator (Agostinis, Morley, & Dowzer, 2008).

Table 15: *Reliable and Clinically Significant Change Outcomes*

Recovered	Reliable change is significant and the individual has passed the normative score of the measure.
Improved but not recovered	Reliable change is significant, but the participant remains in the "dysfunctional" range.
No change	RCI is not significant.
Deterioration	Reliable change, but worsening of scores.

4.10.1 Reliable and Clinically Significant Change (RCSC)

HADS Total, Anxiety Subscale, Depression Subscale

When attempting to determine RCSC it is important to use normative data (means and standard deviations) of a population that best represents the population used in one's research. As the current population are individuals who have been diagnosed with CLL or LGL, and not a mental health population, and it was attempted to find data on the HADS questionnaire that had been validated in a population with individual with CLL or LGL. However, there was no data for the HADS on individuals with a diagnosis of CLL or LGL, and therefore data from a large scale study on individuals with cancer were used to produce normative data for the HADS in a cancer population (Osborne, Elsworth & Hopper, 2003). Jacobson and Truax also indicate three methods one can use in assessing RCSC, and as there are normative data for the cancer or clinical group and the comparison group, criterion c is recommended; wherein, the individual level of functioning should move the individual closer to the mean of the normative group rather than the mean of the clinical group (Agostinis, Morley, & Dowzer, 2008).

Table 16: *Means and Standard Deviation Cancer for Normative Population*

	Cancer Population (Cronbach's Alpha)		General Population (Cronbach's alpha)	
Variable	Mean	SD	Mean	SD
Anxiety	6.73	4.40	6.14 (0.82)	3.46
Depression	3.88	3.40	3.68 (0.77)	3.07
HADS-Total	11 (0.90)	3.90	9 (0.86)	2.50

Table 17: *Reliable and Clinical Pre and Post Effect Size (Anxiety, Depression, and HADS-total)*

Variable (Time)	Pre Mean (SD)	Post Mean (SD)	Effect Size
Anxiety (time-1 – 3 Months)	7.35 (5.30)	7.04 (4.99)	0.06
Anxiety (3 Months – 6 Months)	6.91 (5.28)	7.17 (4.80)	-0.05
Anxiety (6 Months – 12 Months)	4.33 (3.79)	3.00 (2.65)	0.35
Anxiety (time-1 – 6 Months)	7.17 (5.20)	7.17 (4.80)	0.00
Depression time-1– 3 Months)	3.42 (3.43)	4.31 (4.09)	-0.27
Depression (3 Months – 6 Months)	4.43 (4.09)	3.65 (3.48)	0.20
Depression (6 Months – 12 Months)	2.00 (1.73)	2.33 (2.31)	-0.19
Depression (time-1 – 6 Months)	3.70 (3.43)	3.65 (3.48)	0.05
HADS (time-1 – 3 Months)	10.15 (5.55)	11.19 (8.72)	-0.20
HADS (3 Months – 6 Months)	11.17 (8.72)	11.30 (8.32)	-0.01
HADS (6 Months – 3 Months)	6.33 (4.73)	5.33 (4.04)	0.21
HADS (time-1 – 6 Months)	10.17 (5.3)	11.30 (8.32)	-0.20

Table 18: *Individual Change: HADS (Anxiety)*

ID	Time-1 – 3-Months	3-Months – 6-Months	Time-1- 6-Months	6-Months – 12-Months
1	Improve (CSC)	No change	No change	No change
2	No change	No change	No change	No change
3	No change	Improve	Improve	No change
4	Deteriorate	Improve	No change	
5	No change	No change	No change	
6	Improve	No change	No change	
7	No change	No change	No change	
8	Deteriorate	No change	Deteriorate	
9	Improve (CSC)	Deteriorate	No change	
10	No change	No change	Deteriorate	
11	No change	No change	No change	
12	No change	No change	No change	
13	No change	No change	No change	
14	Deteriorate	No change	Deteriorate	
15	No change	No change	No change	
16	No change	No change	No change	
17	No change	No change	Deteriorate	
18	No change	No change	No change	
19	No change	No change	No change	
20	Improve (CSC)	No change	Improve	
21	No change	No change	No change	
22	No change	No change	No change	
23	No change	No change	No change	
24	No change			
25	No change			
26	No change			

Clinical Significant Change (CSC)

Table 19: *Individual Change: HADS (Depression)*

ID	Time-1 – 3-Months	3-Months – 6-Months	Time-1 – 6-Months	6-Months – 12-Months
1	No change	No change	No change	No change
2	No change	No change	No change	No change
3	No change	Improve (CSC)	No change	No change
4	Deteriorate	Improve	No change	
5	No change	No change	No change	
6	No change	No change	No change	
7	No change	No change	No change	
8	No change	No change	No change	
9	Improve (CSC)	No change	Improve	
10	Improve (CSC)	No change	No change	
11	Improve (CSC)	No change	Improve	
12	No change	No change	No change	
13	Deteriorate	No change	No change	
14	Deteriorate	No change	Deteriorate	
15	No change	No change	No change	
16	No change	No change	No change	
17	No change	No change	No change	
18	No change	No change	No change	
19	No change	No change	No change	
20	Deteriorate	No change	No change	
21	Deteriorate	Improve	No change	
22	No change	No change	No change	
23	Deteriorate	No change	No change	
24	Deteriorate			
25	Deteriorate			
26	No change			

Clinical Significant Change (CSC)

As table 17 indicates, the largest effect that occurred was a decrease in anxiety level between 3-months following a diagnosis to 6-months following a diagnosis; but according to Cohen's guidelines on effect size, it would still be considered a small effect (Cohen, 1988). Overall, there was no consistent pattern in regards to whether anxiety increased or decreased over time as measured by the reliable change index. Specifically, there were 2 time points where there was a small effect in terms of psychological distress

decreasing (anxiety 3-months – 6-months and depression 3 – months to 6-months) and there were 3 time points with a small effect where psychological distress increased (depression time-1 – 3 months, HADS total time-1 – 3-months and HADS total time-1to 6-months).

In regards to individual change as indicated by tables 18 and 19, it is clear that there was no real impact of time on an individual's psychological well-being following a diagnosis of CLL or LGL. There were 2 time points where 3 individuals had a clinical significant improvement in regards to anxiety and depression. It is also important to note that there were 4 individuals who deteriorated in terms of level anxiety (time-1 – 6-months). Again, there was no clear pattern in terms of whether levels of anxiety and depression increased or decreased over time, and it is clear that the impact of time as an independent variable had no significant effect on the vast majority of participants.

4.10.2 Reliable and Clinically Significant Change (RCSC)

Post-Traumatic Stress (IES-R Total and Subscales)

As highlighted previously, when attempting to determine RCSC one attempts to find normative data (means and standard deviations) of a population that best represents your population under study, as well as a comparison or community sample. For the IES-R and the subscales (intrusion, avoidance, hyperarousal) there were data that highlighted the means, standard deviations, and alpha coefficient in a population of individuals who have received a diagnosis of cancer, but not a specific diagnosis of CLL or LGL (Mystakidou et al., 2007). When one only has access to the clinical sample data and not the comparison sample, Jacobson and Truax indicate that criterion-a is the only option available when attempting to determine reliable change. When using criterion-a, reliable

change occurs when the data falls out of the range of the clinical population (1.96 standard deviations) (Agostinis, Morley, & Dowzer, 2008).

Table 20: *Mean Standard Deviation IES-R Cancer Population*

	Cancer Population (Cronbach's Alpha)	
Variable	Mean	SD
IES-R Total	24.14 (0.85)	18.34
Avoidance	12.32 (0.77)	4.88
Hyperarousal	7.92 (0.85)	3.48
Intrusion	12.40 (0.72)	4.60

Table 21: *Reliable and Clinical Pre and Post Effect Size (IES-R Total, Intrusion, Avoidance, Hyperarousal)*

Variable (Time)	Pre Mean (SD)	Post Mean (SD)	Effect Size
Intrusion (Time-1 – 3 Months)	10.54 (7.60)	10.31 (8.31)	0.03
Intrusion (3 Months – 6 Months)	10.74 (8.62	9.17 (7.91)	0.18
Intrusion (6 Months – 12 Months)	3.00 (2.65)	3.67 (2.52)	-0.25
Intrusion (Time-1– 6 Months)	10.78 (7.60)	9.17 (7.91)	0.20
Avoidance (Time-1 – 3 Months)	10.15 (6.28)	9.42 (7.39)	0.12
Avoidance (3 Months – 6 Months)	9.52 (7.39)	9.22 (6.54)	0.04
Avoidance (6 Months – 12 Months)	4.67 (4.36)	5.33 (1.53)	-0.16
Avoidance (Time-1 – 6 Months)	10.22 (6.24)	9.22 (6.54)	0.16
Hyperarousal (Time-1 – 3 Months)	5.54 (6.00)	5.38 (5.71)	0.03
Hyperarousal (3 Months – 6 Months)	5.74 (5.89)	4.39 (4.11)	0.23
Hyperarousal (6 Months – 12 Months)	1.67 (1.53)	2.33	-0.44
Hyperarousal (Time-1– 6 Months)	5.96 (6.20)	4.39 (4.11)	0.25
IES-R (Time-1 – 3 Months)	25.00 (16.84)	25.88 (19.05)	-0.03
IES-R (3 Months – 6 Months)	25.35 (19.11)	22.35 (17.01)	0.30
IES-R (6 Months – 12 Months)	9.33 (8.08)	10.33 (5.51)	-0.12
IES-R (Time-1 - 6 Months)	26.30 (17.03)	22.35 (17.01)	0.33

Table 22: *Individual Change: IES-R (Avoidance)*

ID	Time-1 – 3-Months	3-Months – 6-Months	Time-1 – 6-Months	6-Months – 12-Months
1	Improve	No change	Improve	No change
2	No change	No change	No change	No change
3	No change	No change	No change	No change
4	No change	No change	No change	
5	No change	No change	No change	
6	No change	No change	No change	
7	No change	No change	No change	
8	No change	No change	No change	
9	No change	No change	No change	
10	No change	No change	No change	
11	Deteriorate	No change	No change	
12	No change	No change	No change	
13	No change	No change	No change	
14	No change	No change	No change	
15	Improve	No change	No change	
16	No change	No change	No change	
17	No change	No change	No change	
18	No change	No change	No change	
19	No change	No change	No change	
20	No change	No change	No change	
21	No change	No change	No change	
22	Deteriorate	No change	No change	
23	No change	No change	No change	
24	No change			
25	No change			
26	No change			

Clinical Significant Change (CSC)

Table 23: Individual Change: IES-R (Intrusion)

ID	Time-1 – 3-Months	3-Months – 6-Months	Time-1 – 6-Months	6-Months – 12-Months
1	No change	No change	No change	No change
2	No change	No change	No change	No change
3	No change	Improve	Improve	No change
4	No change	Deteriorate	Deteriorate	
5	No change	No change	No change	
6	No change	No change	No change	
7	No change	No change	No change	
8	No change	No change	No change	
9	No change	No change	No change	
10	No change	No change	No change	
11	No change	No change	No change	
12	No change	No change	No change	
13	No change	No change	No change	
14	No change	No change	No change	
15	No change	No change	Improve	
16	No change	No change	No change	
17	No change	No change	No change	
18	No change	No change	No change	
19	No change	No change	No change	
20	No change	No change	No change	
21	Deteriorate	No change	No change	
22	No change	No change	No change	
23	No change	No change	No change	
24	No change			
25	No change			
26	No change			

Clinical Significant Change (CSC)

Table 24: Individual Change: IES-R (Hyperarousal)

ID	Time-1 – 3-Months	3-Months – 6-Months	Time-1 – 6-Months	6-Months – 12-Months
1	Improve (CSC)	No change	No change	No change
2	No change	No change	No change	No change
3	No change	Improve	Improve	No change
4	No change	No change	Improve	
5	No change	No change	No change	
6	No change	No change	No change	
7	No change	No change	No change	
8	No change	No change	No change	
9	No change	No change	No change	
10	No change	No change	No change	
11	No change	No change	No change	
12	Improve	No change	No change	
13	No change	No change	No change	
14	No change	Improve	Improve	
15	No change	No change	Improve	
16	No change	No change	No change	
17	No change	No change	No change	
18	No change	No change	No change	
19	Deteriorate	No change	No change	
20	No change	No change	No change	
21	No change	No change	No change	
22	No change	No change	No change	
23	No change	No change	No change	
24	No change			
25	No change			
26	No change			

Clinical Significant Change (CSC)

As can be seen in Table 21, there were 6 points where there was a small effect due to change in time. The greatest effect was an increase in regards to hyperarousal from 6 months – 12 months; however, there were only 3 people measured between those two time points, and one must be cautious about placing a degree of significance on such a result. There was a small effect of time on the IES-R total score between 3 months – 6 months and also time-1 to 6 months. In addition to IES-R total, there was also a small effect of time on hyperarousal at 2 different time points 3-months – 6-months and time-1

– 6-months. Overall, and in contrast to anxiety and depression, there seemed to be more of a positive impact of time on traumatic stress following a diagnosis of CLL or LGL.

Tables 22, 23, and 24 highlight individual change that occurred in regards to an individual's post-traumatic stress following a diagnosis of CLL or LGL. Similar to anxiety and depression, time did not seem to have a great impact on whether an individual's post-traumatic stress following a diagnosis of CLL or LGL would increase or decrease. There was essentially no change that was clinically significant, but there were 13 people who improved, as opposed to 9 people who deteriorated. Overall, there was no real change in the vast majority of participants as measured by the reliable change index.

4.10.3 Reliable and Clinically Significant Change (RCSC)

Uncertainty in Illness

Similar to the IES-R, data could only be found for the MIUS-SF in regards to the clinical population, and again, this population was not specific to CLL or LGL, but was validated on a population of women who had received a diagnosis of breast cancer. As there was only data on the clinical population and not on the comparison population, again, criterion A was used to analyse the data, where reliable change occurs when the data falls out of the range of the clinical population (1.96 standard deviations) (Agostinis, Morley, & Dowzer, 2008).

Table 25: Mean and Standard Deviation MIUS-SF

	Cancer Population (Cronbach's Alpha)	
Variable	Mean	SD
MIUS – SF	11.00 (0.70)	7.34

Table 26: *Reliable and Clinical Pre and Post Effect Size (Uncertainty in Illness)*

Variable (Time)	Pre Mean (SD)	Post Mean (SD)	Effect Size
MIUS-SF (Time-1 – 3 Months)	11.15 (2.98)	11.15 (2.94)	0.00
MIUS-SF (3 Months – 6 Months)	11.22 (3.10)	11.17 (3.28)	0.01
MIUS-SF (6 Months – 12 Months)	11.00 (5.57)	10.67 (6.03)	0.06
MIUS-SF (Time-1 – 6 Months)	10.91 (2.89)	11.17 (3.28)	-0.09

Table 27: *Individual Change: MIUS-SF (Uncertainty in Illness)*

ID	Time-1 – 3-Months	3-Months – 6-Months	Time-1 – 6-Months	6-Months – 12-Months
1	No change	No change	Deteriorate	No change
2	No change	No change	No change	No change
3	No change	Improve	Improve	No change
4	No change	No change	Improve	
5	No change	Deteriorate	Deteriorate	
6	No change	No change	No change	
7	No change	No change	No change	
8	No change	No change	No change	
9	No change	No change	No change	
10	No change	Deteriorate	Deteriorate	
11	No change	No change	No change	
12	Deteriorate	No change	No change	
13	No change	No change	No change	
14	No change	Deteriorate	No change	
15	No change	Improve	No change	
16	Deteriorate	No change	No change	
17	No change	No change	No change	
18	Improve	Improve	No change	
19	No change	No change	No change	
20	No change	No change	No change	
21	No change	No change	No change	
22	Improve	No change	No change	
23	No change	No change	No change	
24	No change			
25	Improve			
26	No change			

Clinical Significant Change (CSC)

Table 26 highlights how there were essentially no effect of time on the psychological construct of uncertainty in relation to one's illness. The greatest effect of time on uncertainty in illness was between time-1 to 6-months following diagnosis and there was an increase in uncertainty in illness, which is not what had been initially hypothesized. However, to take an overall perspective on the uncertainty in illness data, there seems to be no positive or negative change on the participant following their cancer diagnosis.

In regards to more individual change as it relates to uncertainty in illness, again, there was no overall pattern of an increase or decrease with regards to the MIUS-SF score. To be specific, there was no clinical significant change detected by the RCSC analyses and there were also the same exact number of individuals who improved and deteriorated (7) over the 12-month time period.

4.10.4 Summary of RSCS Results

In keeping with the results from the repeated measures analyses, the RCSC analyses indicated some small changes in terms of effect size in variables associated with anxiety, depression, and traumatic stress, although the change that was detected was not consistent across variables. Once again, and similar to the repeated measures analyses, IES-R total score had the strongest effect size in terms of change over time and the largest effect found (d = 0.33) in the RSCS analyses was in keeping with the most significant change in the post-hoc repeated measures analysis (3-months – 6-months).

In regards to individual improvement, the highest percentage of improvement as measured by clinical change indicators was HADS-total and depression, although these numbers were a small percentage in comparison to the percentage of individuals where there was no reliable or clinical change detected

5.0 Discussion Chapter

5.1 Discussion Overview

The following chapter will provide a summary and will also outline the findings that were yielded from the current study. It will also be determined whether the findings were in keeping with the initial aims and hypotheses of the current research. The chapter will also investigate whether the findings are in keeping with the previous research and consider the clinical and theoretical implications of the study. Finally, the discussion chapter will highlight the limitations and strengths of the current research, and will provide recommendations on how research in this area can possibly move forward.

5.2 Aim 1: Psychological Variables at Time-1

The first aim of the research was to determine the impact of a diagnosis of CLL or LGL and then being placed on the standard watch and wait pathway would have on the individual's level of anxiety, depression, traumatic stress, and uncertainty in illness. The initial hypothesis was that the mean data for the psychological variables would be indicative of psychological distress, which could possibly be attributed to the diagnosis of CLL or LGL. To determine the impact of the diagnosis, certain psychological variables were measured: uncertainty in illness, anxiety, depression, and post-traumatic stress. To achieve this aim, the measure of central tendency was examined for the psychological variables, and how the median value of the data compared with the recommended clinical cut-offs of the outcome measures. However, as the data were positively skewed, and the standard deviations for each of the psychological variables at time-1 were quite high, and it was determined that the measure of central tendency (median) would not be indicative of the participants' initial level of distress. Therefore, it

was deemed prudent to go beyond the measure of central tendency and further explore the data. Therefore, the frequency of the psychological variables at time-1 were examined, in regards to percentage of participants who would be above the clinical cut-offs as recommended by the different outcome measures. When the median values for the clinical cut-offs were initially examined, they were all under the clinical cut-off for what would be considered mild levels of distress, and many of the variables were under it by a distinct margin. However, when examining the percentage of individuals who were above the clinical cut-off; the initial understanding shifted, as there were a high percentage of participants who were above the recommended clinical cut-offs for the outcome measures. For anxiety, uncertainty in illness, and post-traumatic stress, approximately 40% of individuals were over the recommended clinical cut-offs, which could be considered to be a high proportion of the participants under study. Of note was that 41% of individuals would be considered to be in the moderate range as it relates to uncertainty with regards to their illness. As MIUS-SF is a measure directly related to the individual's diagnosis of cancer and such high levels of uncertainty in illness at time-1 would suggest that there could be difficulty in understanding the approach and process of managing the CLL or LGL. Another important finding was that a high percentage of individuals scored in the severe range for anxiety and post-traumatic stress following their diagnosis. Specifically, 15% of the participants would be considered to be in the severe range for level of anxiety as measured by HADS. What was even more surprising was that 27% of participants would be considered to be in the severe range for post-traumatic stress as measured by the IES-R. Such high levels of severity, as it relates to psychological distress, would suggest that the diagnosis of CLL or LGL, and being

placed on the watch and wait pathway could be factors attributing to the psychological distress of the participants.

5.2.1 Support for Hypothesis 1

It is difficult to determine whether or not the hypothesis for the initial aim had been met, as median data for the psychological variables at time-1 did not accurately capture the level of distress, due to the high level of variance and the data being skewed. As reported above, the percentages of individuals who were above the clinical cut-off for anxiety, uncertainty in illness, and post-traumatic stress were quite high. Because of what was deemed to be a high portion of the study population who indicated psychological distress at time-1 in terms of anxiety, post -traumatic stress, and uncertainty in illness, it was determined that the hypothesis was partially met, and the diagnosis of CLL or LGL had an impact on the psychological well-being of the participants.

5.2.2 Aim 1: Theoretical Perspective and Past Research

The previous research in regards to the impact of a diagnosis of CLL or LGL and then being placed on the watch and wait pathway in relation to psychological well-being are rather varied. One of the difficulties with the previous research in relation to psychological well-being and CLL or LGL were the variation in regards to disease progression, as some patients were on watch and wait and others were involved in active treatment. Three of the previous studies (Montgomery et al., 2003; Levin et al., 2007; Morrison et al., 2016) used data that specifically examined anxiety and depression for those individuals' diagnosed with CLL or LGL, who were on the watch and wait pathway. The data from the aforementioned two studies in terms of those participants who would be considered in the clinical range for anxiety and depression were different.

For the Montgomery and colleagues (2003) study, the data demonstrated that 14% of participants would meet "caseness" for anxiety and depression, as measured by the HADS; whereas, for the Levin and colleagues (2007) study, the participants' mean scores on the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI) found the participants in the "normal range" for anxiety and depression. For the most recent study conducted by Morrison and colleagues (2016), 13% of participants were above the clinical cut-off for depression as measured by the Center for Epidemiology Studies Depression Scale (CES –D) and 4% of participants were above the clinical cut-off for anxiety as measured by the Generalized Anxiety Disorder Questionnaire (GAD-Q). The data from the above studies was not in keeping with what was found in the current study, as the percentage of individuals who were above the clinical cut-off was much higher than the studies cited above, although the median level of depression was similar to what was found by Montgomery and colleagues. An important distinction between the current study and the previous research was that the data that were collected from our participants immediately following the diagnosis of CLL or LGL. Additionally, in the other studies, the distinction is not made in terms of how long they have had the diagnosis or how long the participants have been on the watch and wait pathway. Therefore, the finding from the current study that approximately 40% of participants were above the clinical cut-off level of anxiety following a diagnosis of CLL or LGL is novel, and it is important in understanding the level of anxiety that is possibly associated with not only the diagnosis, but the impact of time, as it relates to the diagnosis and then being placed on the watch and wait pathway.

Once again, and similar to the previous research with anxiety and depression, the various studies that have attempted to determine post-traumatic stress following a diagnosis of CLL and LGL found variable results. The two studies (Geffen et al. 2003; Morrison et al., 2016) that examined post-traumatic stress in individuals with a diagnosis of CLL or LGL had results that were completely different. The initial study that was completed by Geffen and colleagues (2003), found that approximately 24% of the individuals in their sample would be considered as having difficulties related to posttraumatic stress as measured by the Post- Traumatic Stress Disorder Checklist (PTSD-C), but the mean data from the Morrison and colleagues (2016) study found the participants to be in the "normal range" as measured by the IES-R. An important difference between the two studies was that the Geffen and colleagues study (2003) was completed with participants who had survived LGL and no information was given about what course of treatment they had received and the level of severity of the cancer; whereas, the Morrison (2016) study examined participants with CLL who were on the watch and wait pathway. The sample from the current study was similar to that of the Morrison study (2016), as the participants were on the watch and wait pathway, although the findings from the current study were different as they relate to post-traumatic stress. As noted above, in the current study, 43% of participants with a diagnosis of CLL or LGL on watch and wait would be considered as having difficulties relating to post-traumatic stress and 27% of the same participants would be considered to have severe difficulties related to post-traumatic stress. Similar to the above findings related to anxiety, the findings in this study relating to post-traumatic stress are novel, in that, there seems to be no previous research in the literature that measured post-traumatic stress immediately following a diagnosis of CLL or LGL and being placed on watch and wait, as the current study has done. What

differentiates the current findings from previous research is again, time, as the previous research was not clear on how long individuals had the diagnosis of CLL or LGL, and the implications of the current findings could be that one's anxiety and stress are high not only because they have received a diagnosis of cancer, but because it is also so close to having received this diagnosis.

As there has been no previous research into uncertainty in illness with patients with a diagnosis of CLL or LGL, it was important to draw comparisons to other form of cancers that have used Mishel's uncertainty in illness theory and her developed outcome measures. The problem is that there is a mix of different cancers that have been used in the theory, which have studied the participants at different time-points along the illness trajectory, and where the physical severity of the cancer is also quite varied. Because of this level of variation, it is difficult to draw conclusions or make generalizations about the findings, as they relate to uncertainty in illness and cancer. However, if one is attempting to draw on specific themes, one of them would be that those individuals who had survived the treatment for cancer or their cancer was deemed benign had seemingly lower levels of uncertainty in illness (Maste et al., 1998; Sarmmarco, 2001; Sammarco & Konecny, 2008; Liao et al., 2008; Kazer et al., 2012; Hall et al., 2014). The other trend among papers that studied uncertainty in illness, as it relates to a diagnosis of cancer, was that those who were involved in treatment or had greater physical illness reported higher levels of uncertainty in illness as measured by Mishel's outcome measures (Suzuki, 2012; Kurita et al., 2014; Lin Lin et al., 2014). It is also important to note that the means were examined for the studies and this is not to suggest that a statistically significant difference exists between the two groups, or a relationship was found in terms of greater

physical symptoms being predictive of greater uncertainty in illness. The research suggests that when individuals have higher severity or are engaged in a direct form of intervention, it could possibly result in greater uncertainty in relation to one's illness, especially as it relates to the overall outcome. Based on previous literature, this is the only study that has attempted to look at the impact of the uncertainty in illness as it relates to CLL or LGL and being placed on watch and watch and wait and therefore the findings that a relatively high percentage of individuals would be considered to have moderate levels of uncertainty is new for the literature.

Overall, when one is comparing the percentages of anxiety, uncertainty in illness, and post-traumatic stress following a diagnosis, it would be helpful to provide context in regards to how these percentages compare to other cancer diagnosis and mental health populations. A recent meta-analysis attempted to determine prevalence of mental health difficulties (depression, anxiety and adjustment difficulties) in oncology and hematology settings; the results from the study were that the percentage of individuals who would have difficulties related to depression was 16.3% and those with difficulties associated with anxiety was 10.3%, which is a lower percentage from what was found in the current study (Mitchell et al., 2011). When compared to percentage of individuals dealing with mental health difficulties drawn from normative population, without a diagnosis of cancer, the percentages indicate that individuals identified with having difficulties associated with anxiety at being approximately 6% and with low mood at approximately 4% (Alonso et al., 2000; Kessler et al., 2007). However, one must be cautious making comparisons between studies and using percentages as an indicator, as different studies of course use different measures, different cut-offs, and different standards for what is

deemed as being “difficulties” with anxiety or mood. Yet, while remaining cautions and skeptical, the percentages in the study compared to previous research seem to be high, and therefore one must attribute a degree of the anxiety, stress, and uncertainty in illness in this current sample to the diagnosis of CLL or LGL.

5.3 Aim 2: Relationship between Psychological Variables at Time-1

Another goal of the study was to determine the relationships that existed between uncertainty in illness and indicators of psychological distress (anxiety, depression, and traumatic stress) following a diagnosis of CLL or LGL. At time-1, following the diagnosis of CLL or LGL, there was only a moderate positive relationship with anxiety but not depression as measured by the HADS. The above result suggests that the more uncertainty the individual had about their diagnosis of cancer and subsequent treatment, the greater the level of anxiety.

Relationship between Uncertainty in Illness and Post-Traumatic Stress

One of the primary goals of the study was to determine the relationship between uncertainty in illness and post-traumatic stress as measured by the IES-R. At time-1, the only relationship that was detected in relation to post-traumatic stress was between uncertainty in illness and the intrusion subscale of the IES-R, where there was a moderate positive association between the two variables. Such an association between these two variables would lead one to make the determination that as uncertainty in relation to one’s illness increases, so would intrusive thoughts, which could be thoughts that are related to the individual’s diagnosis of cancer.

Relationships between Anxiety, Depression and Post-Traumatic Stress

While uncertainty in illness was the primary psychological construct of interest of this current study, it is also important to outline the relationships that were found between the other psychological variables: anxiety, depression, and traumatic stress. Initially following a diagnosis of CLL or LGL, both anxiety and the HADS total score had a positive and moderate relationship with intrusion, avoidance, and the IES-R total score. Therefore, as the level of anxiety increased for the participant, one would expect that their levels of intrusion, avoidance, and IES-R total score would increase as well.

5.3.1 Support for Hypothesis 2

The relationships that were identified between the psychological variables (anxiety, depression, post-traumatic stress, and uncertainty in illness) provide support for the second hypothesis of the current research. Specifically, the primary construct of study, uncertainty as it relates to one's illness was associated with anxiety, intrusion, and IES-R total scores at time-1. It is also important to note that although a number of moderate to strong relationships were found between the psychological variables, it does not infer a causal relationship, in that, one cannot state that uncertainty in illness is causing anxiety or that anxiety is causing one's uncertainty in relation to their illness, as all the statistically significant relationships that were found only imply an interaction between the two variables. Further exploration of the variables in individuals with CLL or LGL would need to be undertaken to better understand causality.

5.3.2 Aim 2: Theoretical Perspective and Past Research

A number of studies have explored the relationship or associations between variables for those individuals with a diagnosis of CLL or LGL and uncertainty and other forms of

cancer. The results from these studies are in keeping with what one would expect: that higher uncertainty in illness would be associated with greater levels of emotional distress. Different studies have found that greater uncertainty in illness using Mishel's outcome measures and outcome measures that focus on emotional distress (anxiety, depression, stress), have determined the strength of the relationships to be small to moderate (Sammarco, 2001; Liao et al, 2008; Sammarco & Konecny, 2008; Suzuki, 2012; Lin Lin et al., 2013). Yet, all the above studies that measured uncertainty in illness and the relationships with psychological variables were not with a sample of patients who had a diagnosis of CLL or LGL and were not on a watch and wait pathway. Other studies highlighted the relationships between psychological variables such as post-traumatic stress, depression, and anxiety (Geffen et al., 2004; Levin et al., 2007; Morrison et al., 2016). Theoretically, one may hypothesize that as uncertainty in illness is related to an individual being unable to predict outcomes to specific situations (illness related events), and when there are a lack of specific cues or prior knowledge, one would also expect that the inability to predict the outcome of the illness would lead greater psychological distress. As was found in the current study, the strongest relationships that were detected in relation to uncertainty in illness were both anxiety and intrusive thoughts, which one would hypothesize could develop from an inability to predict the future in regards to the cancer diagnosis or a difficulty understanding watch and wait as a form of intervention. There has been research to suggest that intrusions increase following a traumatic event, and these intrusions have been described by individuals as being "relatively brief sensory fragments" of the traumatic event, which take the form of "visual images, sounds, smells, taste of bodily sensations" (van der Kolk & Fisler, 1995; Ehlers et al., 2002). Although intrusions are common following a traumatic event, it is

also important to note that frequency or presence of intrusions are not strong predictors of post- traumatic stress (Shalev, 1992; Michael, Ehlers, Halligan & Clark, 2005), which places more emphasis on the important relationships that were detected at time-1. There is not enough data or information that would make the above inferences definitive in the current study, but it is important that future research possibly examine a relationship between uncertainty about one's illness and intrusions as it relates to post- traumatic stress.

5.4 Aim 3: Psychological Variables at Time-1 Predictive of Psychological Distress at 6-months

The aim of the multiple regression analyses was to determine whether psychological variables following the initial diagnosis would be predictive of psychological distress at 6-months follow-up. It was hypothesized that uncertainty in illness would be the psychological variable that was most predictive of psychological distress at 6-months following an initial diagnosis of cancer; however, it is clear that the results were not as straightforward as was initially hypothesized. The only outcome variables that were analyzed were anxiety, depression, and trauma, as uncertainty in illness did not meet the initial assumption for linearity. Of the three regression models that were run, only two of the models were deemed to be statistically significant and, of those two, anxiety at 6-months was the outcome variable wherein the predicted variance was the highest (62%). Within the regression model where anxiety at 6-months was the outcome variable, post-traumatic stress at time-1 was the strongest predictor when compared to depression, which was also a statistically significant predictor of anxiety at 6-months. Although uncertainty in illness did not have the overall impact that was initially hypothesized, it

was a statistically significant predictor of depression at 6-months. As the findings from the multiple regression models were varied, it is difficult to draw well-defined conclusions in regards to the predictability of distress following a diagnosis of CLL or LGL with the current data. However, as posttraumatic stress was such a strong predictor of anxiety and depression, further analyses may benefit from hierarchal regression where outcomes associated with post-traumatic stress are input into the model first.

5.4.1 Support for Hypothesis 3

The findings from the regression analyses were not in keeping with the initial hypothesis, as it was thought that uncertainty in illness at time-1 would be the strongest predictor of psychological distress at 6-months, following diagnosis of CLL or LGL. Though uncertainty in illness was not the strongest predictor of distress, it was a predictor of depression at 6-months and was also one of the variables that played a role in predicting anxiety at 6-months. Therefore, one could conclude that the hypothesis of the regression analyses were partially met, due to the fact that uncertainty in illness was a factor in predicting psychological distress, even though it was not the strongest psychological predictor.

5.4.2 Aim 3: Theoretical Perspective and Past Research

A number of studies that were examined in the literature review attempted to determine factors that predict psychological distress or uncertainty in illness as they relate to one's diagnosis of cancer. Certain studies from the literature review found that uncertainty in illness was predictive of psychological distress; however, the majority of these studies were with patients with CLL or LGL who were on a watch and wait pathway, but with other forms of cancer (breast, lung, head and neck, prostate), with differing levels of

severity (Sammarco, 2001; Sammarco & Konecny, 2008; Liao et al., 2008; Suzuki, 2012; Hall et al., 2014). The studies that used regression analyses to understand what variables could be predictive of CLL or LGL did not use the construct of uncertainty in illness and also did not use psychological variables as predictor variables; specifically, the two previous studies looked at physical symptom burden as being a coping style, and whether these areas were predictive of post-traumatic stress, anxiety, and depression (Montgomery et al., 2003; Morrison et al., 2016). Another important factor is that the majority of the studies that have been reviewed were cross-sectional in their design, and did not examine whether certain variables had an impact on other outcome variables at a later time-point within the same individual. The results in the study, although preliminary and underpowered are novel in that they highlight a number of psychological variables (uncertainty in illness, post-traumatic stress and anxiety) that could possibly play a role in predicting psychological distress for those individuals with CLL or LGL who have been placed on the watch and wait pathway of care.

5.5 Aim 4: Change in Psychological Variables over Time

The findings in regards to change over time were not what had been initially anticipated, as it was initially theorized that psychological distress related to a diagnosis of CLL or LGL would decrease over time, as participants would gain more knowledge about the watch and wait approach to treatment. It was thought that once the participants had received the diagnosis of CLL or LGL that their level of uncertainty, anxiety, depression, and post-traumatic stress would be at the highest point at time-1. The basis for the hypothesis was that it was believed that being told that you have a diagnosis of cancer, but that there would be no direct intervention, would be antithetical to how individuals in

western societies conceptualize or understand cancer and the subsequent treatment of cancer. For the outcome measures that attempted to capture the psychological constructs of anxiety, depression, and uncertainty in illness, there were higher scores at time-point 3 (6-months) than at time-point 1 (following diagnosis), but the increases that were found were not statistically significant, as the data were rather similar over the three time points.

For the IES-R total each of the three subscales that the outcome measure attempts to capture (avoidance, intrusion, and hyperarousal), there was a decrease between the time-1 scores to 6-months following initial diagnosis. However, the decreases in the scores on the three subscales, over the three time-points, were not found to be statistically significant by the repeated measures analyses. In regards to the IES-R total score, the decrease over the three time-points was found to be statistically significant and, from the post-hoc analysis, the largest, significant decrease occurred between 3-month to 6-months. In addition, the scores at both 3-months and 6-months following diagnosis dropped out of the area of clinical concern as measured by the IES-R, which could suggest that these participants would no longer be struggling with post-traumatic stress that could be associated with their diagnosis of CLL or LGL.

Individual Change over Time – Reliable and Clinically Significant Change

It was decided to investigate whether change occurred at an individual level using Jacobson and Truax's reliable and clinically significant change analysis. Due to the fact that there was a relatively small sample, and because the data were positively skewed with high standard deviations, it was deemed important to investigate the individual participants in more depth, since the means may not be as indicative of change as

researchers had initially thought. Firstly, in regards to anxiety, the same amount of individuals improved and deteriorated (8-participants) over the three time points. In relation to depression as measured by the HADS, there were a greater number of individuals who improved over the three time points in comparison to those who deteriorated. However, it is important to highlight that in comparison to the other psychological variables that were measured using RCSC, depression had the highest number of participants who deteriorated between 2 time-points and this occurred between time-1 and three-months following diagnosis.

In addition to more individual level change that was investigated in relation to anxiety and depression, the post-traumatic stress individual outcomes indicated changed had occurred. As a whole there were not substantial differences in terms of number of participants who improved in comparison to the number of participants who deteriorated over the different time-points, but when examining all of the subscales (avoidance, intrusion, hyperarousal) and the IES-R total, more individuals improved as opposed to deteriorated. The highest number of individual improvement was seen in hyperarousal and the IES-R total score, and the most significant time point that saw improvement was between 3 – 6 months (hyperarousal) and time-1 to 6-months (IES-R total).

The final variable that was investigated in terms of individual change outcomes was uncertainty in relation to one's illness. Similar to the post-traumatic stress variables, there was essentially no difference between those individuals who improved and those individuals who deteriorated, as 1 more participant deteriorated when compared to those who improved. This result was the most surprising finding, as one would have expected

that individually, the participants' uncertainty in illness would have decreased as they became more educated about CLL or LGL and the process of watch and wait.

5.5.1 Support for Hypothesis 4

With the exception of one of the variables (IES-R total), the other variables associated with anxiety, depression, post-traumatic stress, and uncertainty in illness in this current population of participants, with a diagnoses of CLL or LGL, did not change in a statistically significant way over the 3 time-points. Although there was a trend with a number of the variables that highlighted a decrease from 3-months to 6-months, one wonders whether any trend would have continued at the 12-month follow-up time-point. Once data has been collected for all the participants and analyses re-run, it will be important to gain insight into whether any significant increase occurred. Yet, for the purposes of this current thesis, and the current write-up, the data does not support the initial hypothesis that there would be a significant decrease in psychological distress as time progressed, as individuals possibly developed a better understanding of CLL or LGL and watch and wait as a form of care. Overall, there was no clear significant trend of whether the participants in this current study improved or deteriorated over time. Although when examining the group data there is a general improvement for most variables over time and for the individual change data more people improved over time, the differences were negligible and not definitive in a way as to draw any specific conclusions.

5.5.2 Aim 4: Theoretical Perspective and Past Research

Previous research has attempted to examine uncertainty and psychological variables associated with well-being in cancer patients, and whether or not these variable increase

or decrease over time. However, as psychological research in cancer patients is not deemed to be of the utmost importance, there are not many studies that have examined uncertainty in illness and also patients with a diagnosis of CLL or LGL who are on the standard watch and wait pathway. The studies that have researched Michel's construct of uncertainty in illness and whether or not the uncertainty in relation to one's illness changed over time have been varied, as two of the studies found that uncertainty in illness decreased over time (Liao et al., 2008; Kazer et al., 2012) and the other study (Suzuki, 2012) found that uncertainty in illness increased, although the increase was not deemed to be statistically significant. The issue with generalizing the results from the above study is that each of the study populations had a different diagnosis of cancer (prostate, head and neck, and breast), and each of the studies were at a different time point in the disease process (pre-diagnosis (biopsy stage), during treatment, after treatment) (Liao et al., 2008; Kazer et al, 2012; Suzuki, 2012). Interestingly, the study where uncertainty in illness increased was the study where the participants had been treated for prostate cancer (Suzuki, 2012). The study that examined individuals with a diagnosis of CLL who were on watch and wait or active treatment was not clear about the change over time in the participants; the questionnaires were given out to the participants at different points making it unclear whether the same participants were given the same questionnaires at another time period, and therefore the results are not helpful in regards to change over time (Holtzer – Goor et al., 2015). Although the forms of cancer were different and the participants were at different points of the disease trajectory, the general trend was that psychological distress and uncertainty in illness would decrease over time, which is not in keeping with the findings from the current study.

A hypothesis as to why the previous research in this area has found a decrease in psychological distress and uncertainty in illness may be related to post-traumatic growth, where individuals have perceived positive changes or personal growth following a traumatic event or a serious crisis in one's life (Tedeschi & Calhous, 1996; Bellizzi, 2004). There has been recent research that has examined post-traumatic growth in individuals who have been diagnosed with cancer and who have undergone treatment. The research suggests that a number of these individuals may experience positive changes and a decrease in psychological distress due to the fact that they have challenged or changed their core-assumptions about the world. Such growth may lead to positive changes in interpersonal relationships, their overall life perspective, how the individual perceives themselves, and their own ability to cope with such a debilitating illness such as cancer (Brix et al., 2003; Morrill et al., 2008; Barskova & Oesterreich, 2009; Morrison & Shakespeare – Finch, 2011). As highlighted previously, and in contrast to the above research, the data from this current study was not in keeping with the previous research in uncertainty in illness and CLL or LGL, as there was no statistically significant pattern or decrease found over time. One must hypothesize as to why this occurred, and some explanations could be that there is still concern about the outcome, that the participants may eventually require a more invasive form of active treatment, and therefore cannot reconceptualise their uncertainty or anxiety in a more positive frame. As one can only speculate, it will be important to analyze the 12-month follow-up data, as it may help with the understanding in relation to psychological change over time.

As there was no distinct or clear pattern in regards to whether psychological distress increased or decreased over time or whether certain psychological variables are

predictive of psychological distress following a diagnosis, it is important to explore if other factors can play a role in how an individual reacts to a diagnosis of cancer. It is also important to note that those individuals who participated in the study remained medically stable throughout and therefore any change that was detected by the RCSC analyses need to be attributed to other factors. There has been research done that has examined how individuals respond to a cancer diagnosis and what factors may be predictive of emotional well-being following such a diagnosis. In regards to a diagnosis of CLL or LGL, a number of studies indicated that greater social support was predictive of psychological well-being following an individual's cancer diagnosis (Sammarco, 2001; Sammarco & Konecny, 2008; Sammarco & Konecny, 2010; Morrison et al., 2016). These studies found that lower social support resulted in greater psychological distress; conversely, greater social support was a protective factor that resulted in less psychological distress following a diagnosis of CLL or LGL. However, similar to the findings in the current study, there were no other clear patterns in regards to factors that had an impact on emotional well-being following the cancer diagnosis. Therefore, it was helpful to explore research into other forms of cancer to determine if there are other factors, which are predictive of psychological well-being. The research into other forms of cancer highlighted a number of factors that may be helpful in determining how an individual will cope after their diagnosis. Specifically, certain factors that were consistent in different studies: social support, physical well-being, severity of the cancer, hopefulness (personal outlook), and ability to function physically (physical activity) (Clutton, Pakenham & Buckley, 1997; Moyer & Salovey, 1999; Dirksen, 2000; Balderson & Towell, 2003; Blank & Bellizzi, 2005; Lynch, Stegingna, Hawkes, Pakenham & Dunn, 2007; Iwatani, Matsuda, Kawabata, Miura & Matsushima, 2013;

Valdes – Stauber, Vietz & Kilian, 2013). Although not as pervasive in the research as the above factors, there has been other research to suggest that previous experiences of trauma, and previous mental health difficulties or diagnoses, are also predictive factors for psychological well-being following a cancer diagnosis (Green, Krupnick, Rowland, Epstein, Stockton, Spertus & Stern, 2000; Kornblith et al., 2001; Palmer, Kagee, Coyne & DeMichele, 2004; Okamura, Yamawaki, Taniguchi & Uchitomi, 2005; Alfano & Rowland, 2006). In terms of future research and based on the above factors, it may be helpful to undertake studies that attempt to investigate the above factors in patients with a diagnosis of CLL or LGL on the watch and wait pathway. Although, it is important to note that it is difficult to generalize the above results, as the research was done with different diagnoses of cancer of varying severity and one must be weary not to conflate these findings for the purposes of future research

5.6 Limitations of Current Research

5.6.1 Sample Size

There are a number of limitations that need to be addressed with regards to the research that was undertaken and the methods used to collect and analyze the data. Firstly, due to the small sample, it is difficult to be definitive in regards to the different relationships that were discovered between the different variables. Although retention rate was high for those individuals who were initially approached to participate in the study, the number of people who were presenting to the Hematology Unit following a diagnosis of CLL or LGL was much lower than we had initially anticipated. The research team made potential participant estimates based on monthly data from the three previous years, for those patients referred to the Hematology Clinic at the local hospital following a

diagnosis of CLL or LGL, and who were subsequently placed on watch and wait pathway. However, during the year that researchers attempted to recruit individuals into this study, the number of individuals presenting to clinic with stage-1 CLL or LGL was markedly lower than what the data had indicated from previous years.

As indicated above, the study did not reach the sample needed to be confident that a relationship existed between the variables based on the a priori power calculations; specifically, the study was underpowered in regards to the correlation analyses and in regards to the multiple regression analyses, and there were not enough participants to be confident in the specific findings.

5.6.2 Homogenous Sample

As was the expectation, there was a lack of diversity in terms of the overall sample as 97% of the sample was White-British. Although the sample was indicative of the population from which the sample was drawn in terms of the diversity in the geographical location of the hospital. A problem with much psychological research is the lack of representation from minority and culturally diverse populations. Such an underrepresentation can lead to incorrect assumptions in terms of generalizability as well as “ethnocentric interpretations” which can lead to stereotyping of these underrepresented groups (Mak, Law, Alvidrez, & Perez-Stable, 2007; Richmond et al., 2015). There is a dearth of research where the primary focus is attempting to determine the psychosocial needs of those individuals from culturally diverse or minority backgrounds (non-white populations) that have a diagnosis of cancer. However, there have been qualitative and quantitative studies that have attempted to gain insight into the needs of such under-represented populations after they have been diagnosed with a form

of cancer. Specifically, there has been research completed that highlighted that, following a diagnosis of cancer, individuals of an ethnic minority background may be less likely to inform members of their extended family of their diagnosis for fear of burdening them. Although these individuals can report higher levels of integration within their family, they may be less likely to use the family structure for support following such serious diagnoses and therefore may require greater support from the staff that provides care (Ashiwa – Giwan et al. 2007; Molina & Beresford, 2014; Molina et al, 2016).

5.6.3 Outcome Measures

The self-report measures used to measure psychological distress (HADS, IES-R) were selected because they have been used in many other psychological well-being and cancer research studies. The measures are also relatively short, not considered to be too time consuming for the participants, and the measures have also not been shown to cause participants any level of distress. In addition, the reliability and the validity of both the HADS and the IES-R have assessed in a number of different studies (Berry & Kennedy, 2003; Woolrich et al., 2006; Creamer et al., 2003; Weiss & Marmar, 1997). The other self-repot measure that was used in this research, MIUS-SF, has not been as widely used as the HADS or the IES-R, and it has only been validated in what is known to be one study. The MIUS-SF was selected as a measure to determine level of uncertainty in illness for the participants, as put forth by Mishel's uncertainty in illness theory. The short-form version of this measure was used because it was understood as being less invasive and time-consuming for the participants, who received no direct benefit from the research. Although, it was deemed important to be mindful of participants who are getting no direct benefit from the study when selecting measures, it is also important to

highlight the limitations of using a measure that has not been widely used in the literature. It was believed that the items on the MIUS-SF were "clear, concise, and specific" (Peterson, 2000; Podsakoff, 2003), but attempting to measure a construct as complex as uncertainty in illness, with an outcome measure of only 5-items, could of course be understood as being a limitation of the current research.

5.6.4 Normative Data – Reliable and Clinically Significant Change

Another limitation of the current study is directly related to Jacobson's and Truax's reliable and clinically significant change (RCSC) analyses, as it relates to the normative data that were used for the clinical. Specifically, the data that were used to provide clinical norms for MIUS-SF and the IES-R were not from individuals who had a diagnosis of either CLL or LGL. Also, the individuals who provided the normative data were not on a watch and wait pathway, and had a more serious form of cancer related illness than the participants in the current study. Therefore, the clinical norms that were used would have presumably been higher due to the fact that the individuals in the studies where the measures were validated could have been experiencing higher levels of distress, as they had a more serious form of illness. Essentially, the impact on the analyses would be that it would have been statistically more possible to detect a significant change due to the fact the mean score of the clinical population would be higher than the CLL or LGL participants. Although, one should not overstate the impact of the clinical norms as the findings from the RCSC analyses did not detect much change across all of the various time-points and all of the different dependent variables. One would be safe in hypothesizing that having clinical normative data for individuals with

CLL or LGL on the specific outcome measures used in the study would not have made much of a difference to the overall results of the study.

5.6.5 Nursing Staff

Another impact on the results of this study was that the initial idea for this research was developed by one of the research nurses, who currently work in the Haematology Clinic, at the local hospital. One could hypothesize that because a member of nursing staff was able to develop such novel research into uncertainty in illness, psychological distress, and cancer, that they may be more attuned to the psychological needs of the patients they see at the hospital - in comparison to other hospitals. If so, the nursing staff at the hospital may have a better understanding of the psychological impact that a diagnosis of cancer and being placed on watch and wait can have, and that understanding may have resulted in greater education and support. In theory, a greater level of exposure about one's illness and the implications of watch and wait may have manifested in lower levels of uncertainty in illness, in comparison to other clinics where nursing staff may not have as much insight into the above psychological constructs or where they may not be as psychologically minded. Therefore, similar to the way in which a homogeneous sample makes it difficult for one to generalize results to a larger population, a nursing team who have greater insight into psychological well-being of their patients would make one wary about generalizing the results to patients with CLL or LGL to other hematology clinics, and, moving forward, it would be of benefit to collect data from different hospitals.

5.7 Strengths of Research

5.7.1 Novelty of Current Research

Based on the literature review in the introduction chapter, there have been no studies that have attempted to follow individuals over time with a diagnosis of CLL or LGL on watch and wait, while attempting to understand the psychological impact that these diagnoses can have on an individual. To be more specific, and again, from examining the literature, the construct of uncertainty in illness has not been investigated in individuals with a diagnosis of CLL or LGL, using any type of research design. Although uncertainty in illness has been investigated in a number of other forms of cancer, it was surprising that it has not been undertaken with CLL or LGL, especially as the prevalence of both of these forms of cancer are quite high and the idea of being put on watch and wait could be confusing and frightening to many individuals.

5.7.2 Longitudinal Design

Another important strength was the design of the study. The longitudinal approach that was taken is unlike much of the research that has been undertaken investigating psychological well-being in cancer patients, which has mostly been cross-sectional. Although we did not have enough individuals at 12-months to analyze the data, because of time limitations, data will be collected for the rest of the participants, and a final analysis will be conducted once each participant has submitted the 12-month outcome measures. Having data over such a time period is not the norm for psychologically based research for patients with CLL or LGLs; as a result, it is a hope that researchers will be able to develop more robust conclusions about the relationships that exist between the psychological variables.

5.7.3 Multi-Disciplinary Approach

A real strength of the current research has been the multi-disciplinary approach, as there have been a number of different discipline specialists who have been involved and have contributed to the research process (nursing, medicine, clinical psychology, and academia). Conducting research in a collaborative way with individuals from various disciplines can provide greater insight or different perspectives when attempting to answer a research question. Individually, and within a particular area of specialty, it is possible for one to develop a degree of "tunnel vision", in that, it may be difficult to think of different methods or ideas when undertaking the research process (Lyons, 2004). The input that this current research received from individuals with varying forms of training and knowledge allowed researchers to think psychologically about a medical problem, which hopefully provided a broader understanding in this specific area of research.

5.8 Clinical Implications

Keeping in mind the size of sample and homogeneity of the sample, there are a number of clinical implications that can be drawn from the current research. Firstly, as a high proportion of individuals at time-1 had scores that would place them in the clinical range for anxiety, post-traumatic stress, and uncertainty, it is important to follow-up with these individuals to determine if they could possibly need any form of mental health support. Specifically, a high proportion of individuals (27 %) would be considered in the severe range for post-traumatic stress and it therefore may be prudent to administer trauma questionnaires to these newly diagnosed patients to determine level of severity; if it is high, consider psychological or trauma informed approaches to assist with their level of

distress. Generally, if following the initial screening the individual's level of distress were still high, the individual could possibly be referred to services that may be able to provide support with regards to difficulties associated with mental health and adjustment following a diagnosis of CLL or LGL. It is important that the medical support the patients receive remains paramount and primary; psychological support could be offered in conjunction with medical treatment if it is determined by the qualified health professionals involved that the patient's level of distress as it relates to their illness is having a negative impact on their overall mental health.

Although the results from the current research study are preliminary, and should be interpreted with caution, it is still important to note the possible implications of the findings, specifically as they relate to uncertainty in relation to one's illness. The results from both the repeated measures and reliable and clinically significant change analyses indicated that uncertainty in illness increased over time, although the increase that was detected was not deemed to be statistically significant. Once there is finalized data from all of the participants at 12-months it will be interesting to determine whether or not this upwards trend of uncertainty in illness continues. If it is determined that the trend continues, it could provide one with some insight that the individuals who have been assigned to watch and wait may still have difficulty understanding the impact of the diagnosis and the implications for treatment on their overall health. Therefore, it may be beneficial to provide these individuals with increased support or increased education in relation to CLL or LGL and watch and wait as a form of care throughout the disease process. Given the current situation in the NHS, and how cuts (see suggestion below) have had an impact on staffing levels which has led to an understaffing of nurses, as well

as nurses having to assume greater workloads (McIvar, 2003; Coombs, Arnolad, Loan-Clarle & Wilkonson, 2007; Keogh, 2013; Mahony, 2014), it may be naive to expect those in health care to be more cognizant of psychological constructs such as uncertainty in illness and an individual's mental health. However, there has been previous research completed that attempted to determine whether providing cancer patients with more information and support in relation to their diagnosis and subsequent treatment could have a positive effect on their psychological well-being. A number of studies examined patient education (PE), which would include more information regarding the illness or symptom(s), the management of said symptom(s), and in-depth discussions on the different treatment options. As health practitioners may not have the time or resources to provide this information in person, booklets, videos, and other educational materials are often used as a means to provide more information (Williams & Schreier, 2004; Weaver, Bell & Sansom-Daily, 2015). The overall goal of supplementary information is to increase understanding for the individual in a manner that is more informed or systematic in comparison to the individual searching for information themselves, which also could serve to increase one's uncertainty in illness and anxiety (Spalding, 2003). A meta-analysis was completed to determine the efficacy of cognitive behavioural therapy (CBT) and PE on those individuals with a diagnosis of various forms of cancer and cancer survivors on their QoL and psychological well-being. The research found that there were similar effects when individuals engaged in CBT or PE, but the effects of the CBT seemed to last longer (Osborne, Demoncada & Feuerstein, 2006). Although there were a number of limitations with the analyses and that CLL or LGL were not cancers that were part of the analyses, it is still an important finding that an increase in patient education

can have a similar effect to a psychological intervention on the well-being of the individuals diagnosed with cancer.

As there were a high percentage of individuals who would be considered as having psychological distress following diagnosis and the distress did not change over time, it may be beneficial to offer support throughout the process in the form of support-groups. Again, due to the current environment within the NHS (Stubbings & Scott, 2003; Duffin, 2009; Snow, 2010; Patters, 2011; Mahony, 2014), with regards to cut-backs and nursing staff not having time to take on more responsibility, it may not be feasible to offer further support, education, or direct psychological input for those individuals whose mental health may have been negatively impacted by their cancer diagnosis. Research has been done that has investigated the impact of peer support groups for those individuals who have a diagnosis of cancer and also the differences between peer-led groups and professional-led groups. The research on peer support has drawn upon coping theory, social comparisons, and helper-therapy principle, in order to understand the positive impact that such groups can have (Campbell, Phaneuf & Dean, 2004; Hooey, Ieropoli, White & Jefford, 2008). Research that has compared peer-led and professional-led groups, found no difference in terms of the impact the group has on those who are involved. Findings that indicate no real difference suggest that it is not the professional background of the group leader, but instead, whether the group provides a "supportive environment, mutuality, a sense of belonging and whether it meets the perceived needs of those attending" (Ussher, Kirsten, Butwow, Sandoval, 2005). Other qualitative research has explored the powerful impact that such groups can have on the individuals who have been diagnosed with cancer. Specifically, qualitative research has highlighted that such

peer-led groups have empowered participants and led to an increase in "personal agency", an increase in "confidence and self-control", and an ability to better live with one's cancer (Gray, Fitch, Davis & Philips, 1997; Cohen & Schulz, 2000; Ussher, Kirsten, Butwow, Sandoval, 2005). Due to the fact that there is seemingly good evidence for the use of peer support for those individuals with a diagnosis of cancer, and that peer-led groups do not lead to different outcomes from professionally-led groups, it may be positive for those individuals with CLL or LGL on watch and wait to engage in such a group. As this study found that the diagnosis of CLL or LGL and being put on watch and wait could have an impact on anxiety, stress, and uncertainty in illness, a group that is facilitated by individuals who have been on the watch and wait pathway for a period of time and who have also developed an understanding of what that entails, could provide others with a sense of normalcy, a degree of knowledge, and support.

Although greater education and peer-support have been researched and have shown to have a positive impact on an individual's anxiety, mood, and stress following a diagnosis of cancer, there are also specific psychological interventions that may prove helpful for these patients with CLL or LGL who have been placed on the watch and wait pathway. Although psychological intervention may not be a priority for those individuals with a cancer diagnosis in comparison to their physical well-being, it is still important to highlight the efficacy that specific interventions have had on the mental-health of those with a diagnosis of cancer. There have been a number of studies that have shown the positive impact of psychosocial interventions (CBT, psychotherapy, mindfulness therapies, etc.) on individuals after their diagnosis of cancer (Devine & Westlake, 1995; Jacobson & Jim, 2008; Trager et al, 2012). Although research on psychological

interventions with cancer patients has been done with different forms of intervention, the research seems to gravitate towards mindfulness-based strategies or mindfulness-based therapy for supporting individuals with their mental health in oncology settings (Hoffman, Sawyer, Witt & Oh, 2010). The understanding is that for cancer patients, using mindfulness-based interventions to pay attention to the "present reality" may prove a respite from past ruminations related to the cancer and diagnosis, or future worries about further psychological or physical pain which may be associated with the cancer (Specca, Carlson, Mackenzie & Angen, 2006; Piet, Wurtzen & Zachariae, 2012). Yet, as with most research, there are those who promote caution in terms of the efficacy of the aforementioned approaches, or the underlying mechanisms that may result in positive change, as much of the outcome data in oncological settings, as it relates to the psychological interventions, are not clear on the methods used in the intervention or the allocation of interventions for the participants (Newell, Sanson-Fisher & Savolainen, 2002). Whether it is further education, peer-support groups, or specific psychological interventions, one cannot deny that there can be a psychological impact that a cancer diagnosis can have on the mental health of certain individuals. The findings from the present study would indicate that individuals with a diagnosis of CLL or LGL should be given options in attempting to manage their psychological difficulties, as a supplement to their cancer treatment.

It is also important to highlight that such specific interventions (CBT, mindfulness), peer support groups, providing greater education, and understanding following a diagnosis of cancer can not only have an impact on an individual's mental health, but can also improve an individual's physical well-being. Although mental health and psychological

constructs have been the focus of this research, mental health and physical health should not be considered as being two disparate entities, as they are very much intertwined. To date, there has been research that has been completed with those individuals with a diagnosis of cancer and the impact that specific psychological or psychosocial interventions can have on both the individual's mental health and their physical health. Specifically, much of the research has focused on psychological interventions and support groups in order to measure the impact that such methods can have on an individual's immune response. The body's immune system is the "chief defence" against disease and is the main function of the immune system is to attempt to eradicate foreign substances (pathogens) that come into contact with the individual's body. Within the literature, studies examined specific immunological or biological markers such as cortisol levels, inflammation cytokine markers (ie. Interlukin-6 or C-reactive protein, immune cell counts, heart-rate, blood-pressure, and other forms of biological measurements) (Miller & Cohen, 2001; Carlson, Speca, Faris & Patel, 2006). The 2001 meta-analyses by Cohen & Miller attempted to examine studies that assessed whether psychological interventions can have a positive impact on immune response; their analysis concluded that psychological interventions can have modest impact on "altering immune parameters" (Miller & Cohen, 2001). However, more recently, further studies and reviews have been completed which have found data to suggest that psychological interventions and support groups can have a more profound impact on both an individual's mental and physical health following a diagnosis of cancer (Richardson et al., 1997; Kiecolt – Glaser, Cruess et al., 2000; McGuire & Robles, 2002; Carlson, Speca, Faris & Patel, 2006; McGregor & Antoni, 2009; Janusek, Tell & Matthews, 2015; Zhao, Cu, Wang, Su, Li & Uw, 2016). Yet, it is important to remain cognizant that the

research in this field have used varying biological markers, different psychological approaches, with different interventions, many of which that have not highlighted the specific program or what specific protocol was used with the cancer patients. More important than the above limitations, is that the findings from these studies were undertaken with different forms of cancer (prostate, breast, lung and others), with different levels of severity, and not with those patients with CLL or LGL. Therefore, one can understand that such findings are not only varied, but preliminary, and must be interpreted with caution. Yet, if one could generalize the above findings, it is that such interventions or approaches may not only be beneficial for an individual's mental health, but may also help those physically following their cancer diagnosis and, therefore, may also be beneficial for those individuals who have a diagnosis of CLL or LGL

5.9 Future Directions

The original goal of the current study was to recruit individuals who have been placed on watch and wait and those who are engaged in active treatment for CLL or LGL; however, given the time constraints and the physical health concerns for those on active treatment, researchers were unable to undertake a study to compare these two groups. Although the findings have shown a preliminary relationship between uncertainty and variables associated with psychological distress following an initial diagnosis, it is important to compare individuals on watch and wait to those engaged in treatment, especially over time. Comparing these two groups would provide more of an understanding as to whether uncertainty in illness is in fact related to being put on watch and wait as opposed to a more direct intervention following a diagnosis of cancer. Again, there seems to be a gap in the literature in comparing individuals on watch and wait and those engaged in a

direct intervention, and the impact these different approaches can have on psychological well-being and uncertainty in illness.

Another method that would provide greater depth and insight in this area would be to conduct qualitative research with individuals who have been diagnosed with CLL or LGL and to query the uncertainty that they are possibly experiencing in relation to the cancer diagnosis. In theory, it would be of benefit to engage in purposive sampling, inviting participants who have participated in the current research, particularly those who not only scored higher on uncertainty in illness at time-1, but also those participants who had high scores over the different time-points. Such purposive sampling would allow one to conduct qualitative interviews into whether that level of uncertainty in relation to their illness is related to being placed on watch and wait, confusion, or lack of understanding about their diagnosis. Conducting qualitative interviews from a sample drawn from the current population would provide greater depth and specificity about whether they are uncertain about other aspects of the cancer diagnosis, or more specifically about the intervention of watch and wait. Using qualitative methodology as a follow-up from this current research would be the ideal way to move forward, as this current research has led to more questions that qualitative research would hopefully be able to answer.

In regards to more specific methods and analysis, it would be helpful to undertake a study with a much larger sample of individuals who have a diagnosis of CLL or LGL and to follow these individuals over time. In the current study, if researchers had a larger sample, it would have been deemed relevant to explore other time-1 variables (demographic data: gender, age, relationship) and determine if such variables are predictive of distress over time. As recruitment was always going to be a challenge for

the current study, it was deemed important to initially examine the psychological variables, as if one were to include demographic variables, the results would have been extremely underpowered. Aside from examining other variables in the regression analyses, it could also be helpful to follow-up the participants longer than the initially planned 12-month period. For the purposes of the doctoral thesis, having the 12-month follow-up was ambitious, and researchers were unable to recruit enough participants before the submission date that would have made the 12-month data informative. However, for research where the time limitations are not as stringent, it would be insightful to follow these individuals with CLL or LGL for years. As CLL and LGL are chronic illnesses, individuals can live with the disease for many years without experiencing symptoms, and would be beneficial to gain further understanding about mental health and general well-being for those patients.

5.10 Research Summary

The research demonstrated that some of the participants in this study who had a diagnosis of CLL or LGL and were on the standard watch and wait pathway were possibly impacted psychologically by their diagnosis and the form of intervention.

At time-1, immediately following their diagnosis, there were a high proportion of participants who were above the clinical cut-off for anxiety, uncertainty in illness, and post-traumatic stress, which was found to be higher when compared to previous research in different cancer and normative populations. Over a quarter of these participants would also be considered to be in the severe range for post-traumatic stress, which could possibly be indicative of the overwhelming impact that such a diagnosis can have on an individual. Also, relationships were found to exist between a number of the

psychological variables at time-1 and one of the strongest relationships that was found was between an individual's uncertainty as it relates to one's illness and intrusion. The other relationship at time-1 that had the strongest association was between the participants' anxiety and overall post-traumatic stress. Such relationships were in keeping with the previous research in this area, although the individuals had other forms of cancer with varying degrees of physical severity.

The participants' level of post-traumatic stress at time-1 was found to be the strongest predictor of psychological distress at 6-months, but other variables such as uncertainty in illness and anxiety were also predictive of psychological distress at 6-months. The above finding was not in keeping with the initial hypothesis, that uncertainty in illness would be the strongest predictor and again such a finding could be attributed to the traumatic experience of a diagnosis of cancer.

From time-1 to 6-months following the initial diagnosis, the analyses of change over time were not indicative of much change, as it related to the psychological variables. Specifically, in regards to the group change and individual change data, there was not a decrease in psychological distress, as was initially hypothesized. However, it was found that post-traumatic stress as measured by the IES-R did decrease from time-1 to 6-months; a change that was determined to be statistically significant. In addition, when one looks at the individual change data, it seems that the strongest effect sizes that were found were a decrease between 3-months to 6-months and one must query whether the psychological distress will continue to decrease once all the data is collected and analyzed at 12-months follow-up.

A diagnosis of cancer can be devastating for the individual, not only in terms of their physical health, but also their psychological well-being. More research needs to be done with these individuals who have a diagnosis of CLL and LGL to determine the impact that their diagnosis has on them psychologically and also to determine if certain methods or support can be helpful in alleviating some of that distress. Cancer has an impact on everyone, and although research will continue to develop new medical treatments to better care for and manage the illness, research that attempts to understand the impact that such illnesses have and the subsequent treatments can have on the individual's mental health must continue.

6.0 Reference List

Abbey, G., Thompson, S. B., Hickish, T., & Heathcote, D. (2015). A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. *Psycho-Oncology*, *24*(4), 371-381.

Acquadro, C., Conway, K., Hareendran, A., Aaronson, N., & Issues, E. R. (2008). Literature review of methods to translate health-related quality of life questionnaires for use in multinational clinical trials. *Value in Health*, *11*(3), 509-521.

Acquadro, C., Bayles, A., & Juniper, E. (2014). Translating patient-reported outcome measures: a multi-step process is essential. *Jornal Brasileiro de Pneumologia*, *40*(3), 211-212.

Akechi, T., Okuyama, T., Sugawara, Y., Nakano, T., Shima, Y., & Uchitomi, Y. (2004). Major depression, adjustment disorders, and post-traumatic stress disorder in terminally ill cancer patients: associated and predictive factors. *Journal of Clinical Oncology*, *22*(10), 1957-1965.

Alfano, C. M., & Rowland, J. H. (2006). Recovery issues in cancer survivorship: a new challenge for supportive care. *The Cancer Journal*, *12*(5), 432-443.

Alter, C. L., Pelcovitz, D., Axelrod, A., Goldenberg, B., Harris, H., Meyers, B., ... & Kaplan, S. (1996). Identification of PTSD in cancer survivors. *Psychosomatics*, *37*(2), 137-143.

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S., Bryson, H., ... & Haro, J. M. (2004). Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta psychiatrica scandinavica*, *109*(s420), 21-27.

Amir, M., & Ramati, A. (2002). Post-traumatic symptoms, emotional distress and quality of life in long-term survivors of breast cancer: a preliminary research. *Journal of Anxiety Disorders*, *16*(2), 191-206.

Ando, N., Iwamitsu, Y., Kuranami, M., Okazaki, S., Nakatani, Y., Yamamoto, K., ... & Miyaoka, H. (2011). Predictors of psychological distress after diagnosis in breast cancer patients and patients with benign breast problems. *Psychosomatics*, *52*(1), 56-64.

Andrykowski, M. A., Cordova, M. J., Studts, J. L., & Miller, T. W. (1998). Posttraumatic stress disorder after treatment for breast cancer: Prevalence of diagnosis and use of the PTSD Checklist—Civilian Version (PCL—C) as a screening instrument. *Journal of consulting and clinical psychology*, *66*(3), 586.

Ardeshna, K. M., Smith, P., Norton, A., Hancock, B. W., Hoskin, P. J., MacLennan, K. A., ... & Linch, D. C. (2003). Long-term effect of a watch and wait policy versus immediate systemic treatment for asymptomatic advanced-stage non-Hodgkin lymphoma: a randomised controlled trial. *The Lancet*, *362*(9383), 516-522.

Armitage, J. O., & Longo, D. L. (2016). Is watch and wait still acceptable for patients with low-grade follicular lymphoma?. *Blood*, *127*(23), 2804-2808.

Bailey Jr, D. E., Mishel, M. H., Belyea, M., Stewart, J. L., & Mohler, J. (2004). Uncertainty intervention for watchful waiting in prostate cancer. *Cancer Nursing*, *27*(5), 339-346.

Bailey, D. E., Wallace, M., & Mishel, M. H. (2007). Watching, waiting and uncertainty in prostate cancer. *Journal of clinical nursing*, *16*(4), 734-741.

Balderson, N., & Towell, T. (2003). The prevalence and predictors of psychological distress in men with prostate cancer who are seeking support. *British journal of health psychology*, *8*(2), 125-134.

Barskova, T., & Oesterreich, R. (2009). Post-traumatic growth in people living with a serious medical condition and its relations to physical and mental health: A systematic review. *Disability and Rehabilitation*, *31*(21), 1709-1733.

Berry, C., & Kennedy, P. (2003). A psychometric analysis of the Needs Assessment Checklist (NAC). *Spinal Cord*, *41*(9), 490-501.

Bhayat, F., Das-Gupta, E., Smith, C., McKeever, T., & Hubbard, R. (2009). The incidence of and mortality from leukaemias in the UK: a general population-based study. *BMC cancer*, *9*(1), 252.

Binet, J. L., Caligaris-Cappio, F., Catovsky, D., Cheson, B., Davis, T., Dighiero, G., ... & Montserrat, E. (2006). Perspectives on the use of new diagnostic tools in the treatment of chronic lymphocytic leukemia. *Blood*, *107*(3), 859-861.

Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale: an updated literature review. *Journal of psychosomatic research*, *52*(2), 69-77.

Blaikie, N. (2007). *Approaches to social enquiry: Advancing knowledge*. Polity.

Blank, T. O., & Bellizzi, K. M. (2006). After prostate cancer: Predictors of well-being among long-term prostate cancer survivors. *Cancer*, *106*(10), 2128-2135.

Bodenheimer, T., Wagner, E. H., & Grumbach, K. (2002). Improving primary care for patients with chronic illness. *Jama*, *288*(14), 1775-1779.

Brewin, C. R., Dalgleish, T., & Joseph, S. (1996). A dual representation theory of posttraumatic stress disorder. Psychological Review, 103, 670–686.

Bryman, A. (2007). Barriers to integrating quantitative and qualitative research. *Journal of mixed methods research*, *1*(1), 8-22.

Bryman, A. (2015). *Social research methods*. Oxford university press.

Brunet, A., St-Hilaire, A., Jehel, L., & King, S. (2003). Validation of a French version of the Impact of Event Scale-Revised. *The Canadian Journal of Psychiatry*, *48*(1), 56-61.

Carlson, L. E., Speca, M., Faris, P., & Patel, K. D. (2007). One year pre–post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. *Brain, behavior, and immunity*, *21*(8), 1038-1049.

Caruana, E. J., Roman, M., Hernández-Sánchez, J., & Solli, P. (2015). Longitudinal studies. *Journal of thoracic disease*, *7*(11), E537.

Cheson, B. D., Bennett, J. M., Grever, M., Kay, N., Keating, M. J., O'Brien, S., & Rai, K. R. (1996). National Cancer Institute-sponsored Working Group guidelines for chronic lymphocytic leukemia: revised guidelines for diagnosis and treatment. *Blood*, *87*(12), 4990-4997.

Cheson, B. D., Pfistner, B., Juweid, M. E., Gascoyne, R. D., Specht, L., Horning, S. J., ... & Rosen, S. T. (2007). Revised response criteria for malignant lymphoma. *Journal of clinical oncology*, *25*(5), 579-586.

Christianson, S., & Marren, J. (2012). The impact of event scale-revised (IES-R). *Medsurg Nurs*, *21*(5), 321-322.

Clayton, M. F., Mishel, M. H., & Belyea, M. (2006). Testing a model of symptoms, communication, uncertainty, and well-being, in older breast cancer survivors. *Research in Nursing & Health*, *29*(1), 18-39.

Cohen, J. (1992). A power primer. *Psychological bulletin*, *112*(1), 155.

Cohen, L., Manion, L., & Morrison, K. (2013). *Research methods in education*. Routledge.

Concato, J., Shah, N., & Horwitz, R. I. (2000). Randomized, controlled trials, observational studies, and the hierarchy of research designs. *New England Journal of Medicine*, *342*(25), 1887-1892.

Coombs, C. R., Arnold, J., Loan-Clarke, J., Wilkinson, A., Park, J., & Preston, D. (2007). Improving the recruitment and return of nurses and allied health professionals: a quantitative study. *Health Services Management Research*, *20*(1), 22-36.

Cordova, M. J., Studts, J. L., Hann, D. M., Jacobsen, P. B., & Andrykowski, M. A. (2000). Symptom structure of PTSD following breast cancer. *Journal of traumatic stress*, *13*(2), 301-319.

Crowley, D. (2008). *An investigation of the relationship between acceptance and adjustment of people who have had a stroke*. (Doctoral Dissertation).

Crowley, D., & Andrews, L. (2017). The longitudinal relationship between acceptance and anxiety and depression in people who have had a stroke. *Aging & mental health*, 1-8.

Cruess, D. G., Antoni, M. H., McGregor, B. A., Kilbourn, K. M., Boyers, A. E., Alferi, S. M., ... & Kumar, M. (2000). Cognitive-behavioral stress management reduces serum cortisol by enhancing benefit finding among women being treated for early stage breast cancer. *Psychosomatic Medicine*, *62*(3), 304-308.

Denscombe, M. (2010). *The Good Research Guide: for small-scale social research*. McGraw Hill.

Devine, E. C., & Westlake, S. K. (1995, October). The effects of psychoeducational care provided to adults with cancer: meta-analysis of 116 studies. In *Oncology Nursing Forum-Oncology Nursing Society* (Vol. 22, No. 9, pp. 1369-1382). [Pittsburgh, PA, etc.] Oncology Nursing Society.

Dighiero, G. (2003). Unsolved issues in CLL biology and anagement. *Leukemia*, *17*(12), 2385.

Dighiero, G. (2005). CLL biology and prognosis. *ASH Education Program Book*, *2005*(1), 278-284.

Dighiero, G., Maloum, K., Desablens, B., Cazin, B., Navarro, M., Leblay, R., ... & Binet, J. L. (1998). Chlorambucil in indolent chronic lymphocytic leukemia. *New England Journal of Medicine*, *338*(21), 1506-1514.

Dighiero, G., & Binet, J. L. (2000). When and how to treat chronic lymphocytic leukemia.

Dighiero, G., Maloum, K., Desablens, B., Cazin, B., Navarro, M., Leblay, R., ... & Binet, J. L. (1998). Chlorambucil in indolent chronic lymphocytic leukemia. *New England Journal of Medicine*, *338*(21), 1506-1514.

Dirksen, S. R. (2000). Predicting well-being among breast cancer survivors. *Journal of Advanced Nursing*, *32*(4), 937-943.

Duffin, C. (2009). Understaffing is threat to success of UK-wide preceptor scheme. *Nursing Standard*, *23*(28), 10.

Durbin, J., & Watson, G. S. (1951). Testing for serial correlation in least squares regression. II. *Biometrika*, *38*(1/2), 159-177.

Ehlers, A., Hackmann, A., Steil, R., Clohessy, S., Wenninger, K., & Winter, H. (2002). The nature of intrusive memories after trauma: The warning signal hypothesis. *Behaviour research and therapy*, *40*(9), 995-1002.

Elphee, E. E. (2008, May). Understanding the concept of uncertainty in patients with indolent lymphoma. In *Oncology nursing forum* (Vol. 35, No. 3).

El-Galaly, T. C., Bilgrau, A. E., Nully Brown, P., Mylam, K. J., Ahmad, S. A., Pedersen, L. M., ... & Pedersen, R. S. (2015). A population-based study of prognosis in advanced stage follicular lymphoma managed by watch and wait. *British journal of haematology*, *169*(3), 435-444.

Else, M., Smith, A. G., Cocks, K., Richards, S. M., Crofts, S., Wade, R., & Catovsky, D. (2008). Patients' experience of chronic lymphocytic leukaemia: baseline health-related quality of life results from the LRF CLL4 trial. *British journal of haematology*, *143*(5), 690-697.

Fay, B. (1996). *Contemporary philosophy of social science: A multicultural approach* (Vol. 1). Oxford: Blackwell.

Farrington, D. P. (1991). Longitudinal research strategies: Advantages, problems, and prospects. *Journal of the American Academy of Child & Adolescent Psychiatry*, *30*(3), 369-374.

Field, A. (2013). *Discovering statistics using IBM SPSS statistics*. sage.

Gelo, O., Braakmann, D., & Benetka, G. (2008). Quantitative and qualitative research: Beyond the debate. *Integrative psychological and behavioral science*, *42*(3), 266-290.

Guba, E. G., & Lincoln, Y. S. (1994). Competing paradigms in qualitative research. *Handbook of qualitative research*, *2*(163-194), 105.

Giddings, L. S., & Grant, B. M. (2007). A Trojan horse for positivism?: A critique of mixed methods research. *Advances in nursing science*, *30*(1), 52-60.

Girgis, A., Lambert, S., Johnson, C., Waller, A., & Currow, D. (2012). Physical, psychosocial, relationship, and economic burden of caring for people with cancer: a review. *Journal of Oncology Practice*, *9*(4), 197-202

Goggin, K., Gqaleni, N., Mbhele, A. L., Makhathini, M. E., Buthelezi, T. D., Ndlovu, S. W., ... & Hlongwane, T. (2010). The translation and cultural adaptation of patient- reported outcome measures for a clinical study involving traditional health providers and bio-medically trained practitioners. *Alternation*, *17*(1), 273.

Glenn, N. D. (2005). *Cohort analysis* (Vol. 5). Sage

Gray, R., Fitch, M., Davis, C., & Phillips, C. (1997). A qualitative study of breast cancer self-help groups. *Psycho-Oncology*, *6*(4), 279-289.

Green, B. L., Krupnick, J. L., Rowland, J. H., Epstein, S. A., Stockton, P., Spertus, I., & Stern, N. (2000). Trauma history as a predictor of psychologic symptoms in women with breast cancer. *Journal of Clinical Oncology*, *18*(5), 1084-1084.

Gribben, J. G. (2010). How I treat CLL up front. *Blood*, *115*(2), 187-197.

Grossman, J., & Mackenzie, F. J. (2005). The randomized controlled trial: gold standard, or merely standard?. *Perspectives in biology and medicine*, *48*(4), 516-534.

Hadorn, D. C., Baker, D., Hodges, J. S., & Hicks, N. (1996). Rating the quality of evidence for clinical practice guidelines. *Journal of clinical epidemiology*, *49*(7), 749-754.

Hagen, K. B., Aas, T., Lode, K., Gjerde, J., Lien, E., Kvaløy, J. T., ... & Lind, R. (2015). Illness uncertainty in breast cancer patients: Validation of the 5-item short form of the Mishel Uncertainty in Illness Scale. *European Journal of Oncology Nursing*, *19*(2), 113-119.

Hall, D. L., Mishel, M. H., & Germino, B. B. (2014). Living with cancer-related uncertainty: associations with fatigue, insomnia, and affect in younger breast cancer survivors. *Supportive Care in Cancer*, *22*(9), 2489-2495.

Hallek, M., & German CLL Study Group. (2005). Chronic lymphocytic leukemia (CLL): first-line treatment. *ASH Education Program Book*, *2005*(1), 285-291.

Halpern-Manners, A., Warren, J. R., & Torche, F. (2014). Panel conditioning in a longitudinal study of illicit behaviors. *Public Opinion Quarterly*, *78*(3), 565-590.

Harrison J and Maguire P (1994) Predictors of psychiatric morbidity in cancer patients. *Br J Psychiatry* **165**: 593–598.

Hayes, N. (2000). *Doing psychological research*. Abingdon: Taylor & Francis Group.

Healy, M., & Perry, C. (2000). Comprehensive criteria to judge validity and reliability of qualitative research within the realism paradigm. *Qualitative market research: An international journal*, *3*(3), 118-126.

Herman, J. L. (2015). *Trauma and recovery: The aftermath of violence--from domestic abuse to political terror*. Hachette UK.

Hoffman, K. J., & Sasaki, J. E. (1997). Comorbidity of substance abuse and PTSD. In C. S. Fullerton, & R. J. Ursano (Eds.), Posttraumatic stress disorder: acute and long-term responses to trauma and disaster. Progress in psychiatry series, No. 51 (pp. 159–174). Washington, DC: American Psychiatric Press.

Hofmann, S. G., Sawyer, A. T., Witt, A. A., & Oh, D. (2010). The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. *Journal of consulting and clinical psychology*, *78*(2), 169.

Holtzer-Goor, K. M., Schaafsma, M. R., Joosten, P., Posthuma, E. F. M., Wittebol, S., Huijgens, P. C., ... & Erjavec, Z. (2015). Quality of life of patients with chronic lymphocytic leukaemia in the Netherlands: results of a longitudinal multicentre study. *Quality of Life Research*, *24*(12), 2895-2906.

Holzner, B., Kemmler, G., Kopp, M., Nguyen-Van-Tam, D., Sperner-Unterweger, B., & Greil, R. (2004). Quality of life of patients with chronic lymphocytic leukemia: results of a longitudinal investigation over 1 yr. *European journal of haematology*, *72*(6), 381-389.

Horning, S. J. (2000). Follicular lymphoma: have we made any progress?. *Annals of oncology*, *11*(suppl_1), S23-S27.

Horning, S. J., & Rosenberg, S. A. (1984). The natural history of initially untreated low-grade non-Hodgkin's lymphomas. *New England Journal of Medicine*, *311*(23), 1471-1475.

Hutchins, E. & Devilly, G.J. (2005). Impact of Events Scale. Victim's Web Site. http://www.swin.edu.au/victims/resources/assessment/ptsd/ies.html

Iwatani, T., Matsuda, A., Kawabata, H., Miura, D., & Matsushima, E. (2013). Predictive factors for psychological distress related to diagnosis of breast cancer. *Psycho-Oncology*, *22*(3), 523-529.

Jacobsen, P. B., & Jim, H. S. (2008). Psychosocial interventions for anxiety and depression in adult cancer patients: achievements and challenges. *CA: a cancer journal for clinicians*, *58*(4), 214-230.

Janusek, L. W., Tell, D., & Mathews, H. L. (2015). Mindfulness based stress reduction improves psychological well-being and restores immune function in women with breast cancer, from diagnosis through 6-months post-cancer treatment. *Brain, Behavior, and Immunity*, *49*, e37-e38.

Jemal, A., Siegel, R., Ward, E., Hao, Y., Xu, J., Murray, T., & Thun, M. J. (2008). Cancer statistics, 2008. *CA: a cancer journal for clinicians*, *58*(2), 71-96.

Johnson, R. B., & Onwuegbuzie, A. J. (2004). Mixed methods research: A research paradigm whose time has come. *Educational researcher*, *33*(7), 14-26.

Kangas, M., Henry, J. L., & Bryant, R. A. (2002). Posttraumatic stress disorder following cancer: A conceptual and empirical review. *Clinical psychology review*, *22*(4), 499-524.

Katon, W., Lin, E. H., & Kroenke, K. (2007). The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. *General hospital psychiatry*, *29*(2), 147-155.

Kaufman, M., Rubin, J., & Kanti Rai MB, B. S. (2009). Diagnosing and treating chronic lymphocytic leukemia in 2009. *Oncology*, *23*(12), 1030.

Kazer, M. W., Bailey Jr, D. E., Chipman, J., Psutka, S. P., Hardy, J., Hembroff, L., ... & Sanda, M. G. (2013). Uncertainty and perception of danger among patients undergoing treatment for prostate cancer. *BJU international*, *111*(3b).

Kessler, R. C., Angermeyer, M., Anthony, J. C., De Graaf, R. O. N., Demyttenaere, K., Gasquet, I., ... & Kawakami, N. (2007). Lifetime prevalence and age-of-onset distributions of mental disorders in the World Health Organization's World Mental Health Survey Initiative. *World psychiatry*, *6*(3), 168.

Keogh, K. (2013). Nursing Standard survey reveals lack of confidence in new NHS. *Nursing Standard (through 2013)*, *27*(37), 12

Kiecolt-Glaser, J. K., McGuire, L., Robles, T. F., & Glaser, R. (2002). Psychoneuroimmunology: Psychological influences on immune function and health. *Journal of consulting and clinical psychology*, *70*(3), 537.

King. B., & Mishel, M. (1986, April). Uncertainty appraisal and management in chronic illness. Paper presented at the Nineteenth Communicating Nursing Research Conference, Western Society for Research in Nursing, Portland, Oregon.

Kornblith, A. B., Herndon, J. E., Zuckerman, E., Viscoli, C. M., Horwitz, R. I., Cooper, M. R., ... & Norton, L. (2001). Social support as a buffer to the psychological impact of stressful life events in women with breast cancer. *Cancer*, *91*(2), 443-454.

Krauss, S. E. (2005). Research paradigms and meaning making: A primer. *The qualitative report*, *10*(4), 758-770.

Kurita, K., Garon, E. B., Stanton, A. L., & Meyerowitz, B. E. (2013). Uncertainty and psychological adjustment in patients with lung cancer. *Psycho‐Oncology*, *22*(6), 1396-1401.

Lavrakas, P. J. (2008). *Encyclopedia of survey research methods*. Sage Publications.

Lazarus RS (1993) Coping theory and research – past, present, and future. *Psychosom Med* 55: 234–247.

Levin, T. T., Li, Y., Riskind, J., & Rai, K. (2007). Depression, anxiety and quality of life in a chronic lymphocytic leukemia cohort. *General hospital psychiatry*, *29*(3), 251-256.

Levy, V., Porcher, R., Delabarre, F., Leporrier, M., Cazin, B., & Chevret, S. (2001). Evaluating treatment strategies in chronic lymphocytic leukemia: use of quality-adjusted survival analysis. *Journal of clinical epidemiology*, *54*(7), 747-754.

Liao, M. N., Chen, M. F., Chen, S. C., & Chen, P. L. (2008). Uncertainty and anxiety during the diagnostic period for women with suspected breast cancer. *Cancer nursing*, *31*(4), 274-283.

Lin, L., Chiang, H. H., Acquaye, A. A., Vera-Bolanos, E., Gilbert, M. R., & Armstrong, T. S. (2013). Uncertainty, mood states, and symptom distress in patients with primary brain tumors. *Cancer*, *119*(15), 2796-2806.

Linden, Wolfgang, Andrea Vodermaier, Regina MacKenzie, and Duncan Greig. "Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age." *Journal of affective disorders* 141, no. 2 (2012): 343-351

Loge JH, Abrahamsen AF, Ekeberg O, Hannisdal E and Kaasa S (1997) Psychological distress after cancer cure: a survey of 459 Hodgkin's disease survivors. *Br J Cancer* 76: 791–796.

Lubkin, I. M., & Larsen, P. D. (2006). *Chronic illness: Impact and interventions*. Jones & Bartlett Learning.

Lynch, B. M., Steginga, S. K., Hawkes, A. L., Pakenham, K. I., & Dunn, J. (2008). Describing and predicting psychological distress after colorectal cancer. *Cancer*, *112*(6), 1363-1370.

Mack, N. W., Macqueen, C., & Guest, K. (2015). G. & Namey, E. 2005. *Qualitative research methods: A data collector's field guide*.

Mackenzie, N., & Knipe, S. (2006). Research dilemmas: Paradigms, methods and methodology. *Issues in educational research*, *16*(2), 193-205.

Mahony, C. (2014). 2013 was a horrible year for nursing—nurses are "burnt out," says chief. *BMJ*, *348*, g126

Mann, C. J. (2003). Observational research methods. Research design II: cohort, cross sectional, and case-control studies. *Emergency medicine journal*, *20*(1), 54-60.

Matutes, E., Owusu-Ankomah, K., Morilla, R., Garcia Marco, J., Houlihan, A., Que, T. H., & Catovsky, D. (1994). The immunological profile of B-cell disorders and proposal of a scoring system for the diagnosis of CLL. *Leukemia*, *8*(10), 1640-1645.

Massie M and Holland J (1990) Overview of normal reactions and prevalence of p psychiatric disorders. In: Holland J and Rowland J. *Handbook of Psycho-oncology*, pp. 273–282. OUP: New York

Mast, M. E. (1998, April). Survivors of breast cancer: illness uncertainty, positive reappraisal, and emotional distress. In *Oncology Nursing Forum* (Vol. 25, No. 3, pp. 555-562).

Mehnert, A., Berg, P., Henrich, G., & Herschbach, P. (2009). Fear of cancerprogression and cancer-related intrusive cognitions in breast cancer survivors. *Psycho-Oncology*, *18*(12), 1273-1280.

Menard, S. (2002). *Longitudinal research* (Vol. 76). Sage.

Menard, S. (Ed.). (2007). *Handbook of longitudinal research: Design, measurement, and analysis*. Elsevier.

McCormick, K. M. (2002). A concept analysis of uncertainty in illness. *Journal of Nursing Scholarship*, *34*(2), 127-131.

McGregor, B. A., & Antoni, M. H. (2009). Psychological intervention and health outcomes among women treated for breast cancer: a review of stress pathways and biological mediators. *Brain, behavior, and immunity*, *23*(2), 159-166.

McVicar, A. (2003). Workplace stress in nursing: a literature review. *Journal of advanced nursing*, *44*(6), 633-642.

Michell, J. (2003). The quantitative imperative: Positivism, naïve realism and the place of qualitative methods in psychology. *Theory & Psychology*, *13*(1), 5-31.

Miller, G. E., & Cohen, S. (2001). Psychological interventions and the immune system: A meta-analytic review and critique. *Health Psychology*, *20*(1), 47.

Mishel, M. H. (1981). The measurement of uncertainty in illness. *Nursing research*, *30*(5), 258-263.

Mishel, M. H. (1983). Parents' perception of uncertainty concerning their hospitalized child. *Nursing research*, *32*(6), 324-330.

Mishel, M. H. (1984). Perceived uncertainty and stress in illness. *Research in Nursing & Health*, *7*(3), 163-171.

Mishel, M. H. (1988a). Uncertainty in illness. Image: Journal of Nursing Scholarship, 4, 225-232.

Mishel, M. H. (1990). Reconceptualization of the uncertainty in illness theory. *Journal of Nursing Scholarship*, *22*(4), 256-262.

Mishel, M. H. (1997). Uncertainty in acute illness. *Annual review of nursing research*, *15*(1), 57-80.

Mishel, M. H. (1999). Uncertainty in chronic illness. *Annual review of nursing research*, *17*, 269-294.

Mishel, M. H., Belyea, M., Germino, B. B., Stewart, J. L., Bailey, D. E., Robertson, C., & Mohler, J. (2002). Helping patients with localized prostate carcinoma manage uncertainty and treatment side effects. *Cancer*, *94*(6), 1854-1866.

Mishel, M. H., & Braden, C. J. (1988). Finding meaning: antecedents of uncertainty in illness. *Nursing Research*, *37*(2), 98-103.

Mishel, M. H., & Clayton, M. F. (2008). Theories of uncertainty in illness. *Middle range theory for nursing*, *2*, 55-84.

Mishel, M. H., Hostetter, T., King, B., & Graham, V. (1984). Predictors of psychosocial adjustment in patients newly diagnosed with gynecological cancer.

Mishel, M. H., & Murdaugh, C. L. (1987). Family experiences with heart transplantation: Redesigning the dream. Nursing Research, 36, 332-338

Mishel, M. H., Padilla, G., Grant, M., & Sorenson, D. S. (1991). Uncertainty in illness theory: a replication of the mediating effects of mastery and coping. *Nursing research*.

Mishel, M. H., & Sorenson, D. S. (1991). Uncertainty in gynecological cancer: a test of the mediating functions of mastery and coping. *Nursing Research*, *40*(3), 167-171.

Mitchell, A. J., Chan, M., Bhatti, H., Halton, M., Grassi, L., Johansen, C., & Meader, N. (2011). Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *The lancet oncology*, *12*(2), 160-174.

Molica, S., Mauro, F., Vignetti, M., Foà, R., & Efficace, F. (2007). What Have We Learned from Measuring Health-Related Quality of Life in Patients with Chronic Lymphocytic Leukemia? A Systematic Review of Published Studies from 1990 to 2007.

Montero, I., & Leon, O. G. (2007). A guide for naming research studies in Psychology. *international Journal of clinical and Health psychology*, *7*(3).

Morgan, D. L. (2007). Paradigms lost and pragmatism regained: Methodological Implications of combining qualitative and quantitative methods. *Journal of mixed methods research*, *1*(1), 48-76

Morrill, E. F., Brewer, N. T., O'neill, S. C., Lillie, S. E., Dees, E. C., Carey, L. A., & Rimer, B. K. (2008). The interaction of post-traumatic growth and post-traumatic stress symptoms in predicting depressive symptoms and quality of life. *Psycho-Oncology*, *17*(9), 948-953

Morris, B. A., & Shakespeare-Finch, J. (2011). Rumination, post-traumatic growth, and distress: structural equation modelling with cancer survivors. *Psycho-Oncology*, *20*(11), 1176-1183.

Moyer, A., & Salovey, P. (1999). Predictors of social support and psychological distress in women with breast cancer. *Journal of Health Psychology*, *4*(2), 177-191.

Moyer, A., Sohl, S. J., Knapp-Oliver, S. K., & Schneider, S. (2009). Characteristics and methodological quality of 25 years of research investigating psychosocial interventions for cancer patients. *Cancer treatment reviews*, *35*(5), 475-484.

Muijs, D. (2010). *Doing quantitative research in education with SPSS*. Sage.

Nelson, J. P. (1996). Struggling to gain meaning: living with the uncertainty of breast cancer. *Advances in nursing science*, *18*(3), 59-76.

Neuman, W., L. (2003). Social Research Methods: Qualitative and quantitative Approaches

Neville, K. L. (2003). Uncertainty in illness: an integrative review. *Orthopaedic Nursing*, *22*(3), 206-214.

Newell, S. A., Sanson-Fisher, R. W., & Savolainen, N. J. (2002). Systematic review of psychological therapies for cancer patients: overview and recommendations for future research. *Journal of the National Cancer Institute*, *94*(8), 558-584.

Nolte, E., & McKee, M. (Eds.). (2008). *Caring for people with chronic conditions: a health system perspective*. McGraw-Hill Education (UK).

Okamura, M., Yamawaki, S., Akechi, T., Taniguchi, K., & Uchitomi, Y. (2005). Psychiatric disorders following first breast cancer recurrence: prevalence, associated factors and relationship to quality of life. *Japanese Journal of Clinical Oncology*, *35*(6), 302-309.

Osborn, R. L., Demoncada, A. C., & Feuerstein, M. (2006). Psychosocial interventions for depression, anxiety, and quality of life in cancer survivors: meta-analyses. *The International Journal of Psychiatry in Medicine*, *36*(1), 13-34.

Palmer, S. C., Kagee, A., Coyne, J. C., & DeMichele, A. (2004). Experience of trauma, distress, and posttraumatic stress disorder among breast cancer patients. *Psychosomatic Medicine*, *66*(2), 258-264.

Patterson, J. (2011). The effects of nurse to patient ratios. *Nurs Times*, *107*(2), 22-5.

Parle M, Jones B and Maguire P (1996) Maladaptive coping and affective disorders among cancer patients. *Psychol Med* 26: 735–744.

Pashos, C. L., Flowers, C. R., Kay, N. E., Weiss, M., Lamanna, N., Farber, C., ... & Kozloff, M. (2013). Association of health-related quality of life with gender in patients with B-cell chronic lymphocytic leukemia. *Supportive Care in Cancer*, *21*(10), 2853-2860.

Pettigrew, A. M. (1990). Longitudinal field research on change: Theory and practice. *Organization science*, *1*(3), 267-292.

Pinquart, M., & Duberstein, P. R. (2010). Depression and cancer mortality: A meta-analysis. *Psychological Medicine, 40,* 1797–1810.

Ponterotto, J. G. (2005). Qualitative research in counseling psychology: A primer on research paradigms and philosophy of science. *Journal of counseling psychology*, *52*(2), 126.

Prieto, J. M., Blanch, J., Atala, J., Carreras, E., Rovira, M., Cirera, E., & Gasto, C. (2002). Psychiatric morbidity and impact on hospital length of stay among hematologic cancer patients receiving stem-cell transplan- tation. *Journal of Clinical Oncology, 20,* 1907–1917.

Rajulton, F. (2001). The fundamentals of longitudinal research: an overview. *Canadian Studies in Population*, *28*(2), 169-185.

Reich, M., Lesur, A., & Perdrizet-Chevallier, C. (2008). Depression, quality of life and breast cancer: A review of the literature. *Breast Cancer Research and Treatment, 110,* 9–17.

Richardson, M. A., Post-White, J., Grimm, E. A., Moye, L. A., Singletary, S. E., & Justice, B. (1997). Coping, life attitudes, and immune responses to imagery and group support after breast cancer treatment. *Alternative Therapies in Health and Medicine*, *3*, 62-71.

Rogosa, D. (1995). Myths and methods: "Myths about longitudinal research" plus supplemental questions. *The analysis of change*, *3*, 66.

Ruspini, E. (2002). *Introduction to longitudinal research*. Psychology Press

Ruspini, E. (1999). Longitudinal research and the analysis of social change. *Quality and Quantity*, *33*, 219-227.

Ryan, A. B. (2006). Post-positivist approaches to research. *Researching and Writing your Thesis: a guide for postgraduate students*, 12-26.

Sackett, D. L., & Wennberg, J. E. (1997). Choosing the best research design for each question. *BMJ: British Medical Journal*, *315*(7123), 1636.

Sale, J. E., Lohfeld, L. H., & Brazil, K. (2002). Revisiting the quantitative-qualitative debate: Implications for mixed-methods research. *Quality and quantity*, *36*(1), 43-53.

Sammarco, A. (2001). Perceived social support, uncertainty, and quality of life of younger breast cancer survivors. *Cancer Nursing*, *24*(3), 212-219.

Sammarco, A., & Konecny, L. M. (2008, September). Quality of life, social support, and uncertainty among Latina breast cancer survivors. In *Oncology nursing forum* (Vol. 35, No. 5).

Sammarco, A., & Konecny, L. M. (2010, January). Quality of life, social support, and uncertainty among Latina and Caucasian breast cancer survivors: a comparative study. In *Oncology Nursing Forum* (Vol. 37, No. 1).

Schneider, S., Moyer, A., Knapp-Oliver, S., Sohl, S., Cannella, D., & Targhetta, V. (2010). Pre-intervention distress moderates the efficacy of psychosocial treatment for cancer patients: a meta-analysis. *Journal of behavioral medicine*, *33*(1), 1-14.

Schmidt, K. R. T., & Teti, D. M. (2005). Issues in the use of longitudinal and cross-sectional designs. *Handbook of research methods in developmental science*, 3-20.

Scriven, M. (2008). A summative evaluation of RCT methodology: & an alternative approach to causal research. *Journal of multidisciplinary evaluation*, *5*(9), 11-24.

Sheard, T., & Maguire, P. (1999). The effect of psychological interventions on anxiety and depression in cancer patients: results of two meta-analyses. *British journal of cancer*, *80*(11), 1770.

Shalev, A. Y. (1992). Posttraumatic stress disorder among injured survivors of a terrorist attack: predictive value of early intrusion and avoidance symptoms. *Journal of Nervous and Mental Disease*.

Shanafelt, T. D., Bowen, D., Venkat, C., Slager, S. L., Zent, C. S., Kay, N. E., ... & Call, T. G. (2007). Quality of life in chronic lymphocytic leukemia: an international survey of 1482 patients. *British journal of haematology*, *139*(2), 255-264.

Shankland, K. R., Armitage, J. O., & Hancock, B. W. (2012). Non-hodgkin lymphoma. *The Lancet*, *380*(9844), 848-857.

Smith, M. J., & Liehr, P. R. (Eds.). (2013). *Middle range theory for nursing*. Springer Publishing Company.

Smith, M. Y., Redd, W. H., Peyser, C., & Vogl, D. (1999). Post-traumatic stress disorder in cancer: a review. *Psycho‐Oncology*, *8*(6), 521-537.

Snow, T. (2010). Agencies claim cuts are leaving wards dangerously understaffed. *Nursing Standard*, *25*(13), 5-6.

Spaner, D. E., & Masellis, A. (2007). Toll-like receptor agonists in the treatment of chronic lymphocytic leukemia. *Leukemia*, *21*(1), 53-60.

Speca, M., Carlson, L. E., Goodey, E., & Angen, M. (2000). A randomized, wait-list controlled clinical trial: the effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. *Psychosomatic medicine*, *62*(5), 613-622.

Stark, D. P. H., & House, A. (2000). Anxiety in cancer patients. *British journal of cancer*, *83*(10), 1261

Streiner, D. L. (2003). Starting at the beginning: an introduction to coefficient alpha and internal consistency. *Journal of personality assessment*, *80*(1), 99-103.

Stubbings, L., & Scott, J. M. (2004). NHS workforce issues: implications for future practice. *Journal of health organization and management*, *18*(3), 179-194.

Suzuki, M. (2012, November). Quality of life, uncertainty, and perceived involvement in decision making in patients with head and neck cancer. In *Oncology nursing forum* (Vol. 39, No. 6).

Tam, C. S., O'Brien, S., Plunkett, W., Wierda, W., Ferrajoli, A., Wang, X., ... & Lerner, S. (2014). Long-term results of first salvage treatment in CLL patients t reated initially with FCR (fludarabine, cyclophosphamide, rituximab). *Blood*, *124*(20), 3059-3064.

Taris, T. W., & Kompier, M. (2003). Challenges in longitudinal designs in occupational health psychology. *Scandinavian journal of work, environment & health*, 1-4.

Taris, T. W., & Kompier, M. A. (2014). Cause and effect: Optimizing the designs of l longitudinal studies in occupational health psychology

Thompson, S. B., Eccleston, L., & Hickish, T. (2011). Post-traumatic stress disorder in cancer survivors: recognising and acknowledging the symptoms.

Tuli, F. (2011). The basis of distinction between qualitative and quantitative research in social science: Reflection on ontological, epistemological and methodological perspectives. *Ethiopian Journal of Education and Sciences*, *6*(1).

Unwin, N., Jordan, J. E., & Bonita, R. (2004). Rethinking the terms non-communicable disease and chronic disease. *Journal of epidemiology and community health*, *58*(9), 801-801

Van der Kolk, B. A., & Fisler, R. (1995). Dissociation and the fragmentary nature of traumatic memories: Overview and exploratory study. *Journal of traumatic stress*, *8*(4), 505-525.

Van Ness, P. H., Fried, T. R., & Gill, T. M. (2011). Mixed methods for the interpretation of longitudinal gerontologic data: Insights from philosophical hermeneutics. *Journal of mixed methods research*, *5*(4), 293-308.

Victora, C. G., Habicht, J. P., & Bryce, J. (2004). Evidence-based public health: moving beyond randomized trials. *American journal of public health*, *94*(3), 400-405.

Wagner, E. H., Austin, B. T., Davis, C., Hindmarsh, M., Schaefer, J., & Bonomi, A. (2001). Improving chronic illness care: translating evidence into action. *Health affairs*, *20*(6), 64-78.

Wagner, E. H., Austin, B. T., & Von Korff, M. (1996). Organizing care for patients with chronic illness. *The Milbank Quarterly*, 511-544.

Warren, J. R., & Halpern-Manners, A. (2012). Panel conditioning in longitudinal social science surveys. *Sociological Methods & Research*, *41*(4), 491-534

Weiss, D. S. & Marmar, C. R. (1997). The Impact of Event Scale-Revised. In: J. P. Wilson & T. M. Keane (Eds.). Assessing psychological trauma and PTSD (pp. 399-411). New York: Guilford Press.

Whitaker, K. L., Watson, M., & Brewin, C. R. (2009). Intrusive cognitions and their appraisal in anxious cancer patients. *Psycho-Oncology*, *18*(11), 1147-1155.

Wild, D., Grove, A., Martin, M., Eremenco, S., McElroy, S., Verjee-Lorenz, A., & Erikson, P. (2005). Principles of good practice for the translation and cultural adaptation process for patient-reported outcomes (PRO) measures: report of the ISPOR task force for translation and cultural adaptation. *Value in health*, *8*(2), 94-104.

Winter, G. (2000). A comparative discussion of the notion of validity in qualitative and quantitative research. *The qualitative report*, *4*(3), 1-14.

Wool, M. S. (1998). Understanding denial in cancer patients. In R. J. Goldberg (Ed.), Psychiatric aspects of cancer (pp. 37–53). Basel, Switzerland: Karger.

Woolrich, R. A., Kennedy, P., & Tasiemski, T. (2006). A preliminary psychometric evaluation of the Hospital Anxiety and Depression Scale (HADS) in 963 people livingwith a spinal cord injury. *Psychology, Health & Medicine*, *11*(1), 80-90.

World Health Organisation. Programme on mental health. Geneva: World Health Organisation; 1996.

Zent, C. S., Kyasa, M. J., Evans, R., & Schichman, S. A. (2001). Chronic lymphocytic leukemia incidence is substantially higher than estimated from tumor registry data. *Cancer*, *92*(5), 1325-1330.

Zhao, X., Cui, L., Wang, W., Su, Q., Li, X., & Wu, J. (2016). Influence of psychological intervention on pain and immune functions of patients receiving lung cancer surgery. *Pakistan journal of medical sciences*, *32*(1), 155.

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta psychiatrica scandinavica*, *67*(6), 361-370.

Appendices

A: Outcome Measures

Hospital Anxiety and Depression Scale (HADS)

Patients are asked to choose one response from the four given for each interview. They should give an immediate response and be dissuaded from thinking too long about their answers. The questions relating to anxiety are marked "A", and to depression "D". The score for each answer is given in the right column. Instruct the patient to answer how it currently describes their feelings.

	I feel tense or 'wound up':	
	Most of the time	3
	A lot of the time	2
	From time to time, occasionally	1
	Not at all	0

	I still enjoy the things I used to enjoy:	
	Definitely as much	0
	Not quite so much	1
	Only a little	2
	Hardly at all	3

	I get a sort of frightened feeling as if something awful is about to happen:	
	Very definitely and quite badly	3
	Yes, but not too badly	2
	A little, but it doesn't worry me	1
	Not at all	0

	I can laugh and see the funny side of things:	
	As much as I always could	0
	Not quite so much now	1
	Definitely not so much now	2
	Not at all	3

	Worrying thoughts go through my mind:	
	A great deal of the time	3
	A lot of the time	2
	From time to time, but not too often	1
	Only occasionally	0

	I feel cheerful:	
	Not at all	3
	Not often	2
	Sometimes	1
	Most of the time	0

	I can sit at ease and feel relaxed:	
	Definitely	0
	Usually	1
	Not Often	2
	Not at all	3

	I feel as if I am slowed down:	
	Nearly all the time	3
	Very often	2
	Sometimes	1
	Not at all	0

	I get a sort of frightened feeling like 'butterflies' in the stomach:	
	Not at all	0
	Occasionally	1
	Quite Often	2
	Very Often	3

	I have lost interest in my appearance:	
	Definitely	3
	I don't take as much care as I should	2
	I may not take quite as much care	1
	I take just as much care as ever	0

	I feel restless as I have to be on the move:	
	Very much indeed	3
	Quite a lot	2
	Not very much	1
	Not at all	0

	I look forward with enjoyment to things:	
	As much as I ever did	0
	Rather less than I used to	1
	Definitely less than I used to	2
	Hardly at all	3

	I get sudden feelings of panic:	
	Very often indeed	3
	Quite often	2
	Not very often	1
	Not at all	0

	I can enjoy a good book or radio or TV program:	
	Often	0
	Sometimes	1
	Not often	2
	Very seldom	3

Reference:

Zigmond and Snaith (1983)

IMPACT OF EVENT SCALE-REVISED

Instructions: The following is a list of difficulties people sometimes have after stressful life events. Please read each item, and then indicate how distressing each difficulty has been for you *during the past 7 days* with respect to the disaster. How much were you distressed or bothered by these difficulties?

		Not at all	A little bit	Mod erate -ly	Quite a bit	Ex- treme -ly
1	Any reminder brought back feelings about it.	0	1	2	3	4
2	I had trouble staying asleep.	0	1	2	3	4
3	Other things kept making me think about it.	0	1	2	3	4
4	I felt irritable and angry.	0	1	2	3	4
5	I avoided letting myself get upset when I thought about it or was reminded of it.	0	1	2	3	4
6	I thought about it when I didn't mean to.	0	1	2	3	4
7	I felt as if it hadn't happened or wasn't real.	0	1	2	3	4
8	I stayed away from reminders about it.	0	1	2	3	4
9	Pictures about it popped into my mind.	0	1	2	3	4
10	I was jumpy and easily startled.	0	1	2	3	4
11	I tried not to think about it.	0	1	2	3	4
12	I was aware that I still had a lot of feelings about it, but I didn't deal with them.	0	1	2	3	4
13	My feelings about it were kind of numb.	0	1	2	3	4
14	I found myself acting or feeling like I was back at that time.	0	1	2	3	4
15	I had trouble falling asleep.	0	1	2	3	4
16	I had waves of strong feelings about it.	0	1	2	3	4

17	I tried to remove it from my memory.	0	1	2	3	4
18	I had trouble concentrating.	0	1	2	3	4
19	Reminders of it caused me to have physical reactions, such as sweating, trouble breathing, nausea, or a pounding heart	0	1	2	3	4
20	I had dreams about it.	0	1	2	3	4
21	I felt watchful and on guard.	0	1	2	3	4
22	I tried not to talk about it.	0	1	2	3	4

MISHEL UNCERTAINTY IN ILLNESS SCALE (Adult)

INSTRUCTIONS:

Please read each statement. Take your time and think about what each statement says in terms of your illness.

Then place an "X" under the column that most closely measures how you are feeling TODAY. If you agree with a statement, then you would mark under either "Strongly Agree" or "Agree." If you disagree with a statement, then mark under either "Strongly Disagree" or "Disagree."

If you are undecided about how you feel, then mark under "Undecided" for that statement.
Please respond to every statement.

1. I have a lot of questions without answers.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
____	____	____	____	____

2. I understand everything explained to me.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
____	____	____	____	____

3. The doctors say things to me that could have many meanings.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
____	____	____	____	____

4. There are so many different types of staff, it's unclear who is responsible for what.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
____	____	____	____	____

5. The purpose of each treatment is clear to me.

Strongly Agree (5)	Agree (4)	Undecided (3)	Disagree (2)	Strongly Disagree (1)
____	____	____	____	____

B: Patient Information Sheets

Participant Consent Form

"Watch and Wait" examining potential uncertainly in illness, depression and anxiety in patients with Chronic Lymphocytic Leukaemia or Low Grade Lymphoma.

Principle Investigators [redacted]
General Hospital
[redacted]
General Hospital
[redacted].

Study Identification number _____

Initial in each box

1. I have read and understood the information sheet for the above study and have had the opportunity to ask questions. ☐
2. I agree to take part in this study and to complete questionnaires. ☐
3. I understand my participation is voluntary and that I am free to withdraw at any time, without giving a reason, and without my medical or legal rights being affected. ☐
4. I agree that sections of my medical notes may be viewed by responsible members of the research team at Colchester General Hospital or by regulatory authorities where
   it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐
5. I agree that my details will be kept on an anonymised database. ☐
6. I agree that my anonymised responses may be shared in scientific publications and at scientific meeting. ☐
7. I agree that the data collected may be used in an anonymised form for research and educational purposes in the future. ☐
8. I agree for my GP to be informed about my participation in the study ☐

Participant:

Print Name_____

Signature_____

Date_____

Researcher:

Print Name_____

Signature_____

Date_____

Original copy of this form must be stored in site file, a copy offered to participant and a copy filed in the clinical notes

GP Information Sheet

[redacted]

[Recipient Name]
[Recipient Address]

[Date]

Dear Dr [Recipient]

Re: [Participant Name] [Participant Address or DOB]

I am writing to inform you that the above patient has consented to participate in a research study investigating the potential impact of uncertainty on depression, anxiety and trauma in patients with untreated Chronic Lymphocytic Leukaemia or Low Grade Lymphoma on "Watch and Wait". The study involves completing questionnaires at regular intervals, and does not affect medical management in any way. The study is being run by [redacted] who is studying for a Doctorate in Clinical Psychology at the University of Essex. The study has received approval from the East of England- Essex Research Ethics Committee (REC reference number: 16/EE/0414).

Please find enclosed a copy of the study information leaflet and signed consent form for your reference and inclusion in the patient's records. Should you have any questions or concerns about your patient participating in this study, please do not hesitate to contact the team on 01206 746421.

Yours sincerely,

[redacted]

Patient Information sheet

Investigators [redacted]

Hospital [redacted]

General Hospital [redacted].

Introduction

You are invited to take part in a research study. It is entirely up to you to decide whether or not you would like to join the study. Before you decide we would like you to understand why the research is being done and what it involves for you. Your participation is completely voluntary, it's up to you.

Please take time to read the following information about the research study carefully. Talk to others about the research study if you wish and please ask your doctor or research nurse if you have any questions or would like more information.

[redacted] will be analysing the data provided by the questionnaires as part of his [redacted]

Purpose of the research study

There is very little research to describe the quality of life patients experience following a diagnosis of Chronic Lymphocytic Leukaemia or Low Grade Lymphoma during the period when your disease is being monitored on "Watch and Wait" and you do not require treatment. Up until now, nearly all studies of quality of life in patients like you have been confined to clinical trials studying the effects of different chemotherapy regimens on your quality of life. Therefore, the lack of knowledge about what quality of life issues patients face limits the ability of the health care team to deliver effective treatments to address your needs.

Firstly, this study aims to collect information about the impact your diagnosis has had on your quality of life, in particular potential levels of uncertainty in illness, anxiety, depression or trauma. Secondly, we would like to understand if levels of anxiety, depression or trauma change over the first year following your diagnosis. Thirdly, does "uncertainty" about how your illness may change or develop have any influence on potential levels of anxiety, depression or trauma as time goes on and you are living with your condition.

People can live with Chronic Lymphocytic Leukaemia or Low Grade Lymphoma for decades without any need for treatment and therefore, the goal of therapy for these patients is to maintain the highest quality of life. Chronic Lymphocytic Leukaemia or Low Grade Lymphoma can be associated with a number of potential issues that could

affect you socially, physically or emotionally and subsequently have an impact on your quality of life.

Why have I been invited to take part?

You have been invited to consider taking part in this study because you have recently been diagnosed with Chronic Lymphocytic Leukaemia or Low Grade Lymphoma and your Hospital Specialist has assessed that at present your disease does not require any intervention or active treatment, but you will be monitored closely to see if and when treatment should start. This approach is commonly called "Watch and Wait" and is based on evidence that suggests immediate or early treatment of patients with "low or intermediate level" of disease does not prolong the life of the patient.

Do I have to take part?

It is up to you whether or not you want to take part as participation is entirely voluntary. Your treatment and monitoring will be the same whether you take part or not. Whether or not you decide to take part you will be given this information sheet to keep, and only asked to sign a consent form if you do decide to take part. You are free to withdraw from the study at any time and without giving a reason. A decision to withdraw from study will not affect the standards of your care.

What will happen to me if I do take part?

We are asking people with a recent diagnosis of Chronic Lymphocytic Leukaemia or Low Grade Lymphoma to complete 3 different questionnaires designed to measure levels of anxiety, depression or trauma. We ask that you complete the questionnaires honestly and answer all questions if you can, though you do not have to give answers if you prefer not to.

1. Hospital Anxiety and Depression Scale (HADS)
2. Mishel's Uncertainty in illness questionnaire (MUIS)
3. Impact of Events Scale-revised (IES-R)

We will approach you when you attend your routine clinic to complete these questionnaires. The first time will be within the first 3 months of diagnosis. These questionnaires will be repeated 3 months later, 6 months later and finally at 12 months.

We anticipate it will take approximately 20 minutes to complete all the questionnaires at each visit.

What will happen if my disease changes and I need treatment?

If your clinical situation changes after signing consent but before the final time point at 12 months, then you will be re-assessed against the study's inclusion and exclusion criteria. If you no longer meet all inclusion/exclusion criteria at any time before

questionnaire completion, then you will be withdrawn from the study. Examples would include disease changing from "watch and wait" pathway to requiring intervention treatment or in the unlikely event that you lose the ability to make your own choices and decisions after the consent process.

Personal Information

Participants who give written consent to participate will have baseline personal data and clinical data recorded. This will include age, gender, ethnicity, religion, occupation, marital status, general well-being, disease stage, date of diagnosis, and any other illnesses. This information may be collected from your medical notes or from you in person. Information that identifies you such as your name and date of birth will be kept confidential.

What are the possible disadvantages and risks of taking part?

The risks of this research are minimal. The proposed questionnaires for this study have not been reported to cause psychological or physical distress. This study does not influence the treatment your Doctor has planned for you. We will ask you to attend an additional visit to complete written consent. You will not need to see your Doctor more often than you normally would but your visit will take longer whilst you complete questionnaires.

What are the possible benefits of taking part?

Participants may receive no direct benefit from this study, however, this study is intended to gain a better understanding of how your disease affects you whilst on “watch and wait” monitoring. Taking part may provide insight and help healthcare professionals support those individuals seeking assistance with their anxiety and depression and design effective interventions to address the needs of future patients.

Will I incur any expense will I be paid to take part?

No. It will not cost you anything to take part in this study. Neither you nor this hospital will be paid for taking part in the study. The questionnaires will be completed when you come to clinic for review with your Consultant Haematologist. You will not receive any financial reward for completing questionnaires even if we ask you to attend additional visit to complete questionnaire or provide written consent.

Will my GP be told that I am part of this study?

Yes. We will inform your GP that you are taking part in this study so that you can access support from them in the unlikely but possible circumstance that the questionnaires’ cause you any distress

What if there is a problem?

Wish to complain formally, you can do this through your local hospitals Patient Advice and Liaison (PALS), or the NHS Complaints Procedure. You can contact PALS by calling the hospital on 01206 747474 and asking to speak to the PALS team.
If you have any questions about the research during this study you may contact: Tina Hickey on 01206 746421 or Clinical Trials Manager on 01206 744496.

Will my taking part in the study be kept confidential?

In you consent to take part in study you will be assigned a unique number which will be used to connect your questionnaire and personal data throughout the study. We will collect your name and initials on consent form with assigned unique number. .The Principal Investigator will ensure any information collected about you during the course of your participation will be kept strictly confidential and stored on a secure, restricted access computer or a locked filing cabinet in the research office at [redacted]
Your anonymized study data will be available for future ethically-approved research and educational purposes, without your identity being made known. Do discuss that with us if that would be a problem for you.

Who has reviewed and approved this study?

This study has been reviewed and approved by the Essex NRES Research Ethics Committee East of England, and by the Research and Development Department of Colchester Hospital.

What will happen to the results of the study?

The results of this research will be published in a medical journal after the study has been completed. Your research team should tell you the results and how you can access the published results.

Patients will not be identified in any report or publication

C: Graphs and Tables: Assumptions Testing

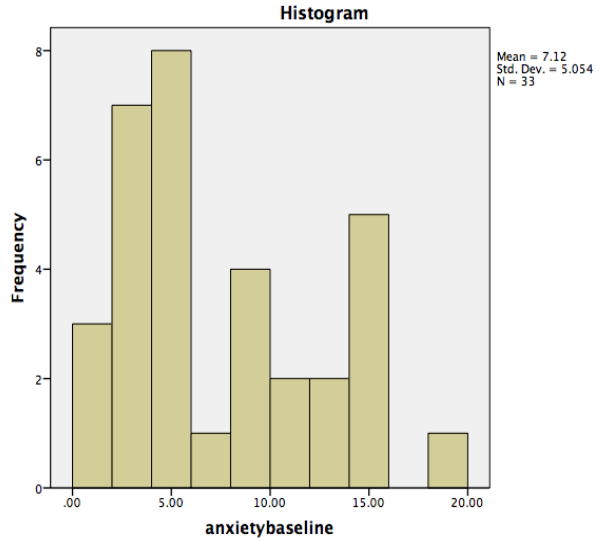
Normality Table – Shapiro Wilk's Test Initial Data

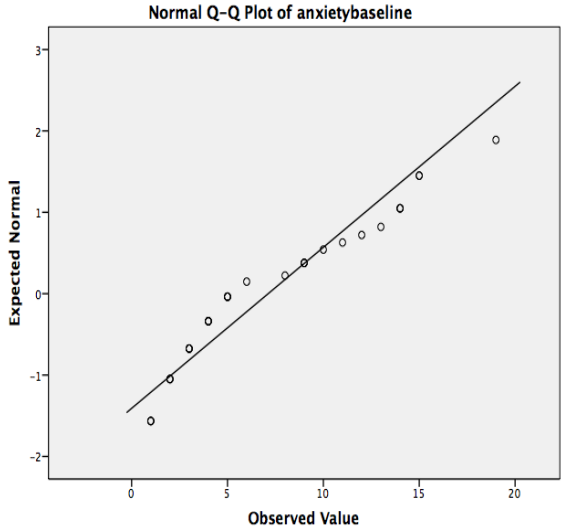
Psychological Measures	**Shapiro – Wilk**		
	Statistic	**df**	**Sig.**
Anxiety Time-1	.887	23	.014
Anxiety 3-Months	.883	23	.013
Anxiety 6- Months	.987	23	.151
Depression Time-1	.812	23	.001
Depression 3-Months	.835	23	.001
Depression 6-Months	.801	23	.000
HADS Total Time-1	.906	23	.033
HADS Total 3-Months	.880	23	.010
HADS Total 6-Months	.857	23	.004
Intrusion Time-1	.907	23	.035
Intrusion 3-Months	.901	23	.027
Intrusion 6-Months	.858	23	.004
Avoidance Time-1	.948	23	.263
Avoidance 3-Months	.925	23	.085
Avoidance 6-Months	.929	23	.102
Hyperarousal Time-1	.844	23	.002
Hyperarousal 3-Months	.868	23	.006
Hyperarousal 6-Months	.793	23	.000
IES-R Time-1	.950	23	.290
IES-R 3-Months	.932	23	.118
IES-R 6-Months	.905	23	.031
MIUS-SF Time-1	.969	23	.657
MIUS-SF 3-Months	.949	23	.273
MIUS-SF 6-Months	.940	23	.176

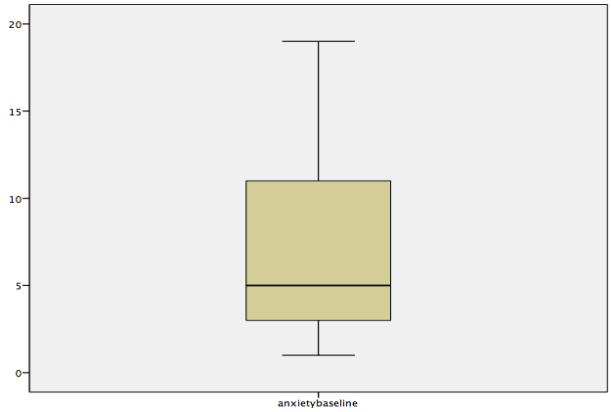
Normality Table Log Transformed Data– Shapiro Wilk's Test

Psychological Measures	**Shapiro – Wilk**		
	Statistic	**df**	**Sig.**
Anxietylog Time-1	.920	23	.076
Anxietylog 3-Months	.927	23	.105
Anxietylog 6-Months	.912	23	.052
Depressionlog Time-1	.922	23	.083
Depressionlog 3-Months	.959	23	.465
Depressionlog 6-Months	.946	23	.263
HADSlog Total Time-1	.950	23	.313
HADSlog Total 3-Months	.958	23	.441
HADSlog Total 6-Months	.947	23	.227
Intrusionlog Time-1	.944	23	.283
Intrusionlog 3-Months	.923	23	.089
Intrusionlog 6-Months	.953	23	.359
Hyperarousallog Time-1	.935	23	.002
Hyperarousallog 3-Months	.890	23	.019
Hyperarousallog 6-Months	.912	23	.046
IES-Rlog Time-1	.877	23	.011
IES-Rlog 3-Months	.936	23	.041
IES-Rlog 6-Months	.906	23	.013

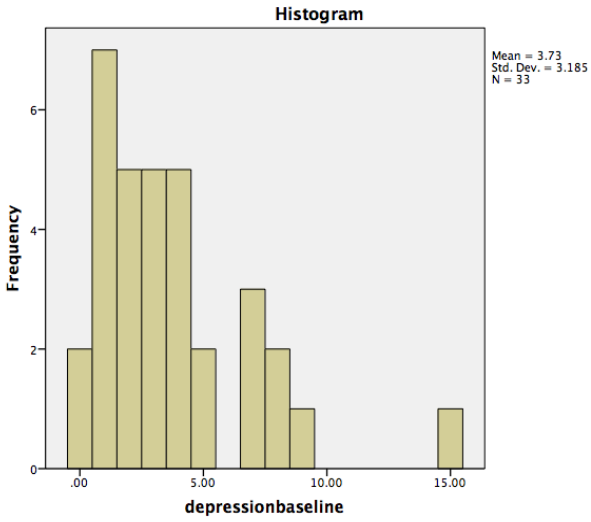
D: Variables: Time-1
Anxiety Histogram, Box Plots and Q-Q Plots

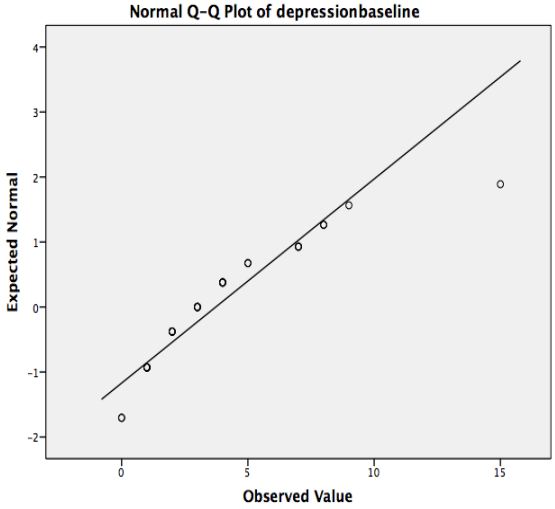


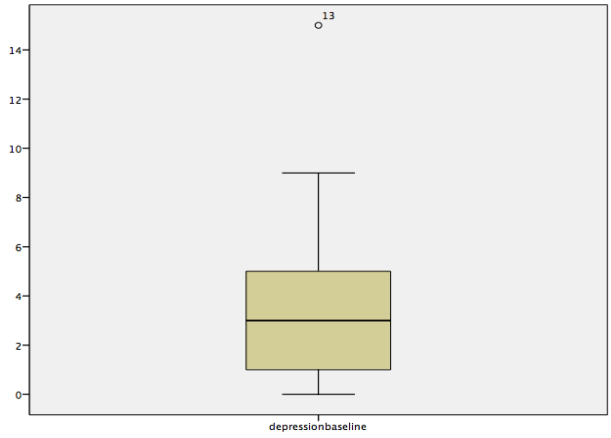




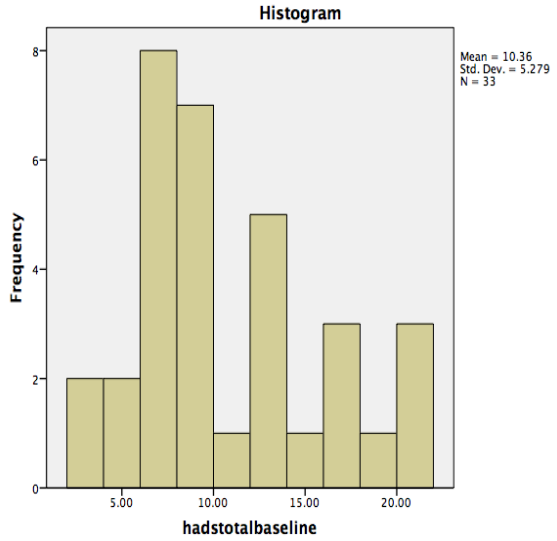
Variables: Time-1
Depression Histogram, Box Plots and Q-Q Plots

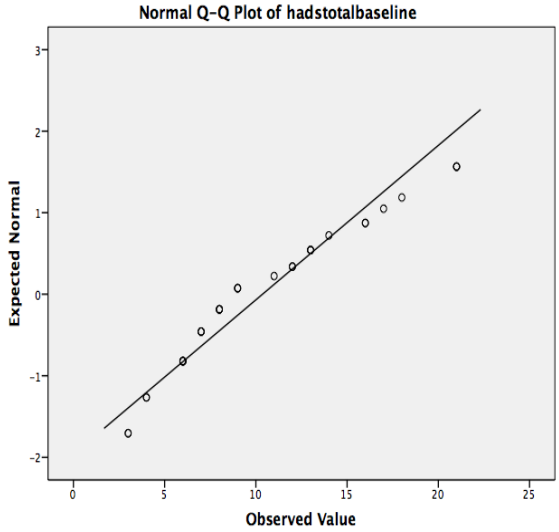


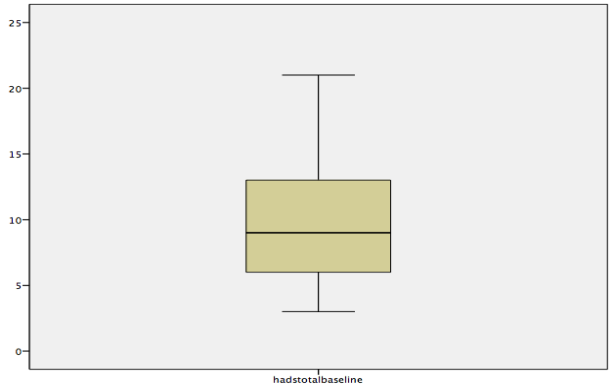




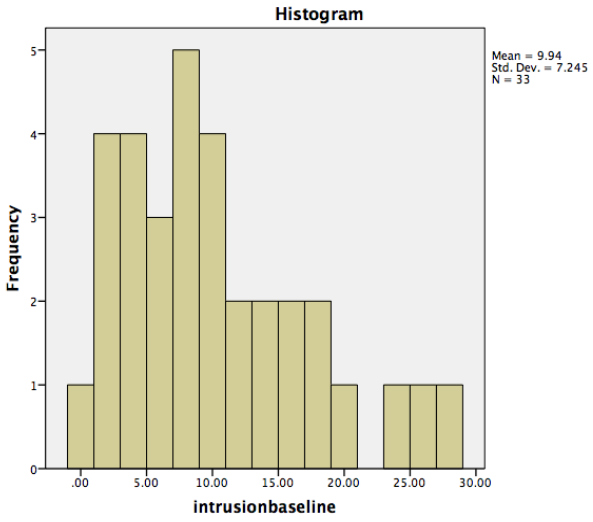
Variables: Time-1
HADS Total Histogram, Box Plots and Q-Q Plots

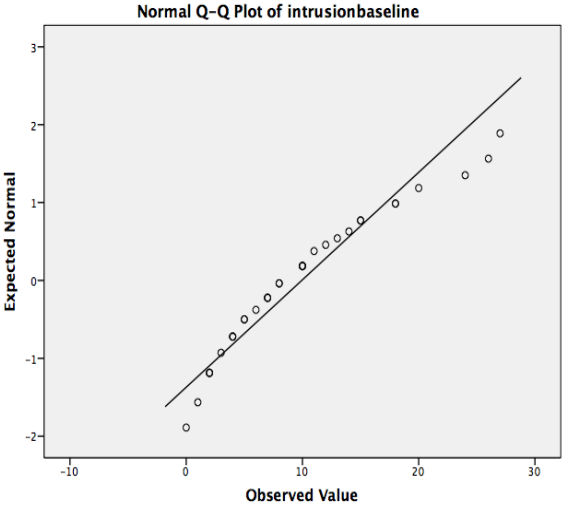




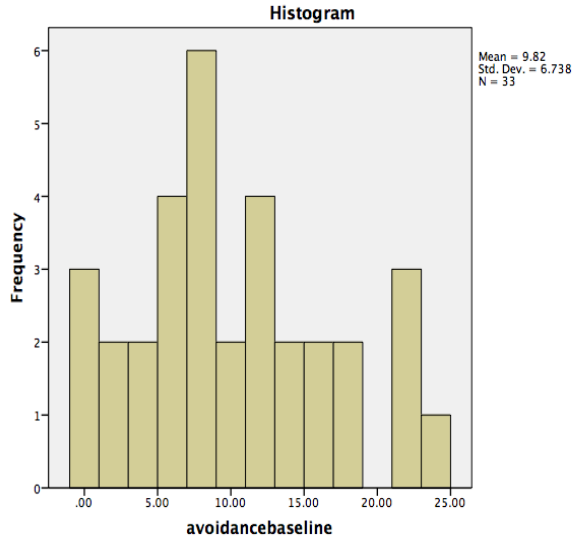


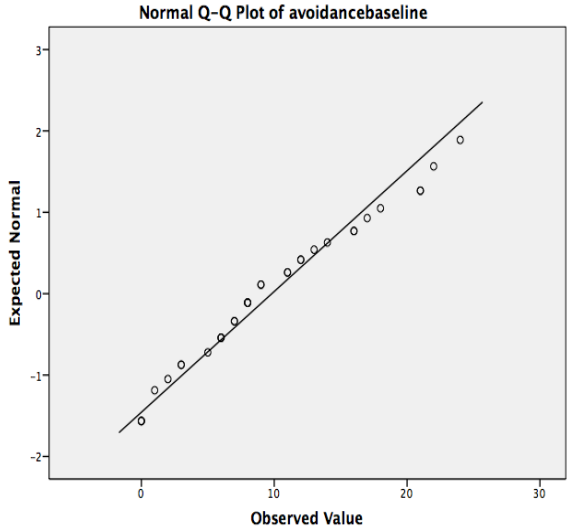
Variables: Time-1
Intrusion Histogram, Box Plots and Q-Q Plots

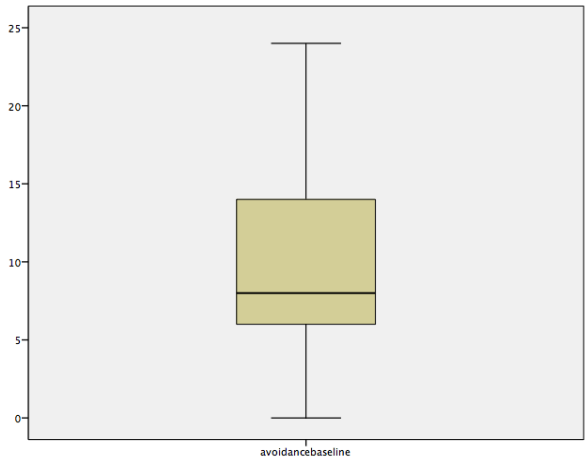




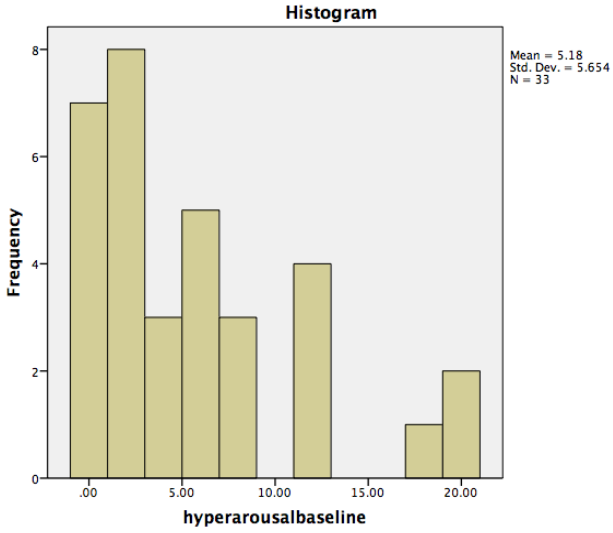
Variables: Time-1
Avoidance Histogram, Box Plots and Q-Q Plots

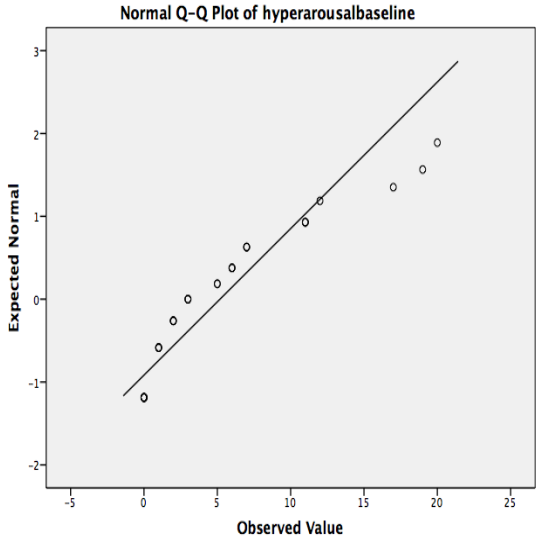


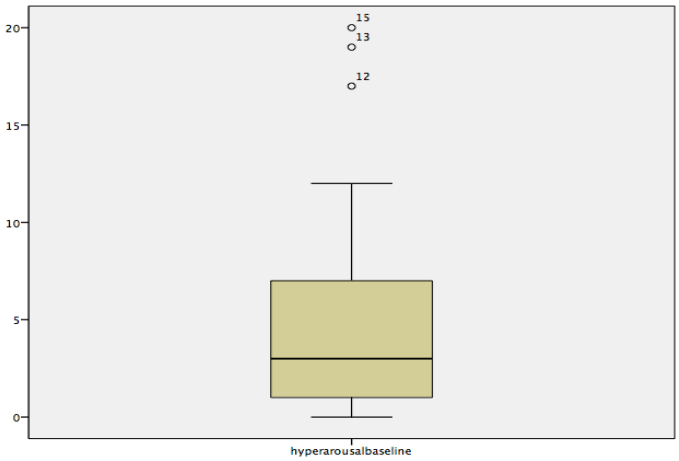




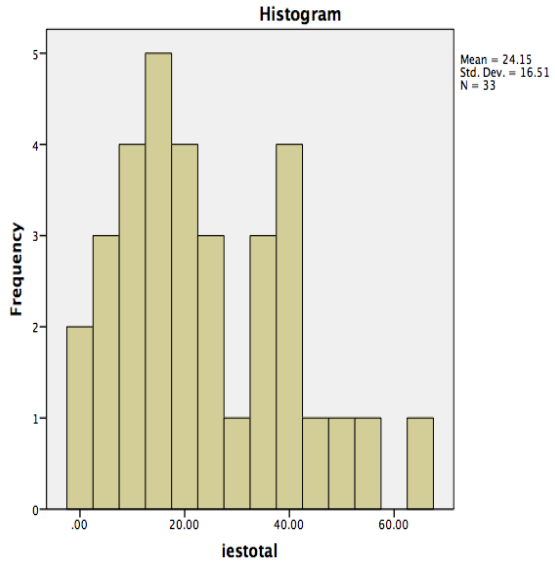
Variables: Time-1
Hyperarousal Histogram, Box Plots and Q-Q Plots

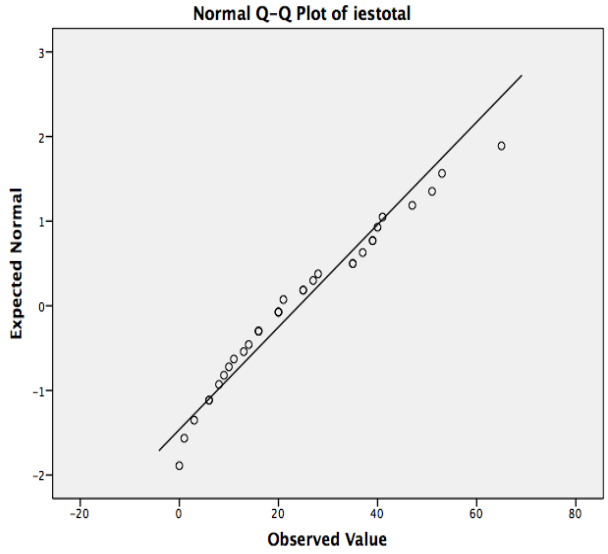


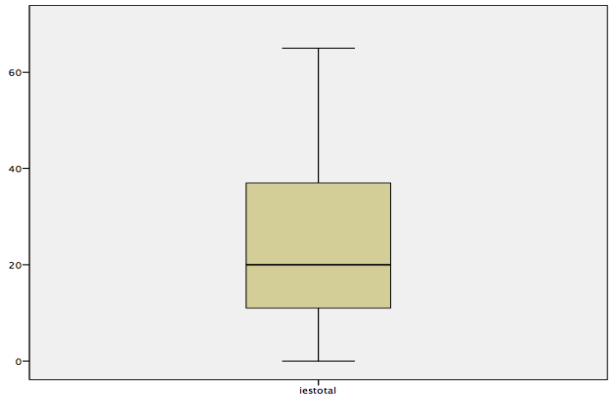




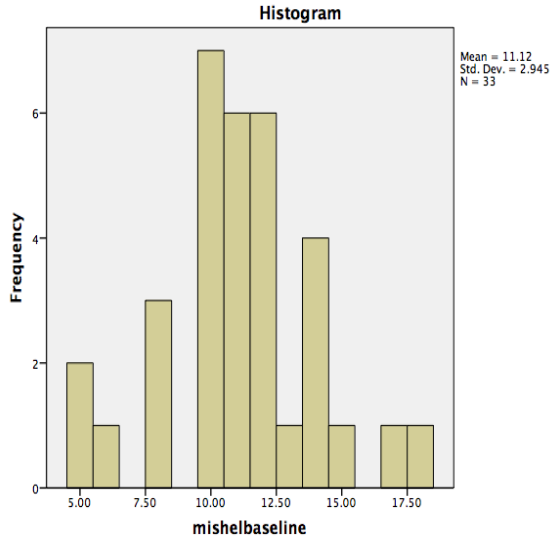
Variables: Time-1
IES-R Total Histogram, Box Plots and Q-Q Plots

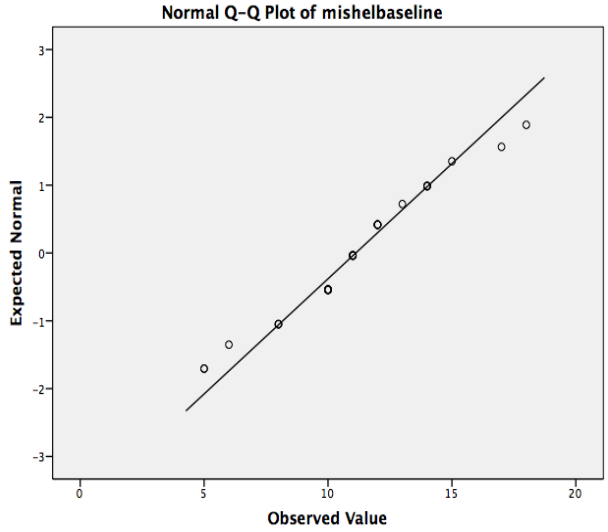


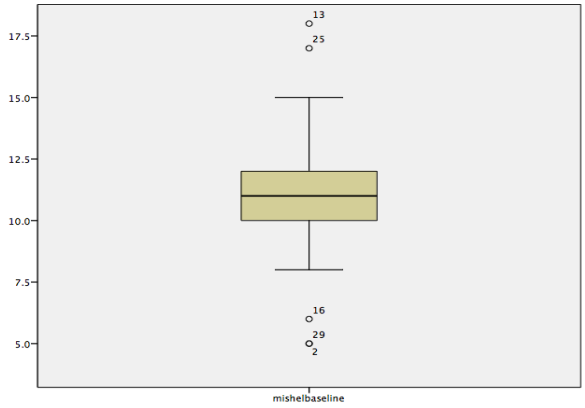




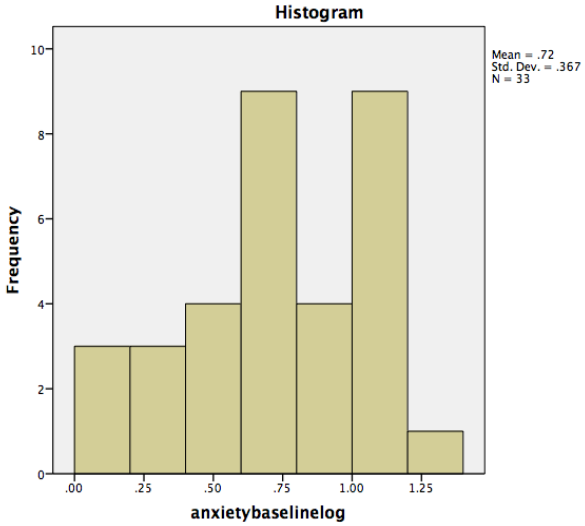
Variables: Time-1
MIUS-SF Histogram, Box Plots and Q-Q Plots

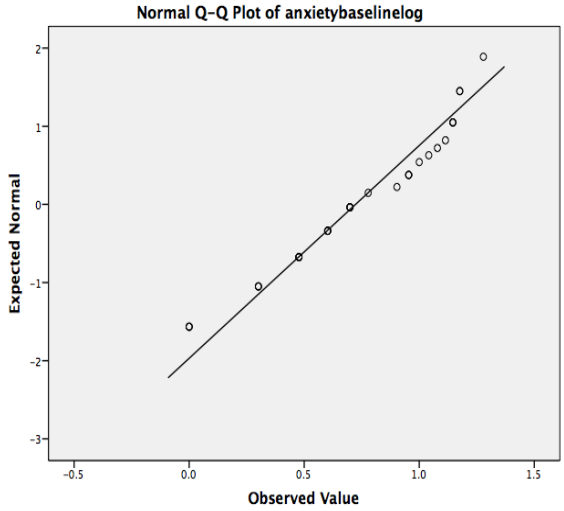


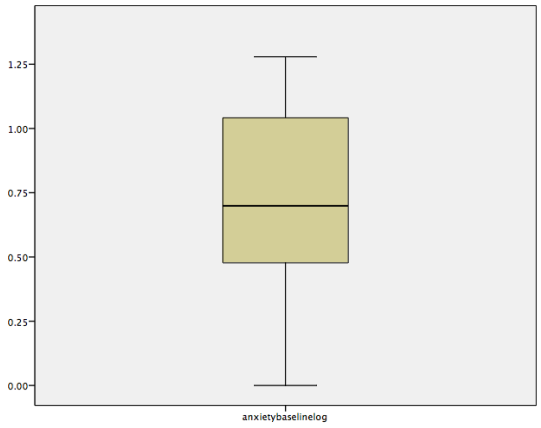




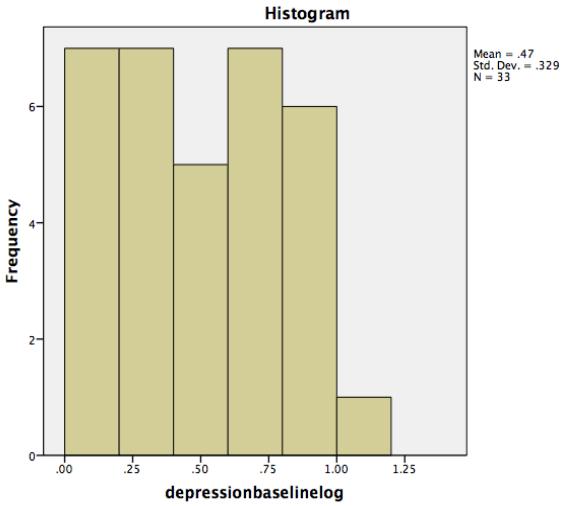
E: Log Transformed Variables: Time-1
Anxiety Histogram, Box Plots and Q-Q Plots

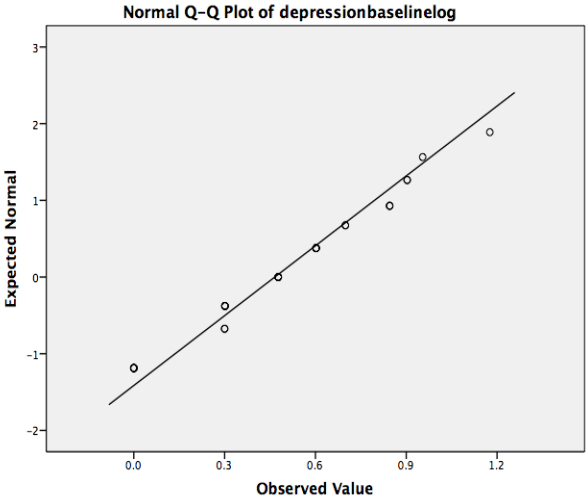


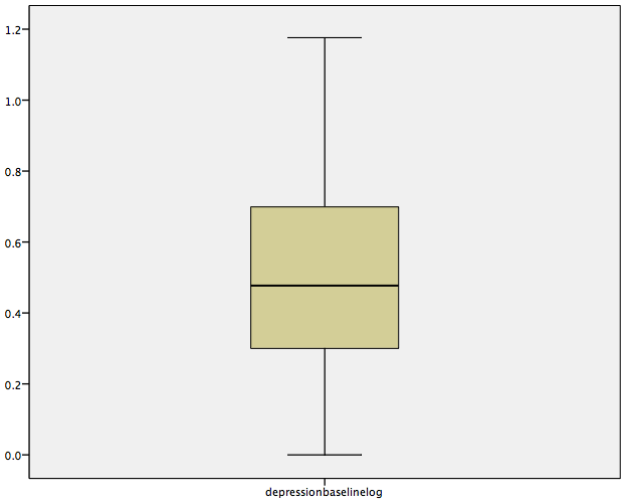




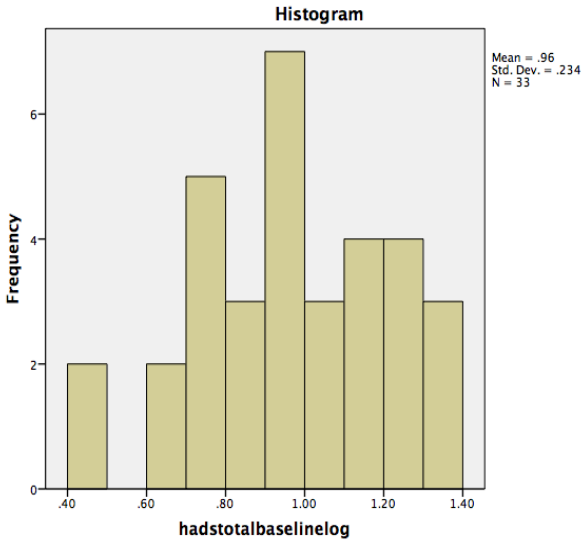
Log Transformed Variables: Time-1
Depression Histogram, Box Plots and Q-Q Plots

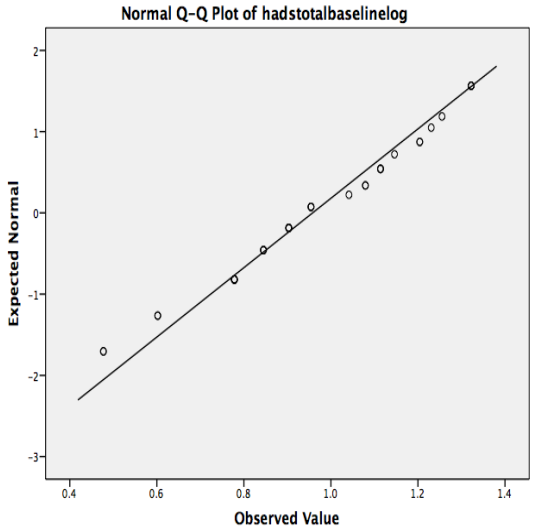


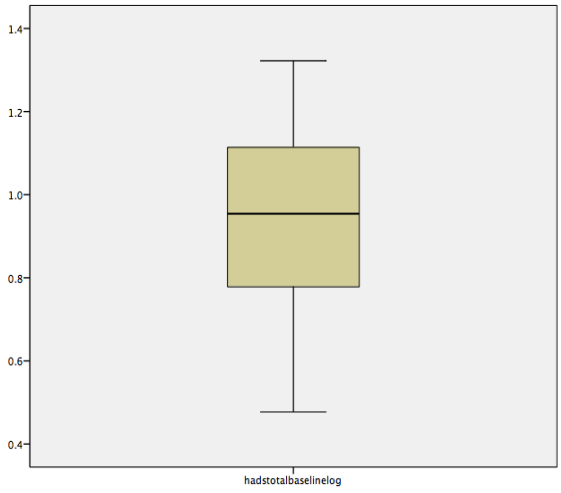




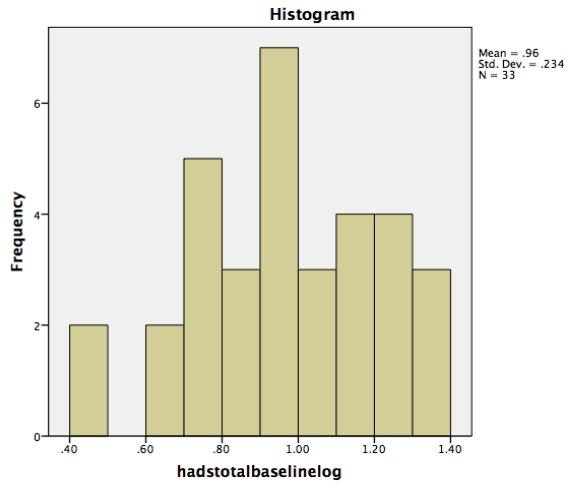
Log Transformed Variables: Time-1
HADS Total Histogram, Box Plots and Q-Q Plots

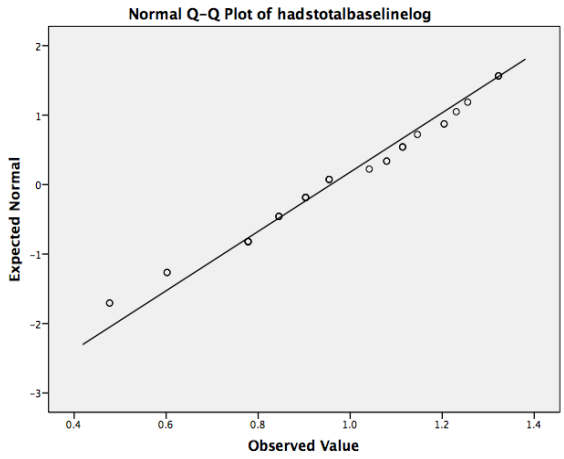


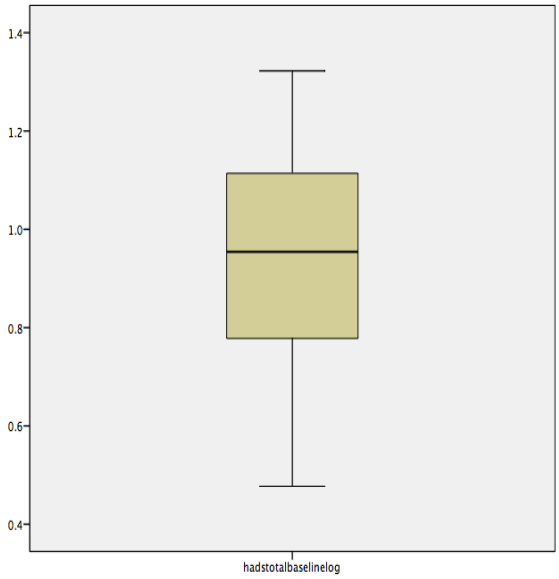




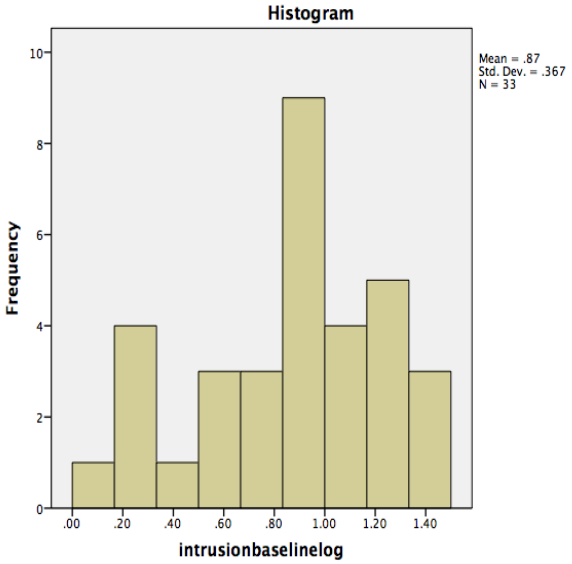
Log Transformed Variables: Time-1
HADS Total Histogram, Box Plots and Q-Q Plots

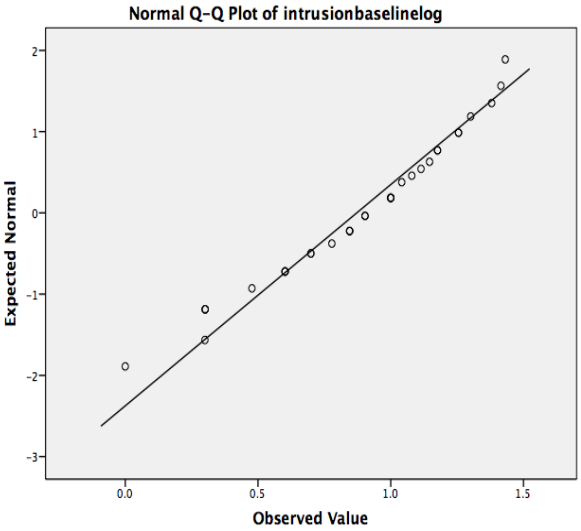


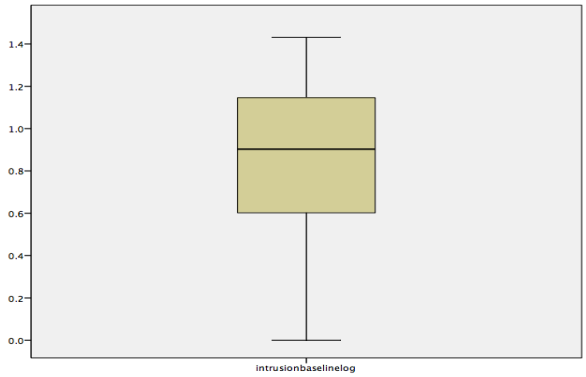




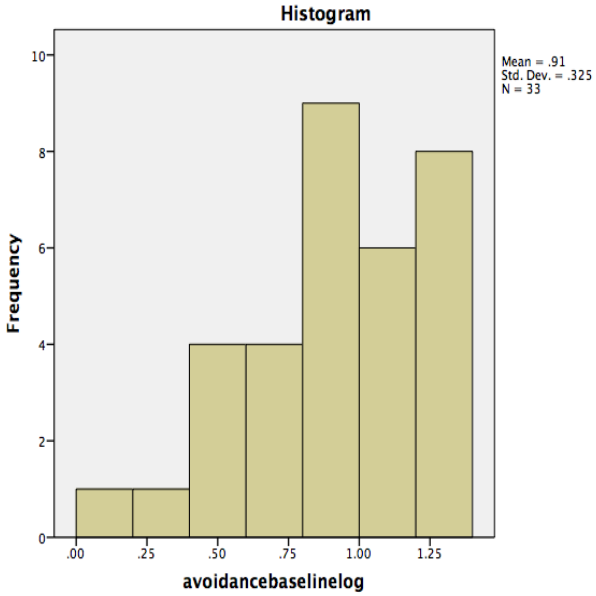
Log Transformed Variables: Time-1
Intrusion Histogram, Box Plots and Q-Q Plots

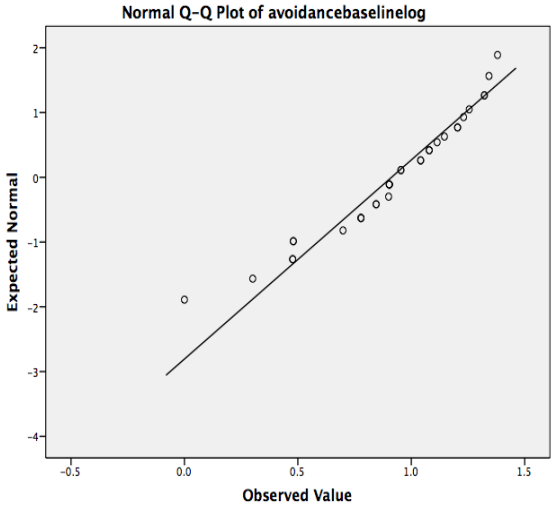


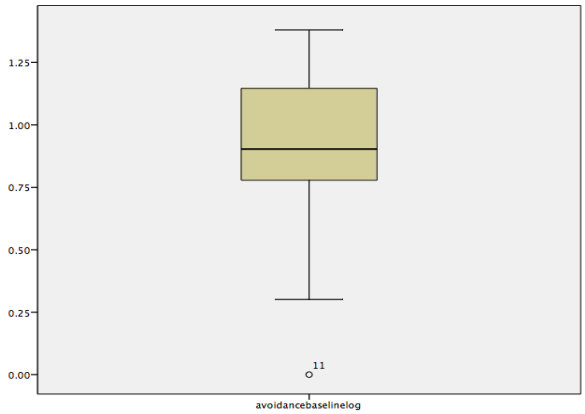




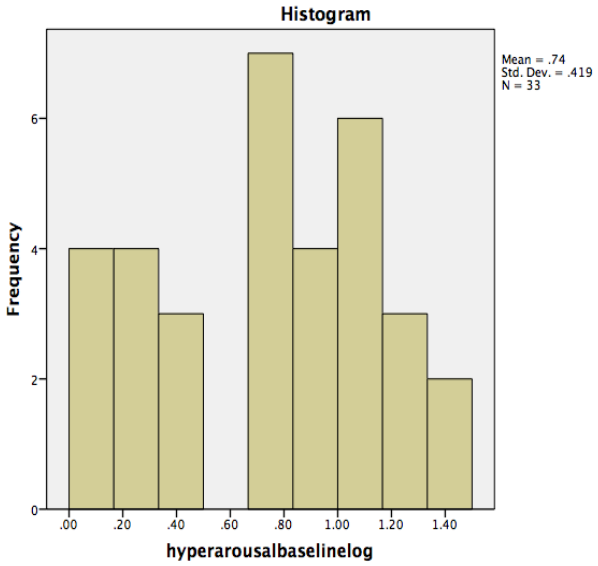
Log Transformed Variables: Time-1
Avoidance Histogram, Box Plots and Q-Q Plots

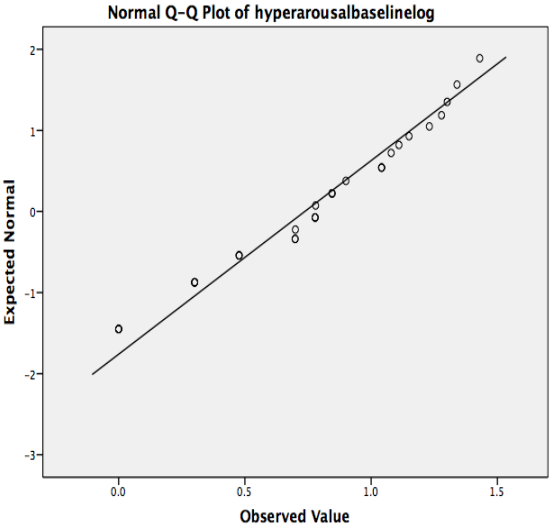


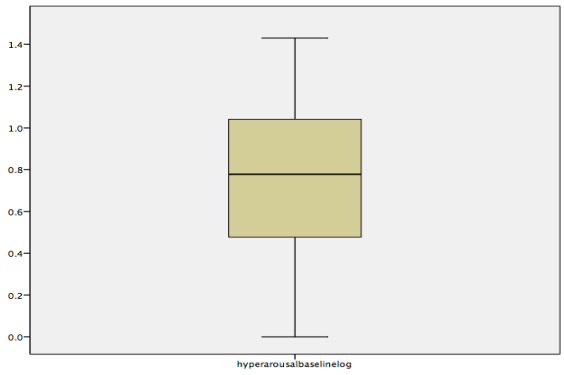




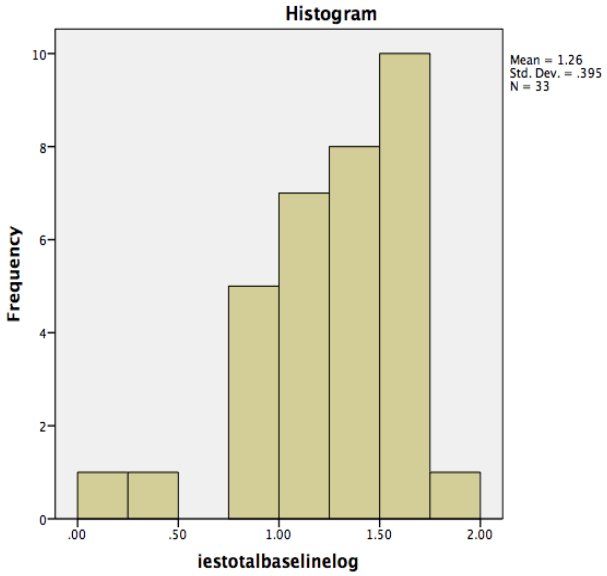
Log Transformed Variables: Time-1
Hyperarousal Histogram, Box Plots and Q-Q Plots

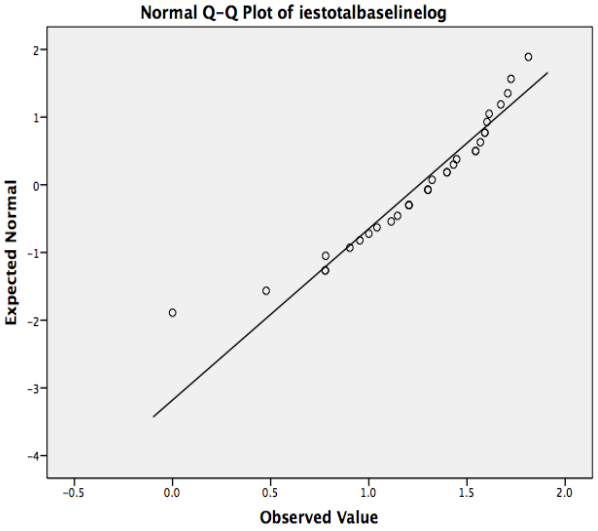


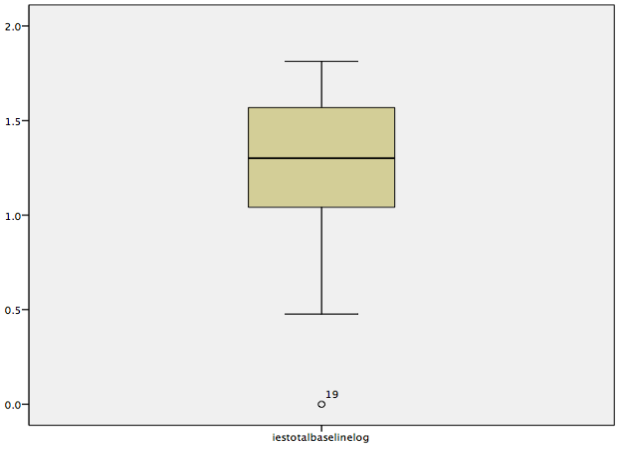




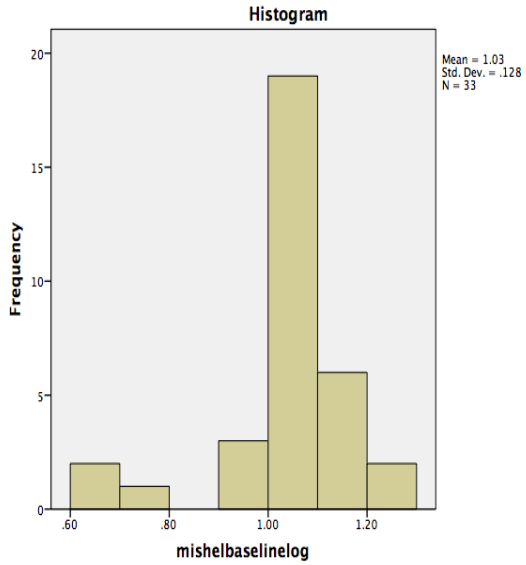
Log Transformed Variables: Time-1
IES-R Total Histogram, Box Plots and Q-Q Plots

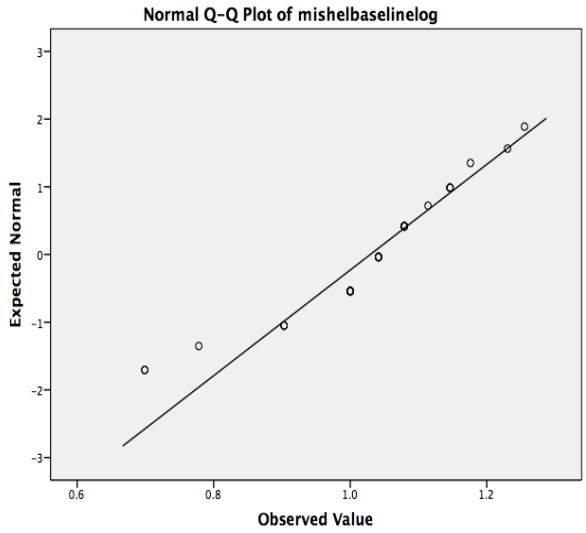


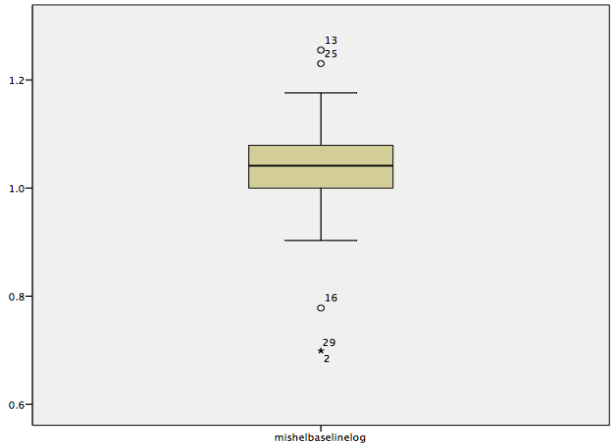




Log Transformed Variables: Time-1
MIUS-SF Histogram, Box Plots and Q-Q Plots

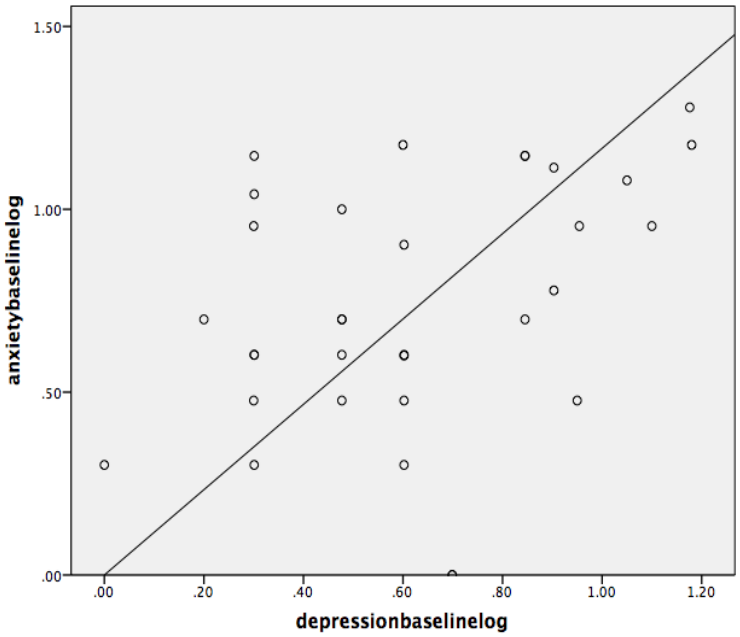




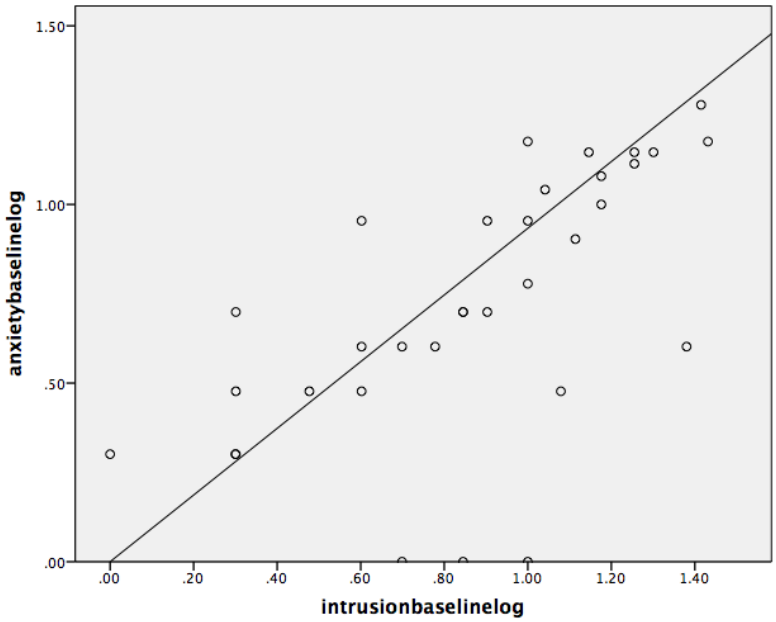


F: Correlation Time-1

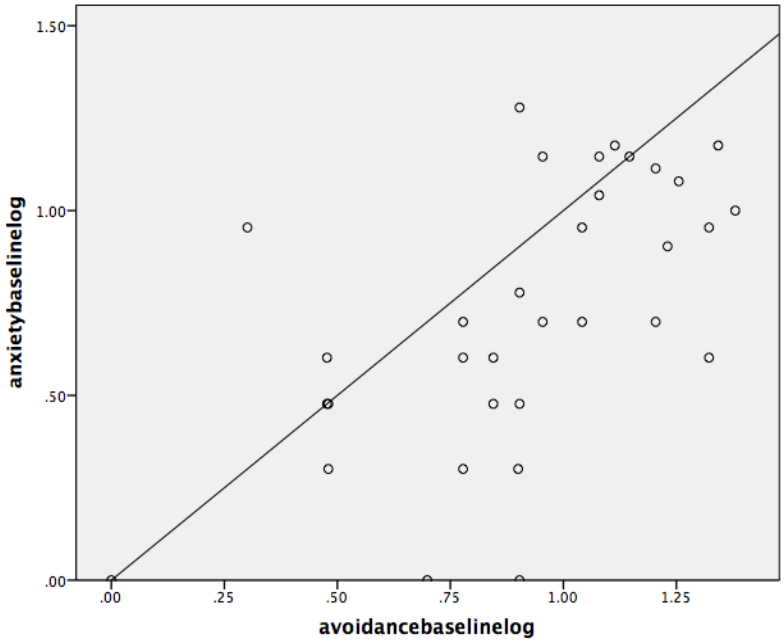
Anxiety and Depression



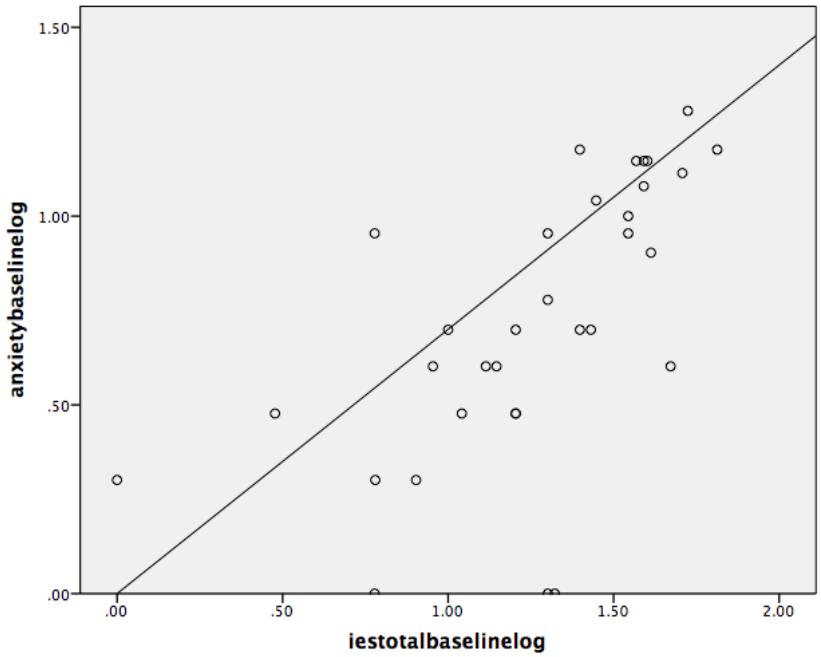
Anxiety and Intrusion



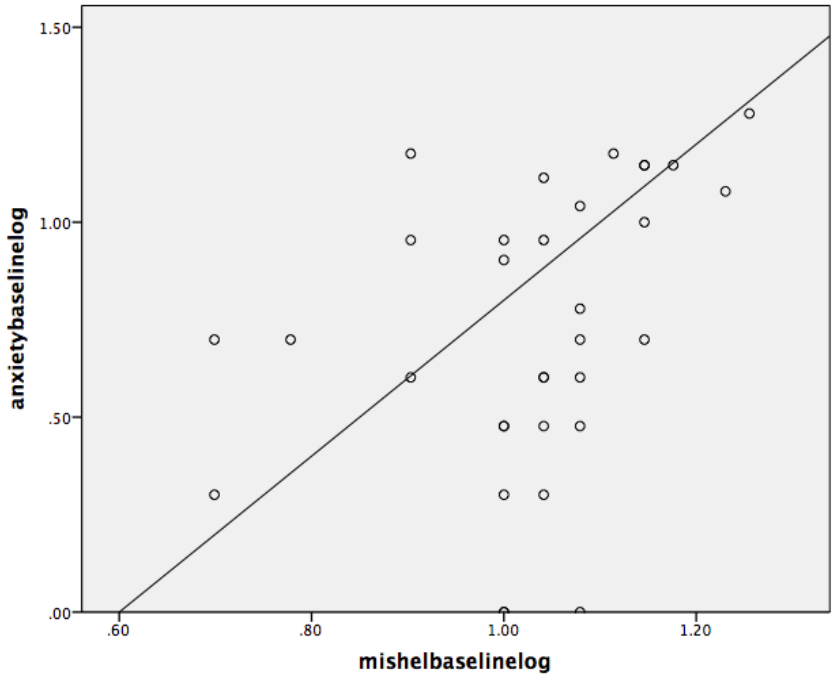
Anxiety and Avoidance



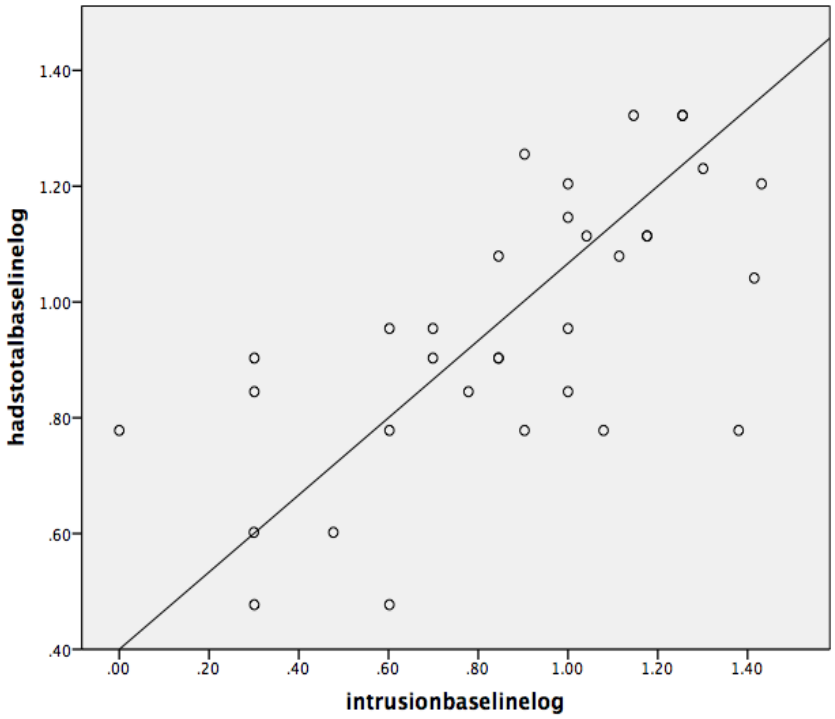
Anxiety and IES-R Total



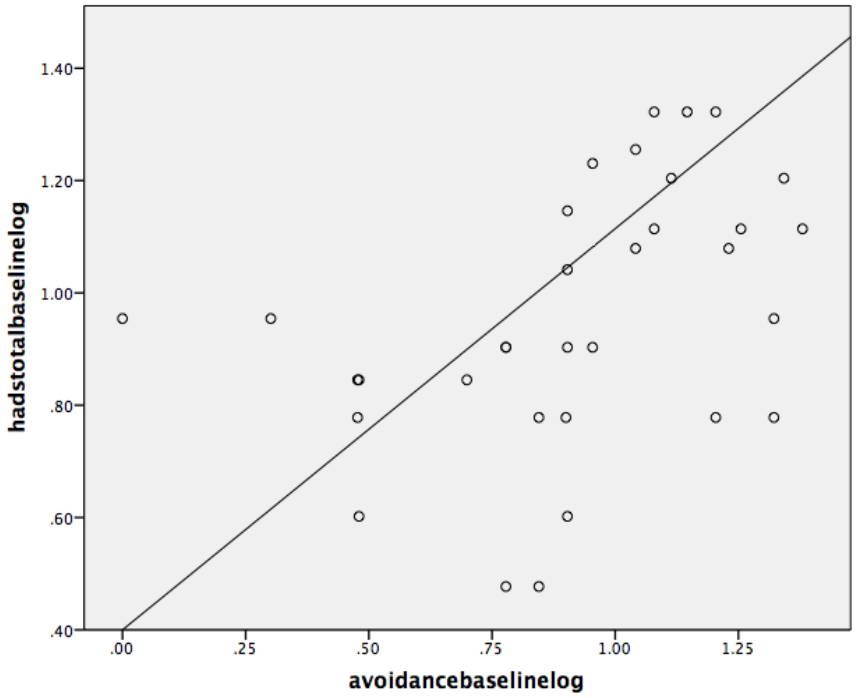
Anxiety and Uncertainty in Illness



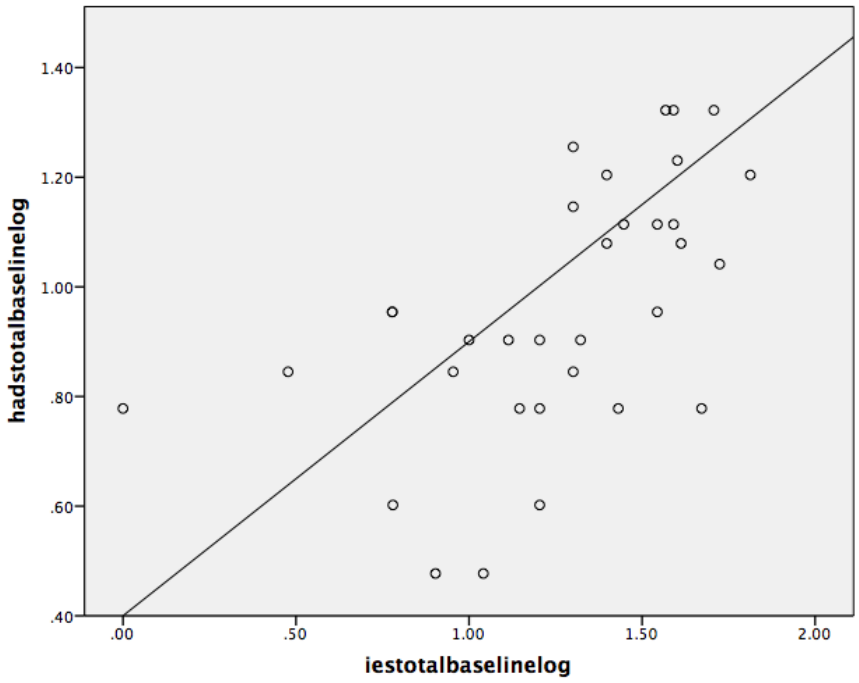
HADS Total and Intrusion



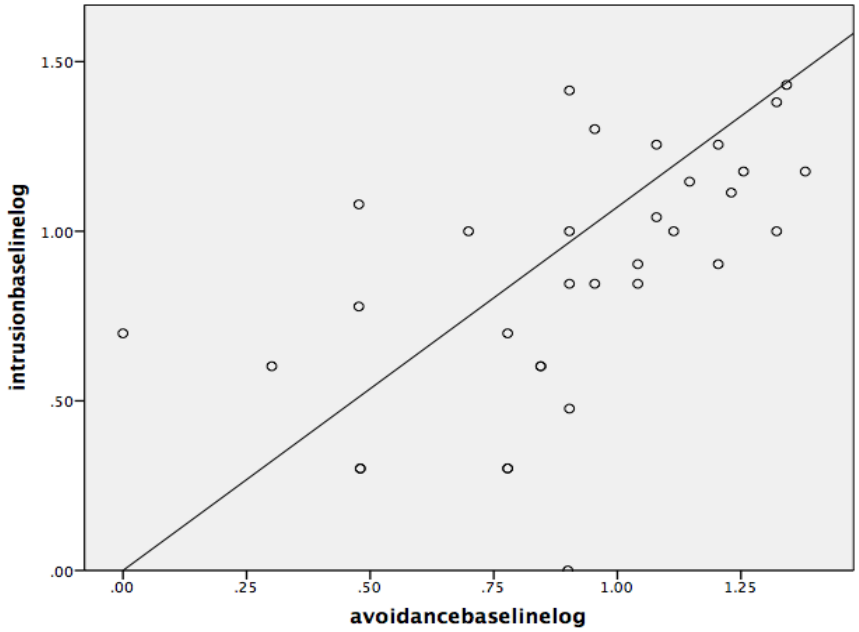
HADS Total and Avoidance



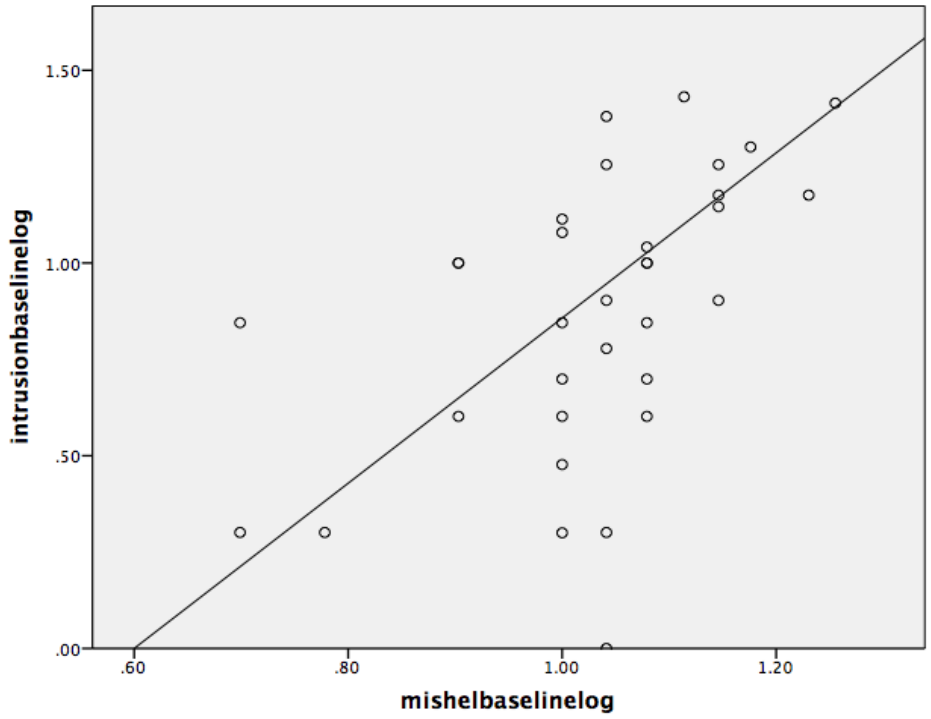
HADS Total and IES-R Total



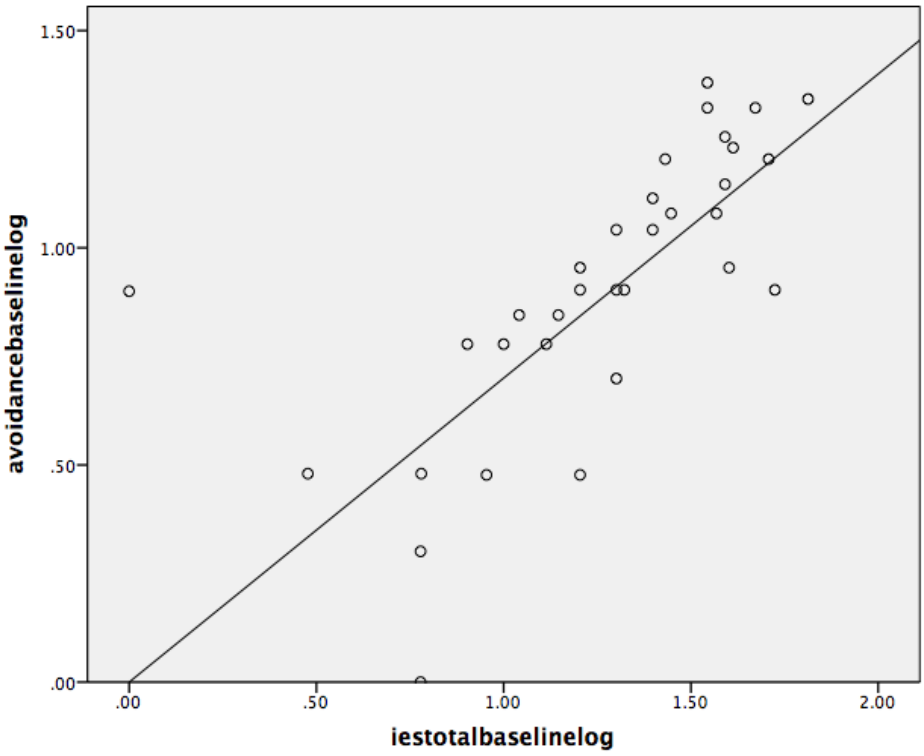
Intrusion and Avoidance



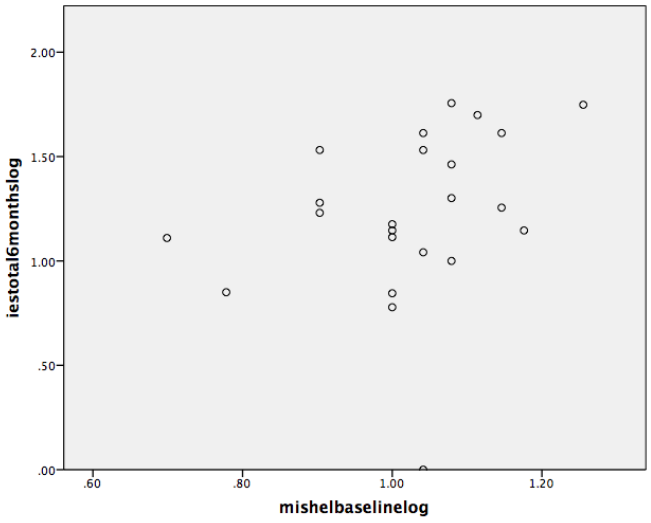
Intrusion and Uncertainty in Illness

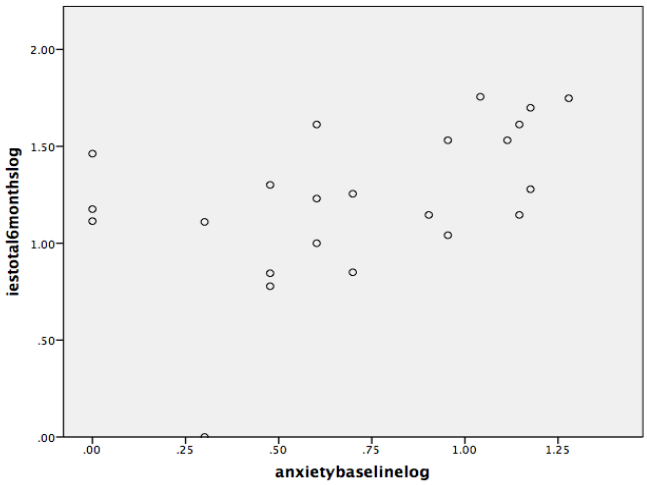


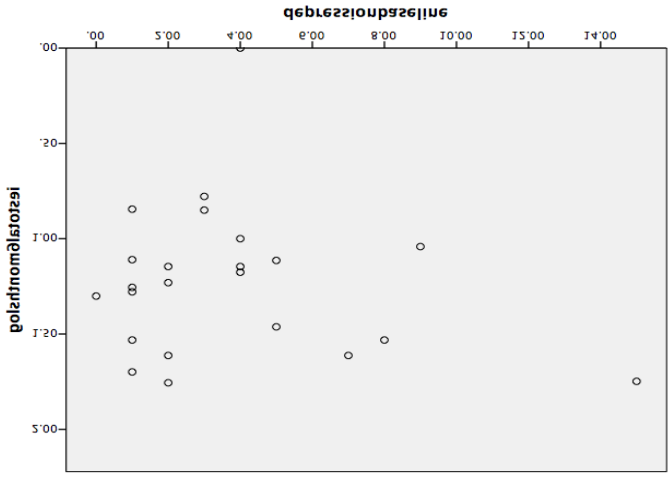
Avoidance and IES-R Total



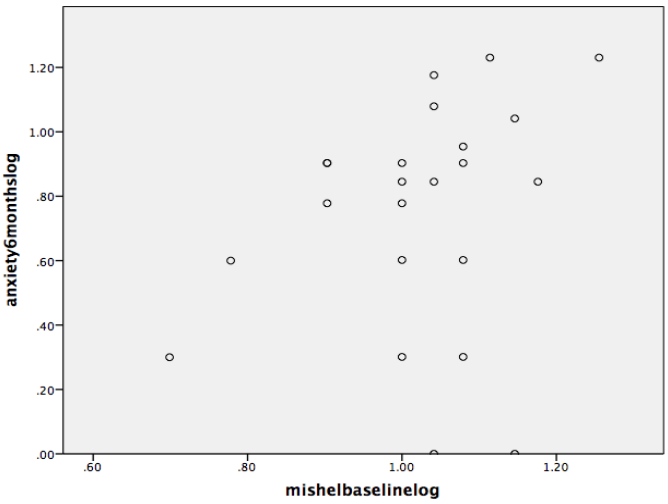
G: Multiple Regression
IESR Outcome Variable Transformed Data

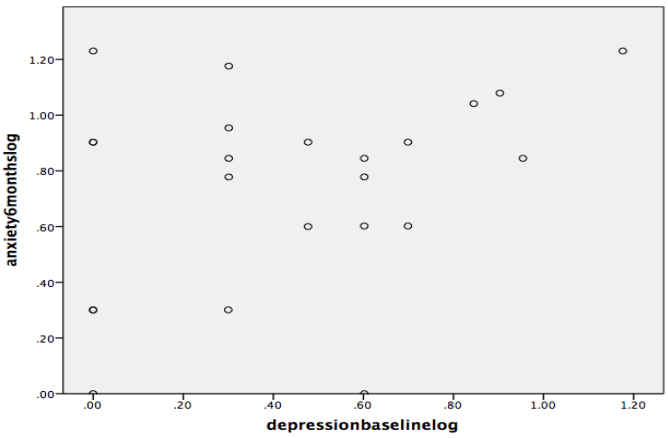


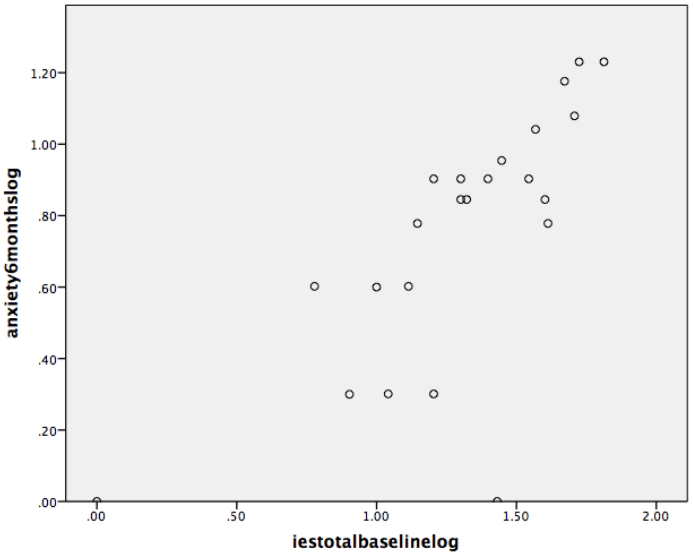




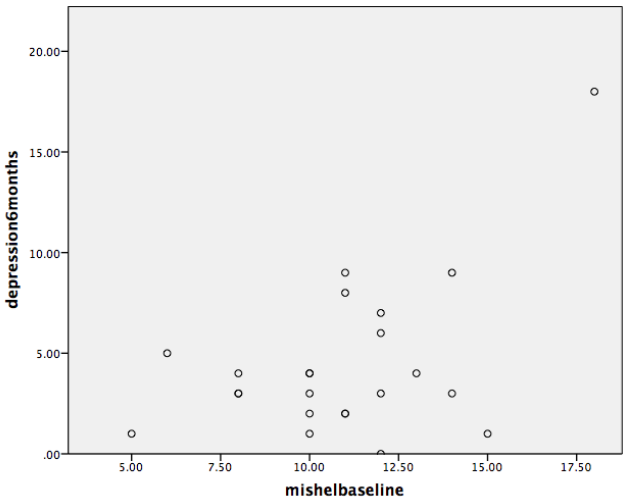
Anxiety Outcome Variable Transformed Data

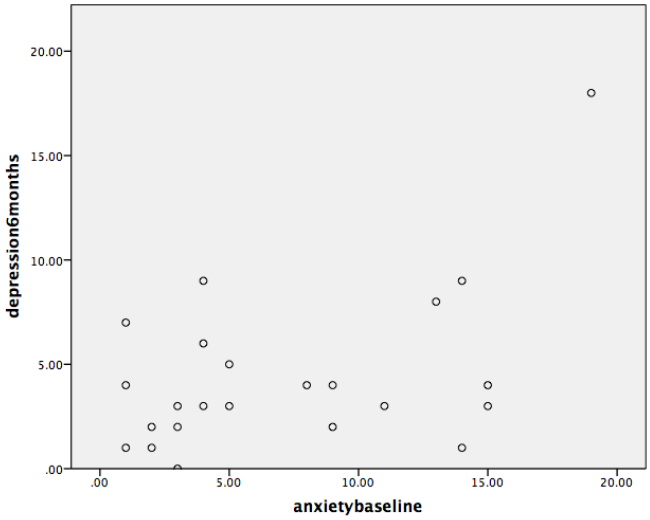


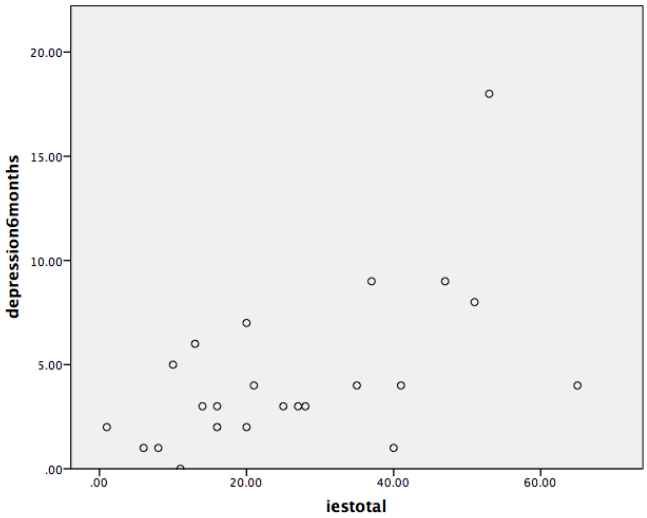




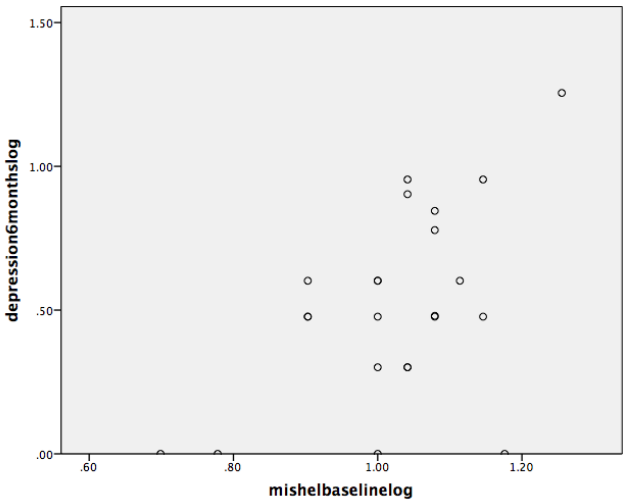
Depression Outcome Variable Normal Data

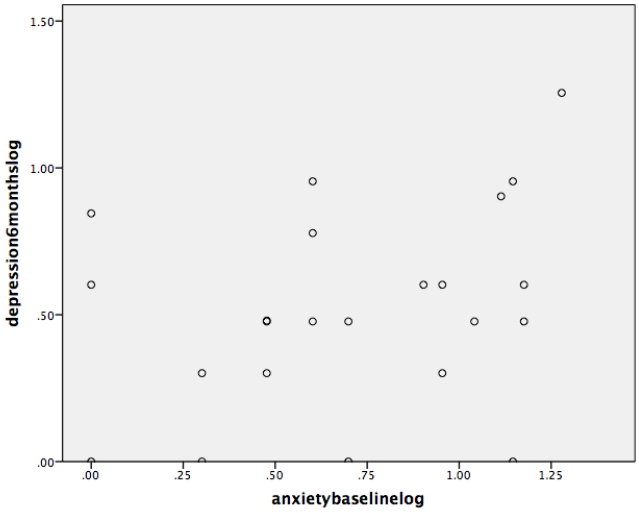


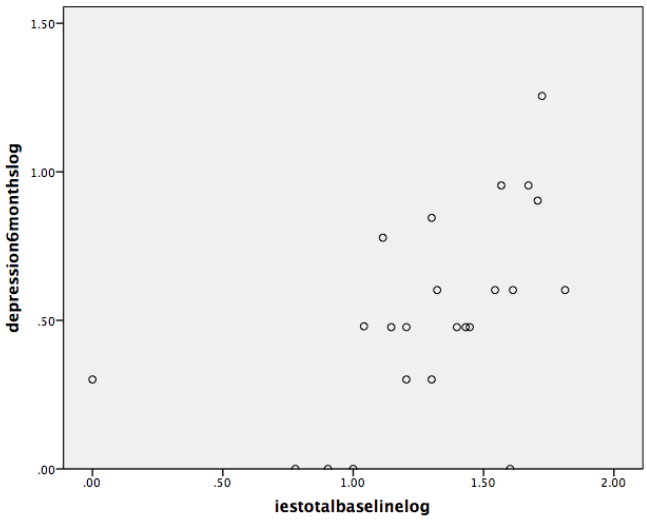




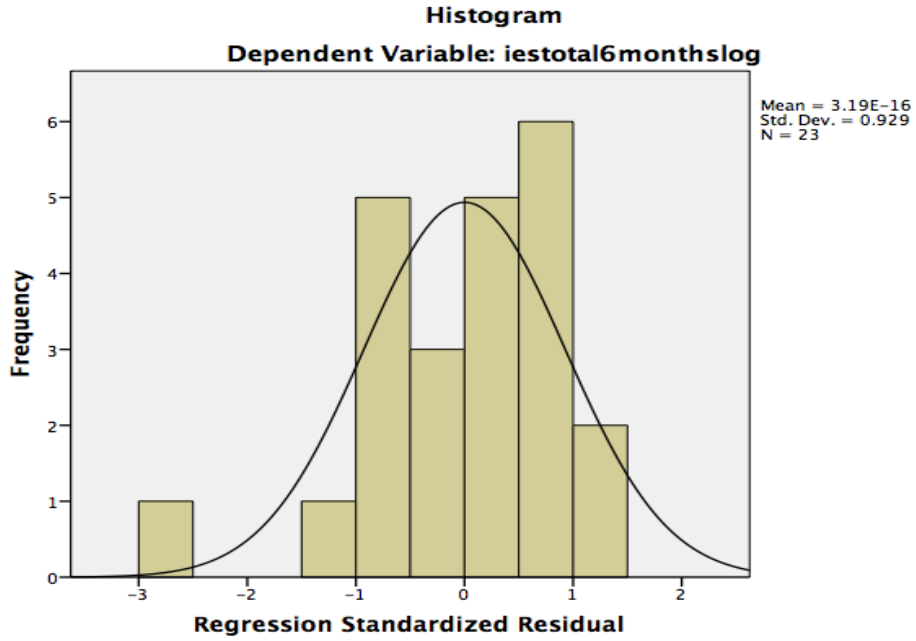
Depression Outcome Variable Transformed Data

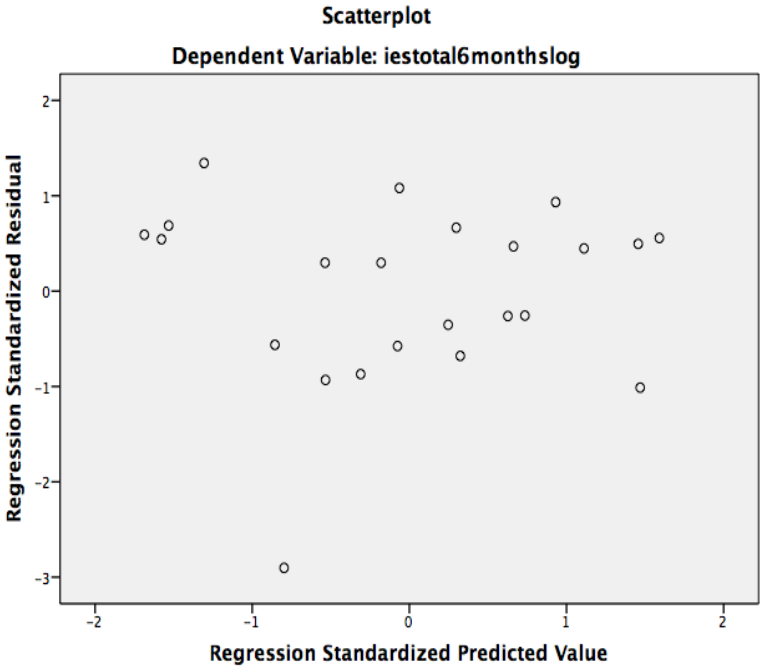




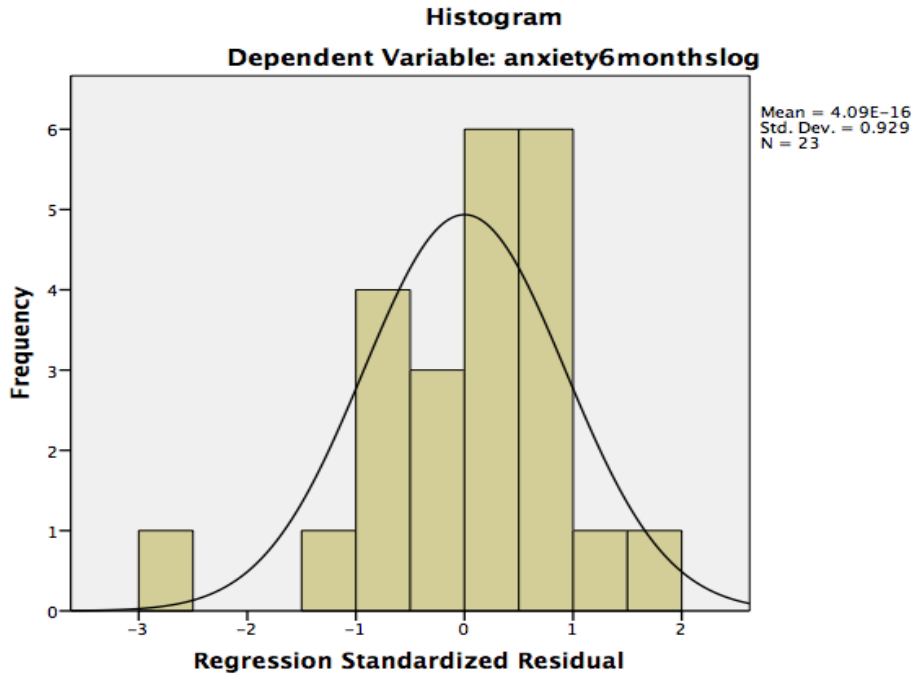


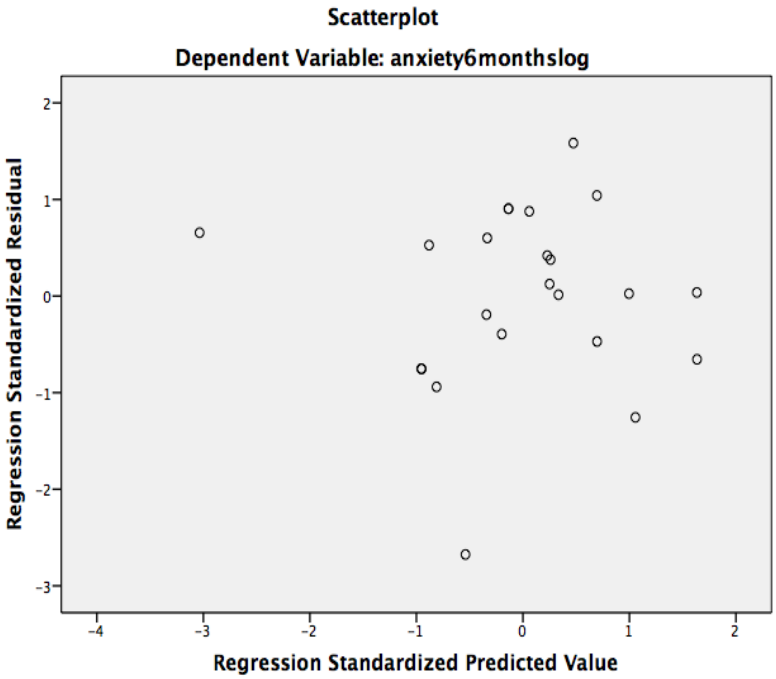
H: Trauma Outcome: Histogram and Scatter Plot Residuals



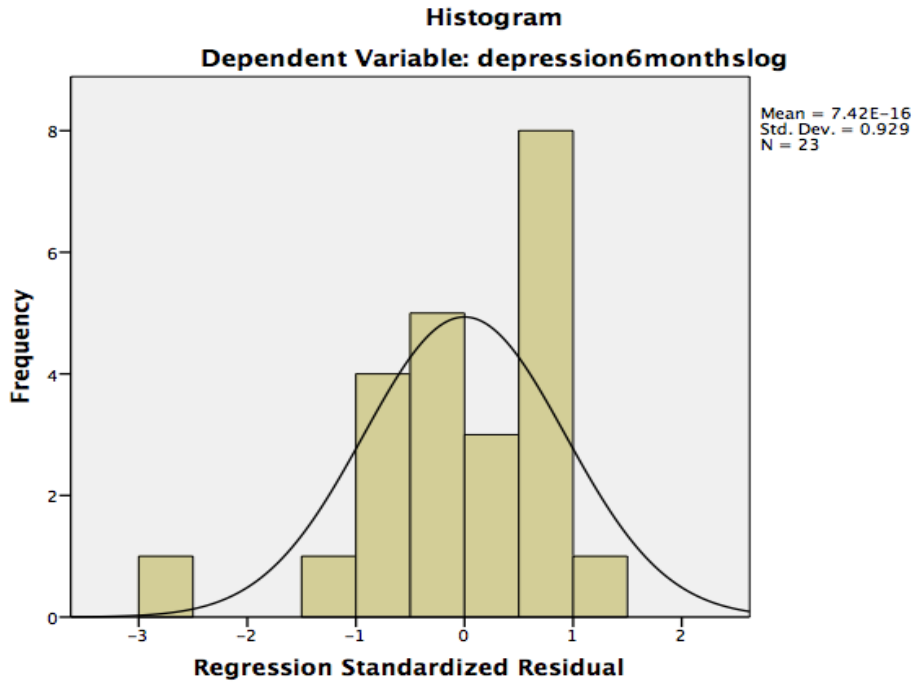


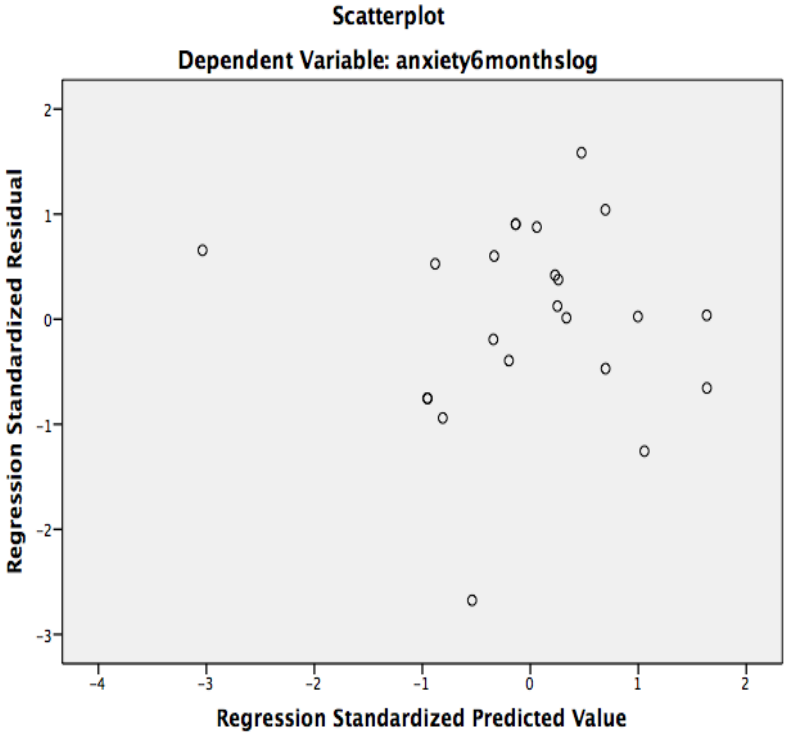
Anxiety Outcome: Histogram and Scatter Plot Residuals





Depression Outcome: Histogram and Scatter Plot Residuals





I: Changes over Time Figures

Group Change (Time-1 to 6-Months)

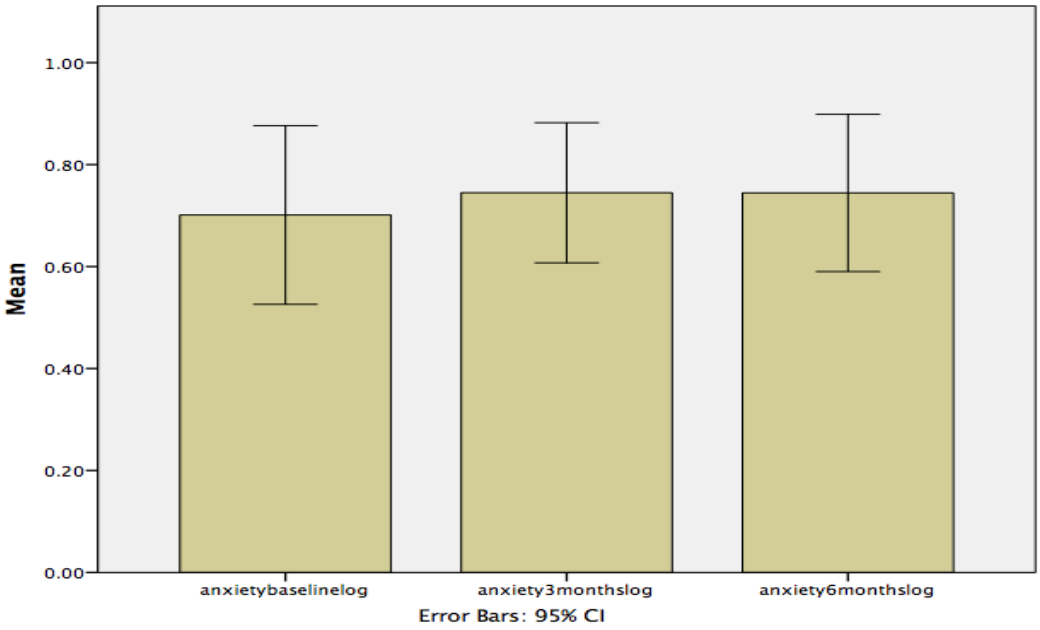


Figure 1: *Repeated Measures: Anxiety*

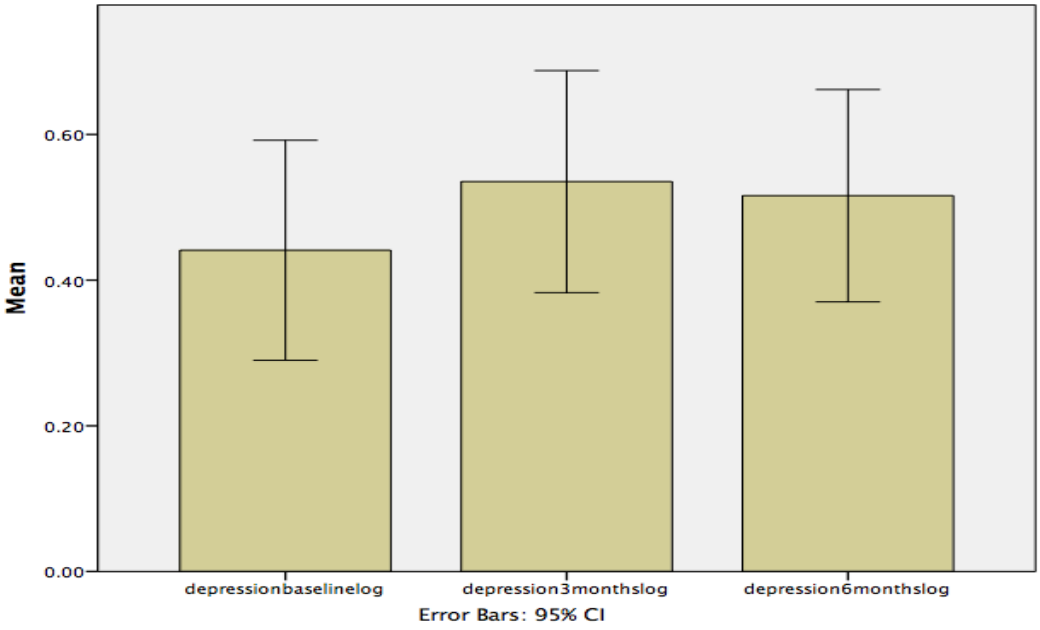


Figure 2: *Repeated Measures: Depression*

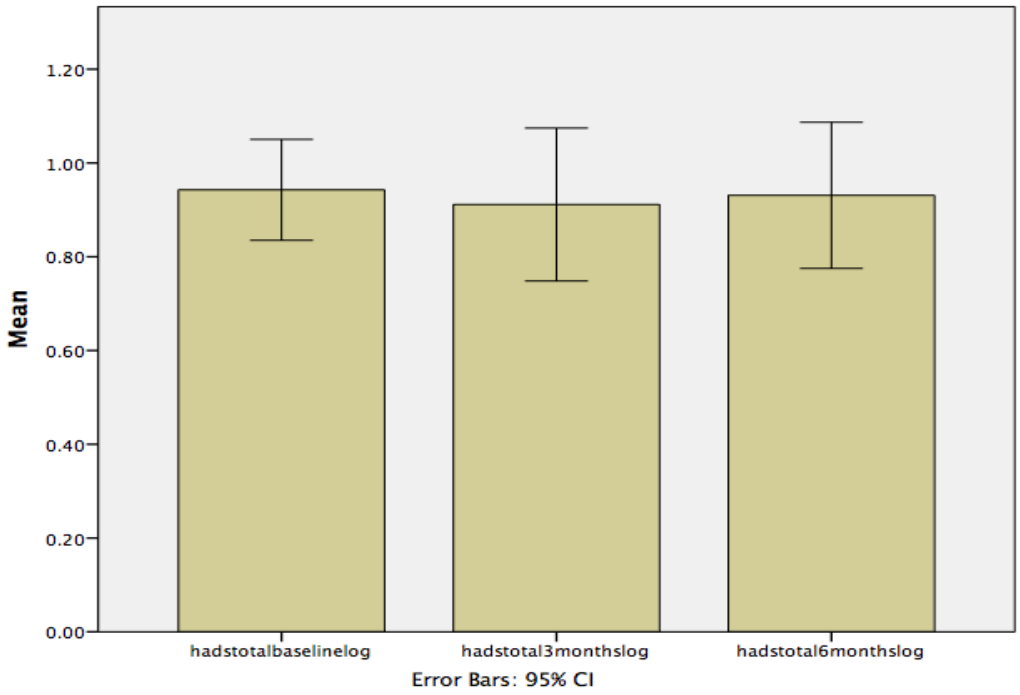


Figure 3*: Repeated Measures: HADS Total Score*

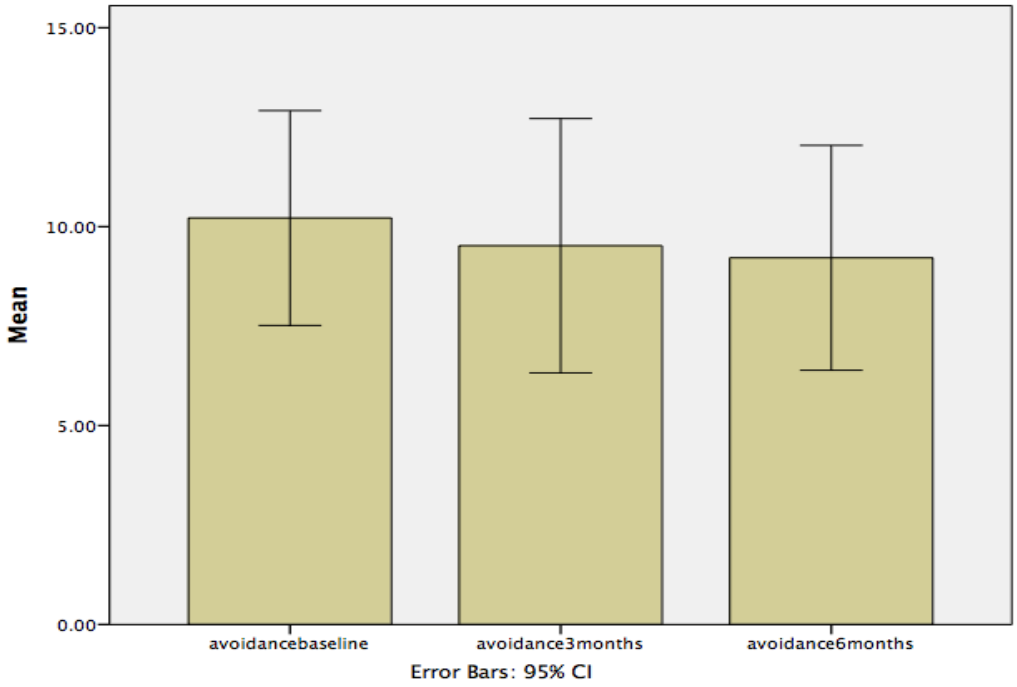


Figure 4: *Repeated Measures: Avoidance Subscale*

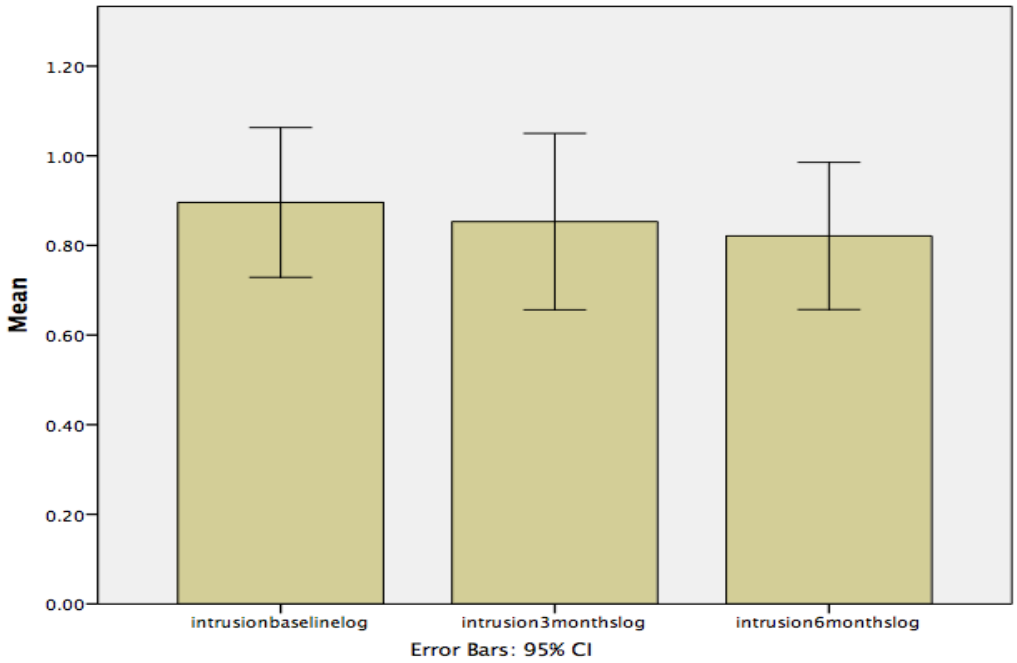


Figure 5*: Repeated Measures: Intrusion Subscale*

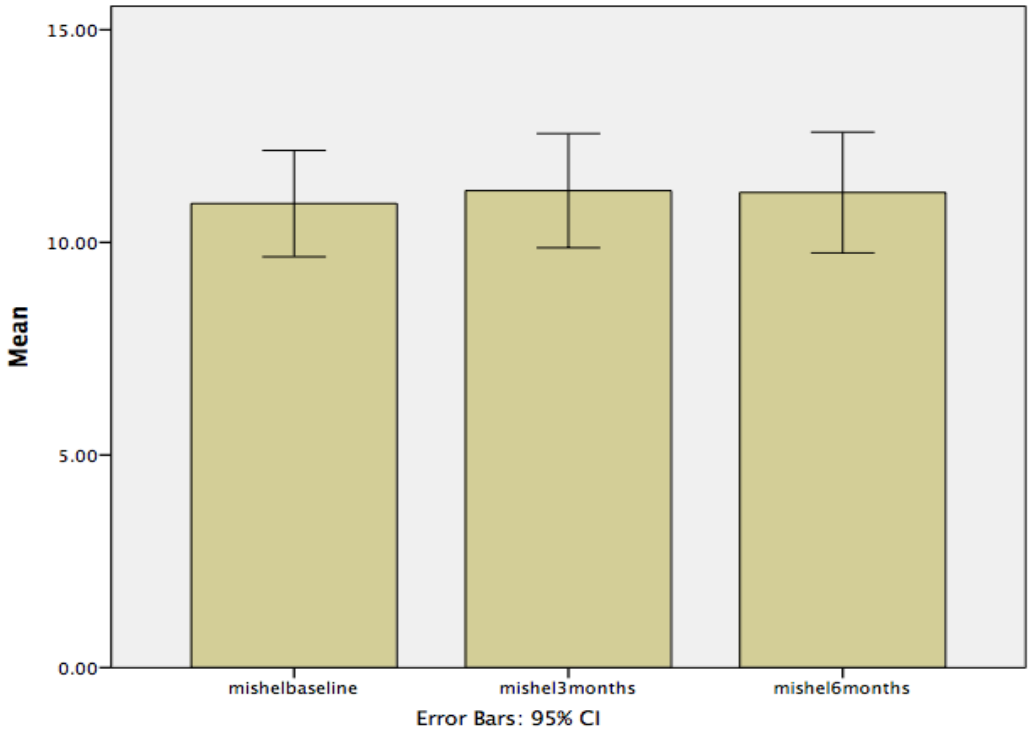


Figure 6: *Repeated Measures: Uncertainty in Illness*

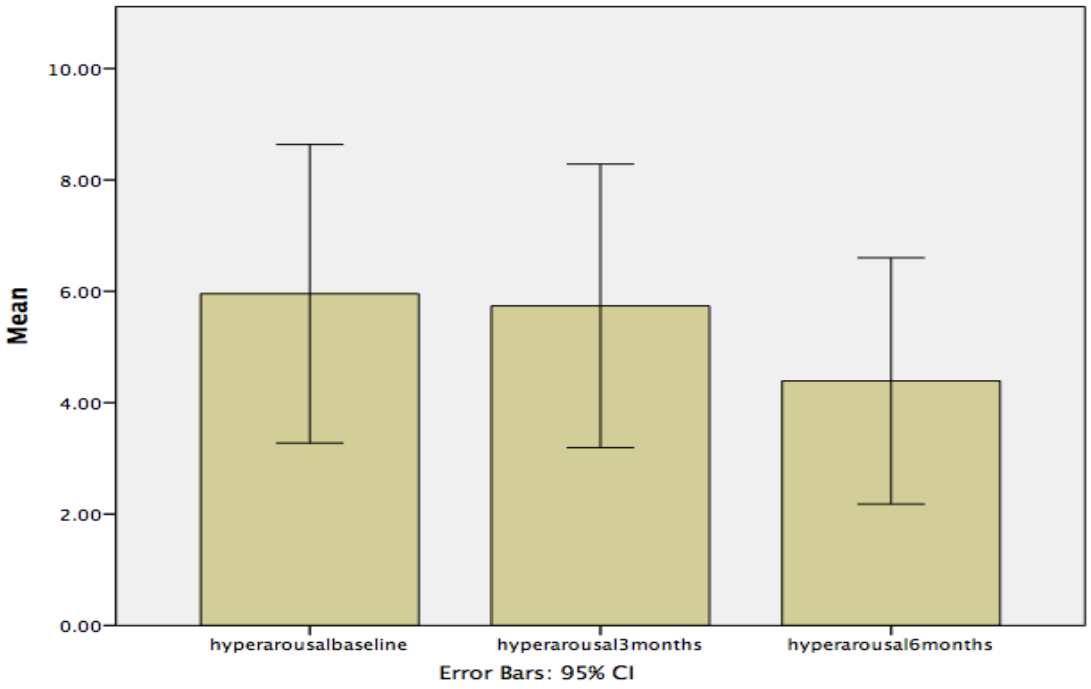


Figure 7: *Freidman's ANOVA: Hyperarousal*

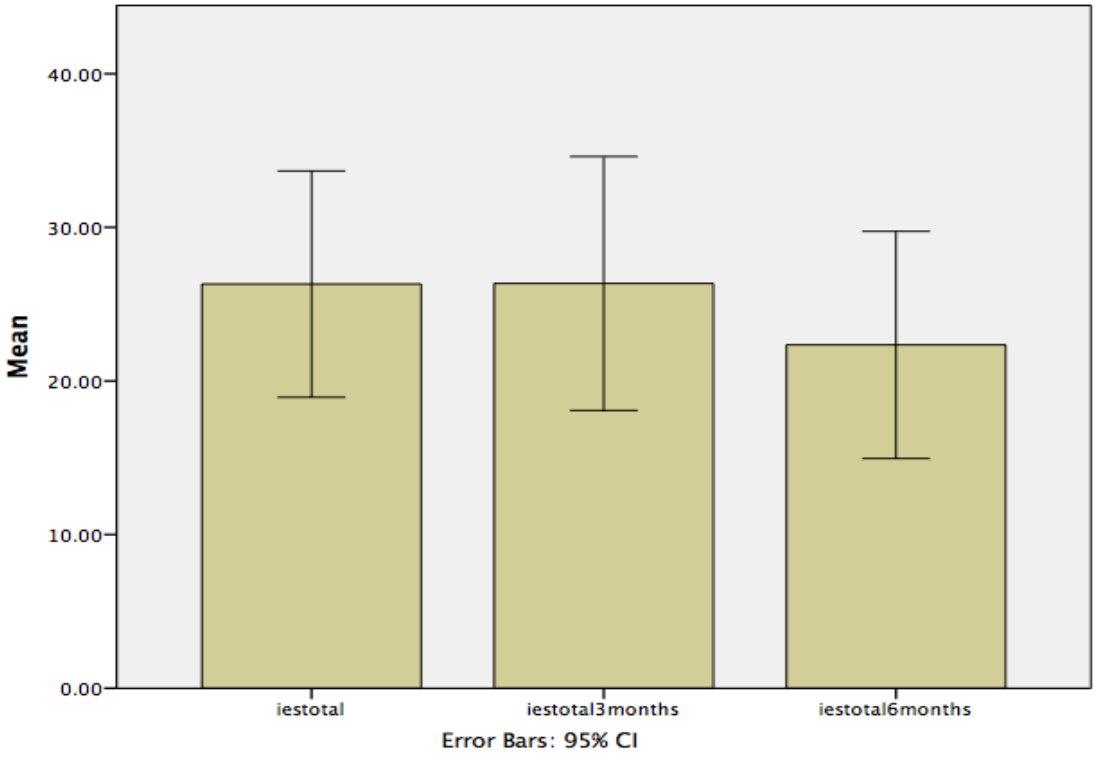


Figure 8: *Freidman's ANOVA: IES-R Total Score*

J: Individual Change (Time-1 to 6-Months)

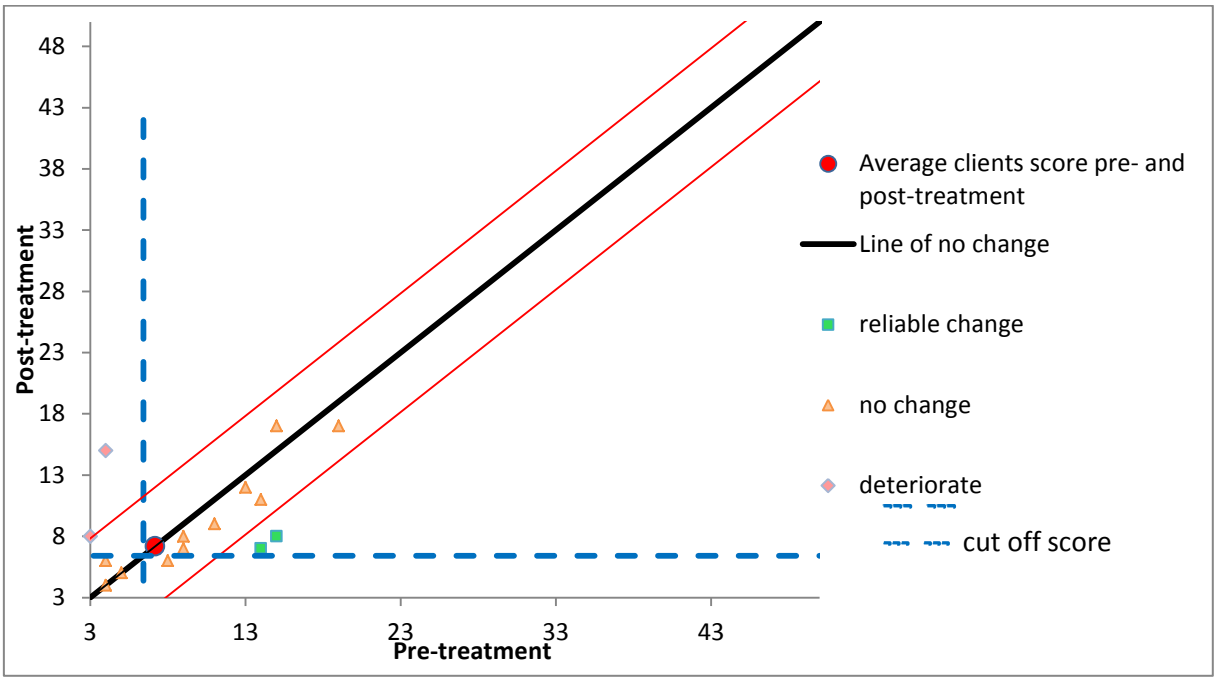


Figure 9: *Anxiety*

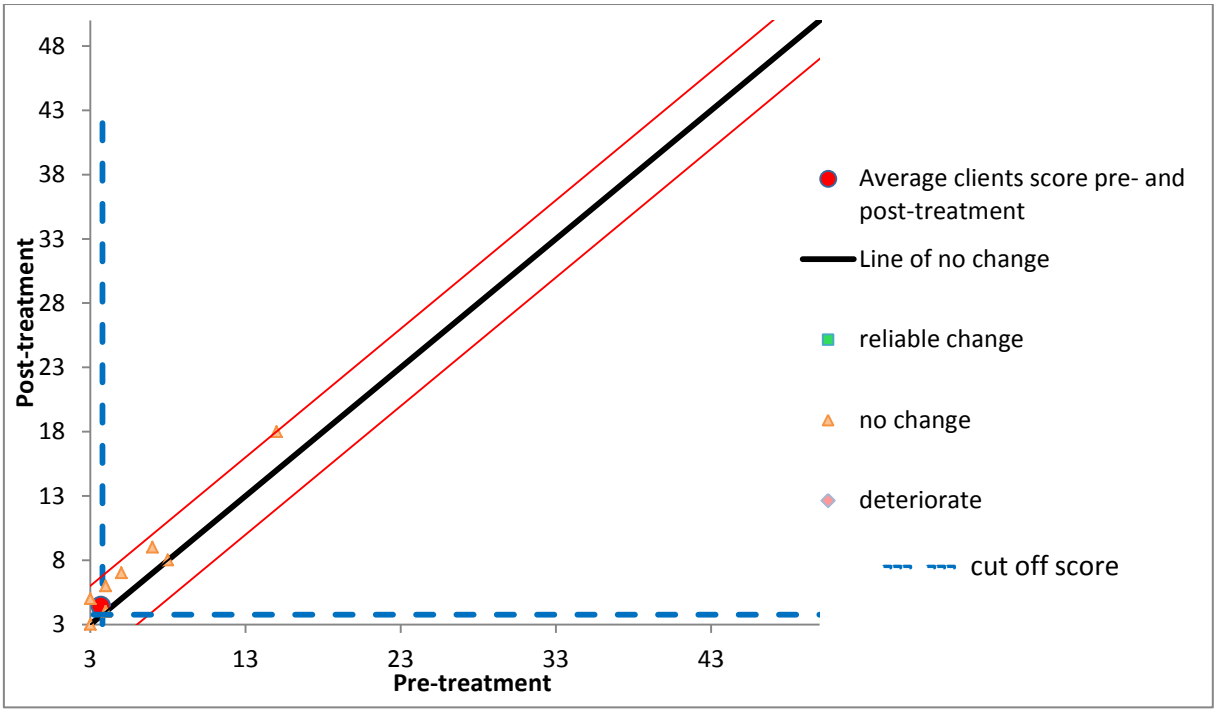


Figure 10: *Depression*

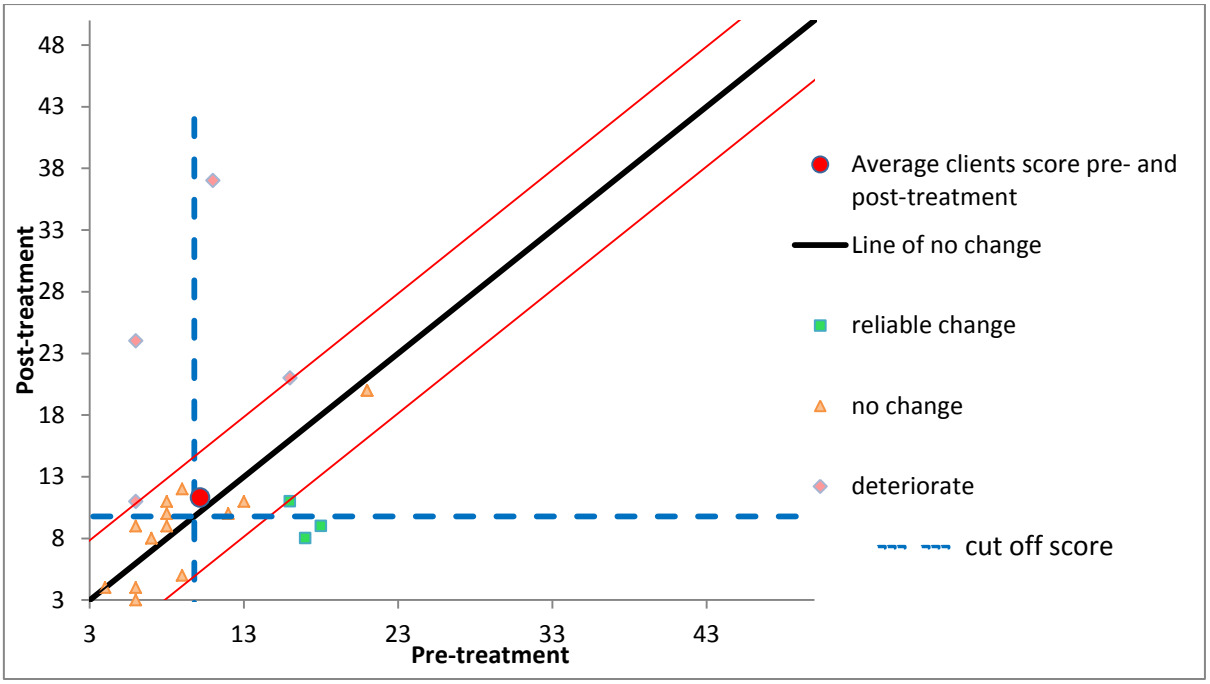


Figure 11: *HADS Total*

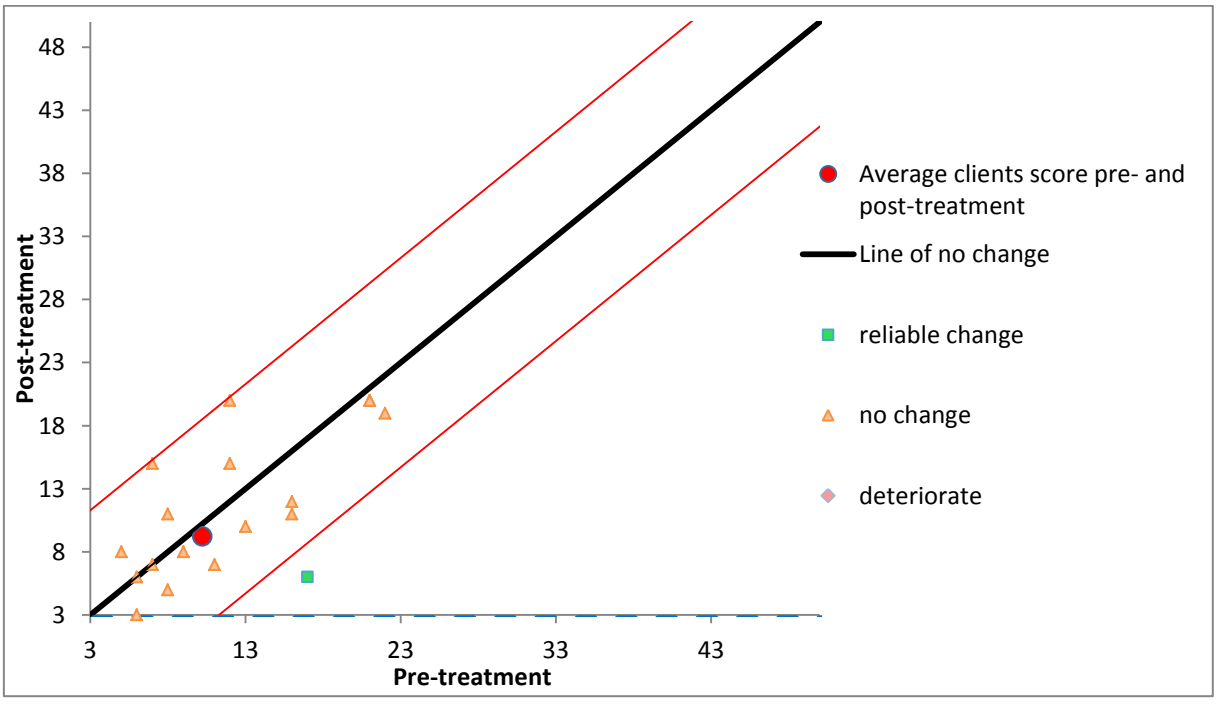


Figure 12: *Avoidance*

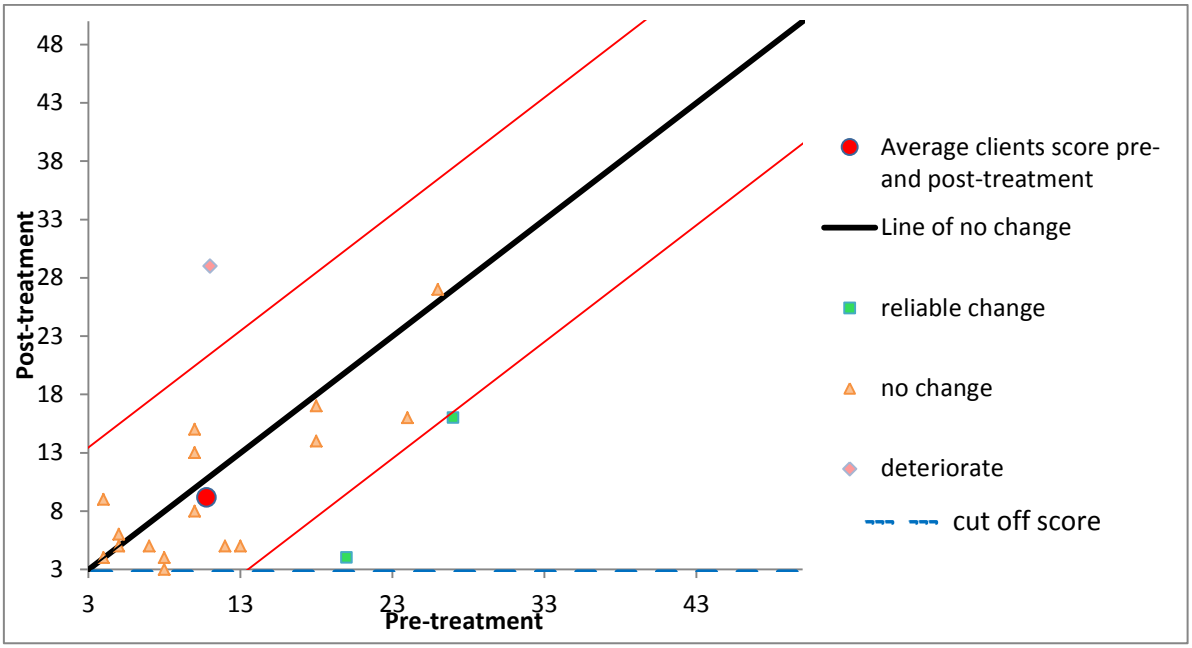


Figure 13: *Intrusion*

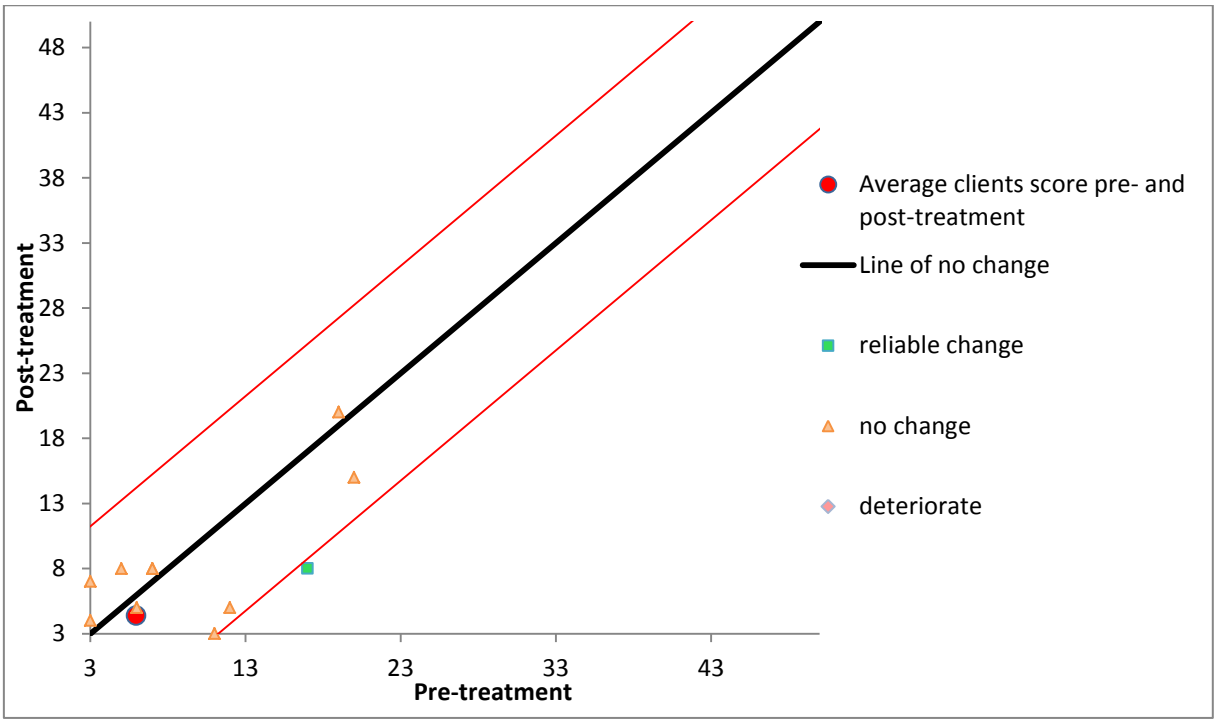


Figure 14: *Hyperarousal*

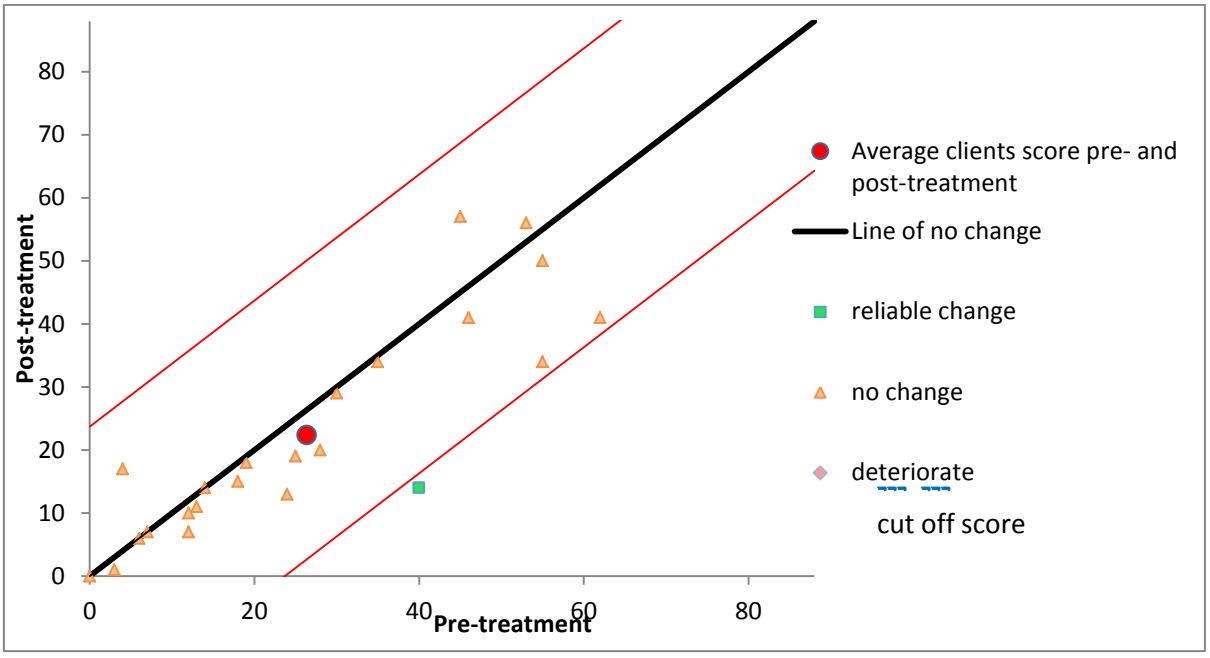


Figure 15: *IES-R Total*

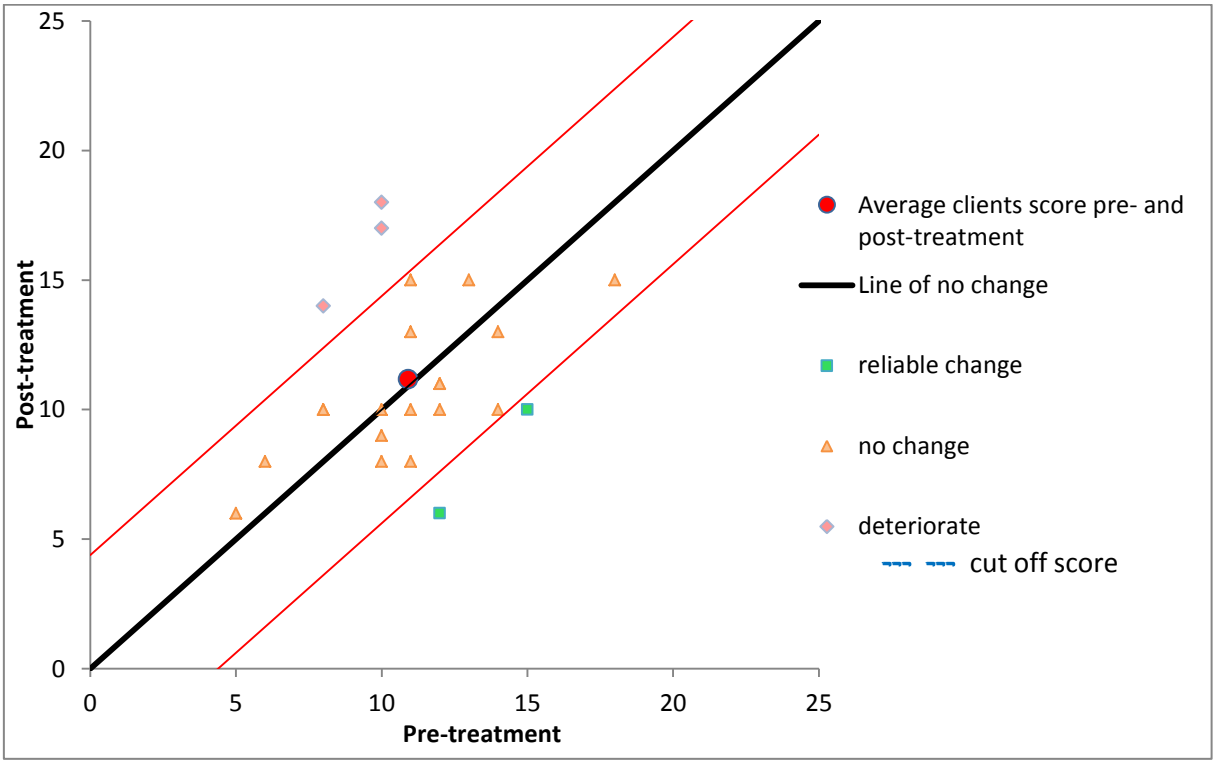


Figure 16: *Uncertainty in Illness*