The Brain-gut-microbiome axis: assessing the relationship between gastrointestinal experiences and mental health

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Declaration

"I declare that this thesis that I have submitted to Dublin Business School for the award of HDip Psychology is the result of my own investigations, except where otherwise stated, where it is clearly acknowledged by references. Furthermore, this work has not been submitted for any other degree."

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Abstract

This study aimed to test whether the relationship between gastrointestinal and mental health observed in clinical samples, extends to a non-clinical sample. This relationship is explained by the brain-gut-microbiome axis. The study also aimed to assess the impact of probiotic use on the axis. An online mixed-methods survey was used to contact participants (N=102). The DASS-21 and PROMIS scales for Belly Pain and Reflux were used. Analysis showed that gastrointestinal experiences significantly predicted stress. Gastrointestinal experiences also significantly predicted anxiety. Depression had a moderate, significant relationship with reflux and a weak, significant relationship with abdominal pain. No significant difference was found in the mental health scores of those that take probiotics. Awareness of the link between gastrointestinal and mental experiences was assessed qualitatively. Thematic analysis revealed gastrointestinal experiences as a theme, demonstrating public awareness. The study provides support for the brain-gut-microbiome axis, this has important implications for mental health interventions.

1. Introduction

1.1 Overview

Physical symptoms are often reported by those who suffer with poor mental health. Of these symptoms gastrointestinal complaints are common among the public (Kroenke & Price, 1993; von Korff, Dworkin, le Resche, & Kruger, 1988). An association between several diagnosed gastrointestinal diseases and mental health has been found in various studies (Hertig, Cain, Jarrett, Burr, & Heitkemper, 2007; Sanna et al., 2013; Shah, Rezaie, Riddle, & Pimentel, 2014; Song, Jung, & Jung, 2013). Although this association is covered in depth in studies involving clinical samples, few studies exist that examine the relationship in a non-clinical sample. These studies often come from medical schools with a focus on gastroenterology or psychiatry, but little research has been done from a psychological perspective. This chapter will review a body of clinical research that has been conducted to date in relation to gastrointestinal disorders and mental health experiences, as well as the limited research that has been conducted in non-clinical samples. The current study will then aim to explore the relationship between mental health and gastrointestinal health among members of the general population and from a psychological perspective. Possible explanations for this apparent relationship will also be explored in this chapter. Recent research has begun to attribute the relationship to what is being called the brain-gut-microbiome axis. This is a system made up of the brain, the gastrointestinal tract and the bacteria within the tract, in which it has been suggested that there may be a bidirectional relationship (Allen, Dinan, Clarke, & Cryan, 2017). The current study will explore this axis as well as the potential impact of probiotics on the axis. The impact of probiotics on mental health that has been suggested in research will be investigated. This impact demonstrates the possible influence that the gastrointestinal tract and the bacteria within the tract may have

over mental health experiences (Pirbaglou et al., 2016). Awareness in relation to the relationship between gastrointestinal and mental health experiences will also be addressed in this study in order to inform future recommendations. Research in the area of the brain-gut-microbiome axis has the potential to impact psychologists in the way that they approach the treatment of complaints such as depression, anxiety and stress, as well as to promote general well-being among the public by promoting particular diet choices or probiotic use (Shi, Balakrishnan, Thiagarajah, Mohd Ismail, & Yin, 2016).

1.2 Mental Health, Psychosomatic Experiences and Gastrointestinal Experiences

Internal mental health factors sometimes occur alongside physical symptoms. It is often suggested that this occurs when internal mental states manifest themselves physically. These psychosomatic symptoms take numerous forms, from stomach-aches and headaches to seizures and rashes (Spencer, 2016). Certain poorly explained syndromes have been found to relate to depression and anxiety. A meta-analysis of data found that irritable bowel syndrome (IBS), non-ulcer dyspepsia, fibromyalgia and chronic fatigue syndrome were all related to high levels of depression and anxiety. Two of these syndromes relate to the gastrointestinal tract (Henningsen, Zimmermann, & Sattel, 2003). Connections between gastrointestinal experiences and mental states were explored early on by Pavlov (1910). His work demonstrated that external sensory experiences that cause emotional reactions could alter function in the gastrointestinal tract. Clinicians had long been aware that experiences such as indigestion and discomfort in the abdomen occurred alongside disturbances in emotional state. However, before Pavlov's work, little had been done in the way of scientific study (Aziz & Thompson, 1998). This connection has more recently been demonstrated in a study by Huerta-Franco, Vargas-Luna, Montes-Frausto, Morales-Mata, and Ramirez-Padilla (2012), where induced psychological stressors brought about changes in the gastric function

of participants. These studies clearly demonstrate the link between psychological experiences and gastrointestinal experiences.

1.3 Previous Theoretical Explanations

Evolutionary and biological theories posit an explanation for the link between psychological experiences and gastrointestinal dysfunction. When an individual is exposed to a stressor the sympathetic nervous system activates the fight-or-flight mechanism. Gastrointestinal function slows down so that energy can be redirected to more pressing functions. This process is evolutionarily important as an adaptive response for humans who were once exposed to life threatening situations, in which a physical reaction was necessary, on a regular basis. Most stressors in modern life do not present a physical threat, however the body displays the same reaction (Hassett & White, 1989). A similar response occurs when an individual experiences anxiety; preparing the body to detect or to deal with a threat (Bateson, Brilot, & Nettle, 2011). This approach may help to explain the link between anxiety and stress and gastrointestinal experiences, however it does little to explain the link between mental health experiences like depression and gastrointestinal experiences. Due to this gap in theory other explanations need to be explored.

1.4 Lower Gastrointestinal Tract and Mental Health

Various studies have looked at the connection between mental and gastrointestinal experiences in clinical samples. Many of these focus on diagnosed disorders of the lower tract such as IBS and Ulcerative Colitis. A review by Shah et al. (2014) found that anxiety and depression were associated with both of these illnesses. A study of women diagnosed with IBS also found that gastrointestinal symptoms were associated with higher levels of stress (Hertig et al., 2007). Another study of IBS patients found that there was a significant relationship between IBS and depression, anxiety and stress (Gaber, 2016). IBS also occurs

more frequently in women than in men (Lee et al., 2007). This could possibly help to explain higher rates of anxiety and depression among women (World Health Organization, 2017). Although the relationship between depression, anxiety and stress and lower gastrointestinal tract experiences has been covered in many clinical studies, there are few studies that have analysed the link in a non-clinical sample. A problem that arises when dealing with an exclusively clinical sample was displayed by Drossman et al. (1988), who showed among a sample of people diagnosed with IBS that psychological factors appeared to be associated with the status of "patient" rather than with IBS symptoms. To establish whether an association between mental health and gastrointestinal experiences does in fact exist, a body of research in non-clinical samples must be conducted.

In addition to the problem of patient status when dealing with clinical samples, it should be considered that gastrointestinal disorders like IBS are characterised by abdominal pain (Windgassen et al., 2017). Abdominal pain or discomfort is a symptom that is often experienced by those who do not meet the criteria for a diagnosis with a gastrointestinal disorder (Walter et al., 2013). Walter et al. (2013) looked at the experience of this symptom in a non-clinical sample and found that scores for anxiety and depression were higher among those who had experienced abdominal pain. This is an important study as it tested whether the relationship between mental health and gastrointestinal experiences extended to those not diagnosed with a gastrointestinal disorder. The current study looks at the relationship between lower gastrointestinal tract experiences and depression, anxiety and stress to test whether the relationship demonstrated in a clinical sample will in fact be extended to a non-clinical sample. The Walter et al. (2013) study used the hospital anxiety and depression scale, which was developed to look at depression and anxiety in an outpatient setting (Zigmond & Snaith, 1983). The current study will analyse these factors using the DASS-21 (see Appendix B.2.1) as the focus is on a non-clinical sample. The DASS-21 is also beneficial as it includes

the added factor of stress. The current study also uses the PROMIS Belly Pain scale (see Appendix B.2.2) over a daily diary, this will be done for increased ease of participation. The use of a standardised questionnaire also lends itself to better reliability and validity tests.

1.5 Upper Gastrointestinal Tract and Mental Health

Many other studies have examined the relationship between mental health and upper gastrointestinal symptoms in clinical samples. One such study looked at gastro-oesophageal reflux disease and its associated symptoms and found that there was a positive relationship with mood and anxiety disorders (Sanna et al., 2013). Yang, Jiang, Hou, and Song (2015) also looked at reflux diseases and found an association with levels of anxiety and depression. The authors suggest that psychological variables could play a role in the occurrence of reflux diseases. Song et al. (2013) focused on a sample of sufferers of reflux-esophagitis and found a significant association between symptoms and levels of psychosocial stress. It was also found in this study that the severity of reflux symptoms correlated with the level of stress that an individual experienced. The current study looks at the relationship between upper gastrointestinal tract experiences and depression, anxiety and stress in a sample of the general population to test whether the relationship demonstrated in these clinical samples extends to a non-clinical sample. A population-based study by Jansson et al. (2007) analysed the depression and anxiety experiences of those that reported severe reflux symptoms in the past year. A strong association was found between anxiety and depression and reflux experiences. This study did not assess a clinical sample, instead investigating the general public, as reflux is often experienced by those without a diagnosis of an upper tract disorder. However, the study solely looked at those who experienced severe levels of reflux in comparison with those who experienced no symptoms of reflux, and did not account for possible varying levels of reflux experiences (Jansson et al., 2007). The PROMIS Reflux scale (see Appendix B.2.3)

will be used in the current study in order to comprehensively examine the varying levels of reflux symptoms, rather than placing a focus on those who experience severe symptoms.

1.6 Mental Health Variables – Stress, Anxiety and Depression

In the examined studies a link between the specific mental health variables, depression, anxiety and stress and gastrointestinal disorders has been observed. These variables are important issues in the field of psychology. Concerning levels of stress, anxiety and depression affect society today. Stress is understood as a relationship between an individual and their environment that is considered by the individual to exceed their capabilities, to be difficult or to threaten their well-being (Lazarus & Folkman, 1984). A person's perceptions about a situation and about their own ability can impact the amount of stress that is experienced (Ogden, 2007). Perceived stress has not only been linked to gastrointestinal problems but also to problems in the cardiovascular system (Holmes, 1994), problems with the immune system (Sternberg, 2001), anxiety (Jones & Daigle, 2018), depression and diabetes (Cotti, Haley, & Miller, 2017), however the direction of causality in these cases is often unclear. A World Health Organisation report estimated that 264 million people were living with anxiety disorders in 2015 (World Health Organization, 2017). Anxiety refers to an emotion that is closely related to fear or worry and that is often experienced in the absence of any real threat (Evans et al., 2005). Anxiety disorders have the highest lifetime incidence of any category of disorder in the Diagnostic and Statistical Manual of Mental Disorders (Kessler et al., 2005). It is also estimated that over 300 million people suffer from depression worldwide (World Health Organization, 2017). The World Health Organisation classifies depression as sadness, loss of interest or pleasure, feelings of low self-worth, guilt or tiredness, poor concentration and changes in sleep or appetite. This state can be chronic or can reoccur, often affecting an individual's ability to function in day-

to-day life. It is a major contributor to suicide. With both anxiety disorders and depression, women are more commonly sufferers (World Health Organization, 2017). It is important that the factors which influence, or occur alongside, experiences of stress, depression and anxiety are identified by psychologists in order to treat and prevent high levels among those who suffer.

1.7 Brain-gut-microbiome Axis

When it comes to understanding the link between the gastrointestinal tract and stress, anxiety and depression, upper and lower gastrointestinal symptoms have often been treated separately in psychological studies (Jansson et al., 2007; Shah et al., 2014). However, in neuroscience and biopsychology, there has recently been an increase in research focusing on the brain-gut-microbiome-axis as a biological explanation for experiences of depression, anxiety and stress. In a review by Allen et al. (2017) it is suggested that there may be a bidirectional relationship within this system, which includes the entire gastrointestinal tract, the bacteria within the tract, and the brain. The current study examines the whole gastrointestinal tract rather than investigating symptoms of the upper and lower tract separately, in order to gain a better understanding of this axis. The apparent bidirectional communication is facilitated by an interconnected neuron network within the tract which is estimated to have a similar number of neurons to the spinal cord (Sasselli, Pachnis, & Burns, 2012). It has been demonstrated that bacteria within the gut produces neurotransmitters which are also found in the central nervous system, further suggesting how this communication may occur. The production of neurotransmitters such as serotonin in the gut may help to explain the impact of the axis on mental state (Wall et al., 2014). Allen et al. (2017) indicate that the brain-gut-microbiome axis impacts experiences of depression, anxiety and stress, although they state that how exactly this occurs is not yet definitively known. The review also suggests

that disorders such as IBS can be explained as a disorder of communication within the axis rather than as originating from a problem with either gastrointestinal or psychological function alone. The possible connectedness and bi-directionality within the axis mean that interventions that are aimed at one part of the axis could potentially impact other parts of the axis. This is a very important suggestion for psychologists given the apparent connection with experiences of depression, anxiety and stress. If further evidence of this link can be provided, interventions that consider both gastrointestinal and mental health could have far reaching impacts.

The understanding of the axis is a relatively new area of study that has been brought about by developments in non-invasive neurophysiological methods. Functional brain imaging allows psychologists to look at brain activation during specific mental processes. It has also allowed gastroenterologists to investigate how brain activity corresponds to gut function (Aziz & Thompson, 1998). A study by Phillips et al. (2003) used imaging to study brain activity responses to non-painful pressure in the oesophagus in different emotional contexts. Participants were shown images of fearful and neutral faces to establish an emotional context. It was found that there was a significant increase in activity in the brain regions associated with perceptions of sensations arising from the body, as well as with psychological state, while in the fearful emotional context in comparison with the neutral context. This study demonstrates the impact of psychological state in the brain-gut-microbiome axis, perceptions of sensations from within the axis can be altered based on the emotion that is experienced. The connection between brain, gut and microbiome can also be observed developmentally, the critical period in which microbes colonize the gut of an infant occurs alongside a period of rapid brain development (Konkel, 2018). The implications of this were demonstrated by Sudo et al. (2004). Germ-free laboratory mice were administered with a microbial intervention containing beneficial bacteria early in their lives. These mice

were less likely to demonstrate anxiety-like behaviours in stressful environments than conventionally raised mice later in life. Findings in relation to the benefits of probiotics have also been demonstrated in human studies. Participants were enrolled in a three week long probiotic treatment in a study by Benton, Williams, and Brown (2007). Individuals with the highest depression scores at the outset saw an improvement in mood, rating themselves as happy rather than depressed. A review by Clapp et al. (2017) highlighted the importance of a healthy microbiome for those suffering with anxiety and depression. The review highlights the impact of a microbial imbalance and inflammation of the gut on mental health. These studies show that probiotics have the potential to correct imbalance, having important implications for those suffering with depression, anxiety and stress.

Although studies that demonstrate the benefits of probiotics suggest a directional relationship where gut health impacts mental health, this is a relatively recent area of study and a causal relationship has not yet been drawn with certainty. For example, in a study that attempted to establish the direction of this relationship it was not determined with certainty whether gastrointestinal illness affected mental health or whether the inverse was true (Shah et al., 2014). It has also been suggested that treatments which reduce psychological distress should be used in order to reduce gastrointestinal symptoms, reinforcing the idea of bi-directionality (Hertig et al., 2007). The current study will ask participants whether they currently take a daily probiotic dose in order to compare depression, anxiety and stress scores between those that do and those that do not. This aims to add to the current body of literature exploring the extent of the impact of probiotics and to inform recommendations that are made in terms of treatment plans.

1.8 Public Awareness

Public knowledge of the connection between gastrointestinal and mental health could potentially aid in promoting wellbeing among the general population. A healthy gut microbiome can be achieved through diet and the use of probiotics (Luna & Foster, 2015; Shi et al., 2016). These can be easily implemented as a treatment plan or promoted through public awareness campaigns. It is important to establish whether the link between gastrointestinal experiences and mental health experiences that has been demonstrated in the literature is known by the general public, as little research exists in this area. The current study will ask participants to list any physical experiences that they are aware of that may be associated with depression, anxiety or stress in order to examine whether gastrointestinal experiences arise as a theme.

1.9 Aims and Rationale

This chapter has demonstrated the link between certain physical experiences and depression, anxiety and stress, particularly highlighting the link with gastrointestinal experiences. Due to the observed association between gastrointestinal symptoms of both the upper and the lower tract and mental health experiences in clinical studies, and less comprehensively in non-clinical studies, the current study will aim to test whether this association does in fact extend to a non-clinical sample. Abdominal pain and reflux have been selected as the gastrointestinal symptoms of interest, as they are representative of experiences of both the upper and lower tract and are commonly experienced by those in a non-clinical sample (Jansson et al., 2007; Walter et al., 2013). Explanations for the apparent association between gastrointestinal function and mental health have varied over time. Currently, evidence is being explored in relation to the brain-gut-microbiome axis in several scientific schools, however little headway has been made in this area from a psychological

perspective (Aziz & Thompson, 1998). In keeping with literature on this axis, the current study looks at the whole gastrointestinal tract, rather than separating out experiences of the upper and lower tract, in order to examine the impact of the gastrointestinal tract on mental health variables. The current study will also ask participants whether they take a daily probiotic so that scores for depression, anxiety and stress can be examined. If it is confirmed that there is a positive relationship between gastrointestinal and mental health experiences, public knowledge of this connection could also have potential benefits. It has been demonstrated that positive mental health outcomes can be achieved through diet choices and probiotic use (Luna & Foster, 2015; Shi et al., 2016). Public awareness campaigns have the potential to improve overall mental health of the population by spreading this information. Therefore, the current study will assess participants' awareness of this link by asking them to list some of the physical experiences that may occur alongside experiences of stress, anxiety and depression.

1.10 Research Hypotheses and Research Question

A positive relationship between gastrointestinal symptoms and depression, anxiety and stress has been demonstrated in all of the examined literature (Jansson et al., 2007; Walter et al., 2013). Thus, the three main hypotheses of the study are:

1. Abdominal pain and reflux will have a positive relationship with stress levels

2. Abdominal pain and reflux will have a positive relationship with anxiety levels

3. Abdominal pain and reflux will have a positive relationship with depression levels

The examined literature also suggests that use of probiotics will positively impact mental health, lowering levels of stress, anxiety and depression (Benton, Williams & Brown, 2007; Sudo et al., 2004). Therefore, it is also hypothesised that:

4. There will be lower levels of depression, anxiety and stress among those that take a daily probiotic in comparison with those that do not.

In order to establish whether knowledge of a connection between mental health and gastrointestinal experiences exists among the general public the study will also ask the research question:

1. Are the general public aware of the gastrointestinal experiences that may be associated with stress, anxiety and depression?

This question will be answered by asking participants to list any of the physical experiences that they are aware of that may be associated with depression, anxiety or stress. Answers will then be analysed using thematic analysis. The hypotheses and research question will be analysed using data collected via an online survey aimed at the general population. A non-clinical sample will be recruited by asking participants if they have any diagnosed gastrointestinal disease or disorder. Clinical participants will answer the qualitative question and are exempt from the remainder of the study.

2. Methodology

2.1 Participants

A link to a survey style questionnaire was circulated online using snowball sampling to recruit participants. The study was aimed at members of the public over the age of 18 and no incentive was offered for taking part. The study was comprised of 102 participants (62 females), ranging from age 21 to 61 (with a mean of 30.98 and standard deviation 12.25). All participants were eligible to complete the first part of the study (Appendix B.1). Eighty-five participants responded to the open-ended qualitative question. Following an exclusion criteria question that ensured a non-clinical sample, 87 participants (51 females), ranging from age 21 to 61 (with a mean of 30.49 and standard deviation 12.28) completed the subsequent parts of the study (Appendix B.2).

2.2 Design

The current study used a mixed-methods design where data was collected using an online survey. Qualitative and quantitative methods were employed, the quantitative part of the study used a correlational design. The survey collected demographic data as well as data relating to probiotic use, depression, anxiety, stress, abdominal pain and gastro-oesophageal reflux. It also contained an open-ended qualitative question that looked at awareness of the link between gastrointestinal experiences and mental health. For hypothesis 1 the predictor variables were abdominal pain and reflux and the criterion variable was stress. For hypothesis 2 the predictor variables were abdominal pain and reflux and the criterion variable was anxiety. For hypothesis 3 the predictor variables were abdominal pain and reflux and the criterion variable was depression. For hypothesis 4 the independent variable was probiotic use and the dependent variables were depression, anxiety and stress. The key variables of

interest for the research question were any psychosomatic experiences that can be associated with stress, anxiety and depression.

2.3 Materials

An online survey comprised of demographic questions regarding sex and age, a question relating to probiotic use, an open-ended qualitative question, and three standardised questionnaires was used in the collection of data. The open-ended qualitative question: "Please list any physical health experiences that you associate with depression, anxiety or stress" was used to assess the awareness of the general population when it comes to the link between gastrointestinal experiences and mental health. The shortened version of the depression anxiety stress scale (DASS-21) (Lovibond & Lovibond, 1995) (see Appendix B.2.1) is a 21-item questionnaire that collects data on participants' experiences over the course of the past week. It examines the occurrence of symptoms from three subscales; depression, anxiety and stress. Each subscale contains seven items. Participants are asked to rate how much each item applied to them personally in the last week on a four-point Likert scale, without spending too much time on any one statement. For example, the following item is from the anxiety subscale, "I felt scared without any good reason." Response options are as follows: Did not apply to me at all; Applied to me to some degree, or some of the time; Applied to me to a considerable degree, or a good part of the time; and Applied to me very much, or most of the time. Higher overall scores indicate increased severity of symptoms. The scores are totalled and multiplied by two, giving a range of 0 to 42. Cut off points for the anxiety sub-scale are as follows: 0–7 (Normal); 8–9 (Mild); 10–14 (Moderate); 15–19 (Severe); ≥20 (Extremely severe). Cut off points for the stress sub-scale are as follows: 0–14 (Normal); 15–18 (Mild); 19–25 (Moderate); 26–33 (Severe); ≥34 (Extremely severe). Cut off points for the depression sub-scale are as follows: 0–9 (Normal); 10–13 (Mild); 14–20

(Moderate); 21–27 (Severe); ≥28 (Extremely severe). Henry and Crawford (2005) demonstrated good levels of validity and reliability for this scale in a non-clinical sample. Each subscale was demonstrated to have good internal reliability, Cronbach's alpha was .88 for the depression subscale, .82 for the anxiety subscale and .90 for the stress subscale. Cronbach's alpha for the total scale was .93, demonstrating excellent internal reliability.

The PROMIS Scale v1.0, GI Belly Pain 5a (PROMIS Health Organization and PROMIS Cooperative Group, 2016) (Appendix B.2.2) and the PROMIS Scale v1.0, GI Reflux 13a (PROMIS Health Organization and PROMIS Cooperative Group, 2016) (Appendix B.2.3) were used to collect information relating to experiences of abdominal pain and reflux in the last week. The Patient Reported Outcome Measurement Information System (PROMIS) was designed to evaluate various areas relating to health-related quality of life, measuring biopsychosocial health. The PROMIS gastrointestinal symptoms scales were designed to be appropriate for the general population as well as for patients with gastrointestinal illnesses. They measure physical symptoms of the gastrointestinal tract and are not disease-targeted, meaning that they are useful across the general population (Spiegel, 2013). The GI Belly Pain scale contains five items and the GI Reflux scale contains 13 items. Participants are asked about their experiences of abdominal pain and reflux in the past 7 days on a five-point scale with scores ranging from 0-4. Some items in each scale are not administered based on the response to the preceding item, if a respondent answers "Never" when asked about a specific experience the following questions that relate to that experience are excluded by a built-in skip pattern. When a question is skipped by this function its score is set to zero. Scores are calculated by adding the item scores for each scale, a person who receives an overall score of 0 is considered "non-symptomatic", a person who receives the highest possible total score for a scale is considered "maximally symptomatic". The range of scores for the GI Belly Pain scale are 0-20 and for the GI Reflux scale the range are 0-52 (as

cited by Spiegel et al., 2014). Examples of the items for each scale are as follows: "In the past 7 days, how much did belly pain bother you?"; "In the past 7 days, how often did you feel burning in your throat?" Spiegel et al. (2014) demonstrated content and cross-sectional construct validity of the scales using data from gastrointestinal patients as well as members of the general population. Correlations with a range of legacy instruments were found to be statistically significant. Internal reliability was also found to be high for each scale with a Cronbach' s alpha of .87 for abdominal pain and .88 for gastroesophageal reflux.

2.4 Procedure

On beginning the study, a cover sheet (Appendix A) outlined the purpose of the research to participants. Participants were informed that the survey focused on depression, anxiety and stress as well as certain physical health experiences. The gastrointestinal focus of the study was not revealed at the beginning of the study so as not to bias answers. However, participants were told that they would receive more details about the study at the debrief stage. The cover sheet also highlighted the voluntary nature as well as the anonymity and confidentiality of the study. A mandatory question establishing consent was also included after the cover sheet, this was the only mandatory question included in the study. The first part of the study (Appendix B.1) was open to all participants. Demographic questions were asked first. Participants were asked not to continue with the study if they were under the age of 18. These were followed by the open-ended qualitative question; this question was presented at the beginning to avoid bias in the responses as the research question focuses on topics that are brought up later in the study. The subsequent parts of the study (Appendix B.2) were subject to the exclusion criteria of diagnosis with a gastrointestinal disorder so that the study could focus on a non-clinical sample. A question that ensured this parameter was included at this point. The following question asked participants about their daily probiotic

use. Next the participants were presented with the three standardised questionnaires which assessed their experiences from the previous week. First the DASS-21, followed by the PROMIS GI Belly Pain and finally the PROMIS GI Reflux. At the close of the study participants were presented with a debrief sheet containing contact information for relevant support services. The gastrointestinal focus of the study was also revealed at this point. No time constraints were applied to the study which contained 44 questions in total.

2.5 Ethics

The Code of Professional Ethics (Psychological Society of Ireland, 2010) was consulted in the design of the study. Prior to beginning research, a proposal was approved by a filter committee at Dublin Business School. Age was collected at the start of the study to prevent those under the age of 18 from taking part. The participants were not asked for their names at any point in the study to ensure de-identified data collection and full anonymity. Participants were informed in advance that they would not be able to withdraw their data once it had been submitted for this reason. The study involved a low level of deception as the focus on gastrointestinal symptoms was not initially stated. This was highlighted to participants at the beginning of the study (Appendix A). Consent was collected from participants after this information was outlined, ensuring informed consent. To combat any deception, debrief information was included (Appendix C).

Questions contained in the DASS-21 may be considered sensitive to some participants, participants were notified of this at the outset. However, the DASS-21 is a commonly utilised tool in psychological studies. To address the issue of sensitivity, relevant contact information was included in the debrief sheet (Appendix C). The time taken to complete the study may have posed a certain level of inconvenience to participants, in order to keep the length of the study to a minimum, short-form questionnaires were used. Data was

stored securely and anonymously on a password protected computer. Participants were informed that research was being conducted as part of the researcher's studies and would be submitted for examination. Participants were also informed that answers to the qualitative part of the study could be included in the write up of the results of the study.

2.6 Data Analysis

Thematic analysis as per Braun and Clarke (2006) was used for the qualitative part of the study. Braun and Clarke outline the decisions about the research approach that should be made before beginning analysis. An inductive, or data driven, approach was chosen. In this type of approach themes are identified from the data itself rather than an approach where the researcher begins analysis with preformed themes chosen from pre-existing theory. A semantic approach was also used. In this type of approach themes arise from the direct meaning of the language used in the data, the researcher "is not looking for anything beyond what a participant has said or what has been written" (Braun & Clarke, 2006, p. 84). The themes were formed keeping in mind the research question: Are the general public aware of the gastrointestinal experiences that may be associated with stress, anxiety and depression? The open-ended question used was phrased so that participants could discuss opinions without being directed by the question. The prevalence of themes as well as their relevance to the research question were taken into consideration. The generation of these themes was conducted using NVivo software and was represented in a model (see Figure 4). The analysis provided a detailed description of the data set. For the quantitative part of the study descriptive statistics were run. Multiple regressions were chosen to address hypotheses 1, 2 and 3. A multivariate analysis of variance (MANOVA) was chosen to address hypothesis 4. Eighty-seven participants took park in the second part of the study, meeting requirements set out by Cohen (1992) for the selected inferential tests.

3. Results

3.1 Descriptive Statistics

Descriptive statistics were run to summarise the data prior to beginning inferential tests.

Table 1 *Descriptive Statistics for Mental Health Measures*

Variable	Mean	Standard deviation	Cronbach's α
Depression	8.64	9.02	.92
Anxiety	8.02	7.98	.84
Stress	12.80	8.37	.85

Table 2 *Descriptive Statistics for Gastrointestinal Health Measures*

Variable	Mean	Standard deviation	Cronbach's α
Abdominal pain	2.39	3.24	.93
Reflux	5.30	5.47	.81

The descriptive statistics for the DASS-21 are demonstrated in Table 1. Cronbach's alpha established that there were good levels of internal reliability for each of the subscales. Mean scores for anxiety were in the mild range, mean scores for stress and depression were in the normal range. The descriptive statistics for each of the PROMIS measures are shown in Table 2. Both scales were also shown to have good internal reliability. Abdominal pain and reflux mean scores were both relatively low, demonstrating low symptomatic levels in the

sample. This was to be expected given the non-clinical nature of the study. The number of

participants who take a probiotic daily are demonstrated graphically in Figure 1.
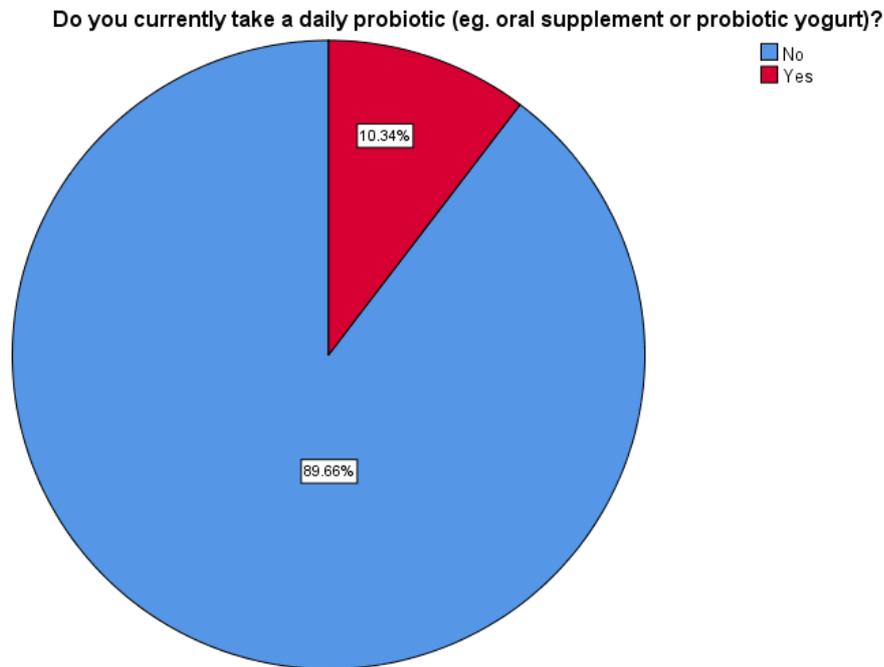
Do you currently take a daily probiotic (eg. oral supplement or probiotic yogurt)?

Figure 1 *Percentage of participants who take a daily probiotic.*

3.2 Inferential statistics

Inferential statistics were employed in order to test the hypotheses of the study

Hypothesis 1. Abdominal pain and reflux will have a positive relationship with stress

levels

After checking whether all mahal distances were below the critical value for two

independent variables (13.82) and correcting for one multivariate outlier, all assumptions for

a multiple regression were met. The data was checked for normality using a histogram

(Appendix D) and was found to be approximately normally distributed. The P-P plot of

regression (Appendix E) did not dramatically deviate from the line. A multiple regression

was then used to test whether abdominal pain and reflux were predictors of stress. The results

of the regression indicated that the two predictors explained 34% of variance (R^2 = .34, F(2,

74) = 20.14, p < .001). As this result is significant the null hypothesis can be rejected. It was found that reflux significantly predicted stress (β = .50, p < .001, 95% CI = .45, 1.11). However, it was found that abdominal pain failed to predict stress on its own (β = .17, p = .104, 95% CI = -.10, 1.08)

Hypothesis 2. Abdominal pain and reflux will have a positive relationship with anxiety levels

After checking whether all mahal distances were below the critical value for two independent variables (13.82) and correcting for one multivariate outlier, all assumptions for a multiple regression were met. The data was checked for normality using a histogram (Appendix F) and was found to be relatively normally distributed. The P-P plot of regression (Appendix G) was checked and did not dramatically deviate from the line. A multiple regression was then used to test whether abdominal pain and reflux were predictors of anxiety. The results of the regression indicated that the two predictors explained 40% of the variance (R^2 = .40, F(2, 74)= 25.90, p < .001). As this result is significant the null hypothesis can be rejected. It was found that reflux significantly predicted anxiety (β = .58, p < .001, 95% CI = .57, 1.17). Abdominal pain failed to predict anxiety on its own (β = .12, p = .24, 95% CI = -.21, .85).

Hypothesis 3. Abdominal pain and reflux will have a positive relationship with depression levels

When doing the checks for a multiple regression it was found that abdominal pain and depression had a correlation of 0.21. As the assumptions for a multiple regression state that each predictor variable should have a correlation above 0.3 with the criterion variable, a multiple regression could not be run. As there is no good non-parametric equivalent for a

multiple regression, scatter plots were generated (see Figure 2 & 3), and Pearson's

correlations were run for analysis. The correlations between each predictor variable and the

criterion variable were looked at separately in two post hoc sub-hypotheses.

Hypothesis 3A. There will be a positive relationship between depression and reflux

A Pearson correlation coefficient found that there was a moderate positive significant

relationship between depression (M = 8.64, SD = 9.02) and reflux (M = 5.30, SD = 5.47) (r

(76) = 0.41, p < .001). Therefore, the null hypothesis is rejected. This relationship can

account for 17% of variation of scores. See Figure 2 for an illustration of this relationship.

Figure 2 *Scatterplot Illustrating the Relationship Between Reflux and Depression Scores*

Hypothesis 3B. There will be a positive relationship between depression and

abdominal pain

On analysis of the initial scatterplot for depression against abdominal pain an outlier

that was over three standard deviations from the mean was identified and raw scores were

removed so as not to skew results. A Pearson correlation coefficient found that there was a weak positive significant relationship between depression (M = 8.75, SD = 9.02) and abdominal pain (M = 2.24, SD = 2.95) (r (78) = 0.23, p = .02). Therefore, the null hypothesis is rejected. This relationship can account for 5% of variation of scores. See Figure 3 for an illustration of this relationship.
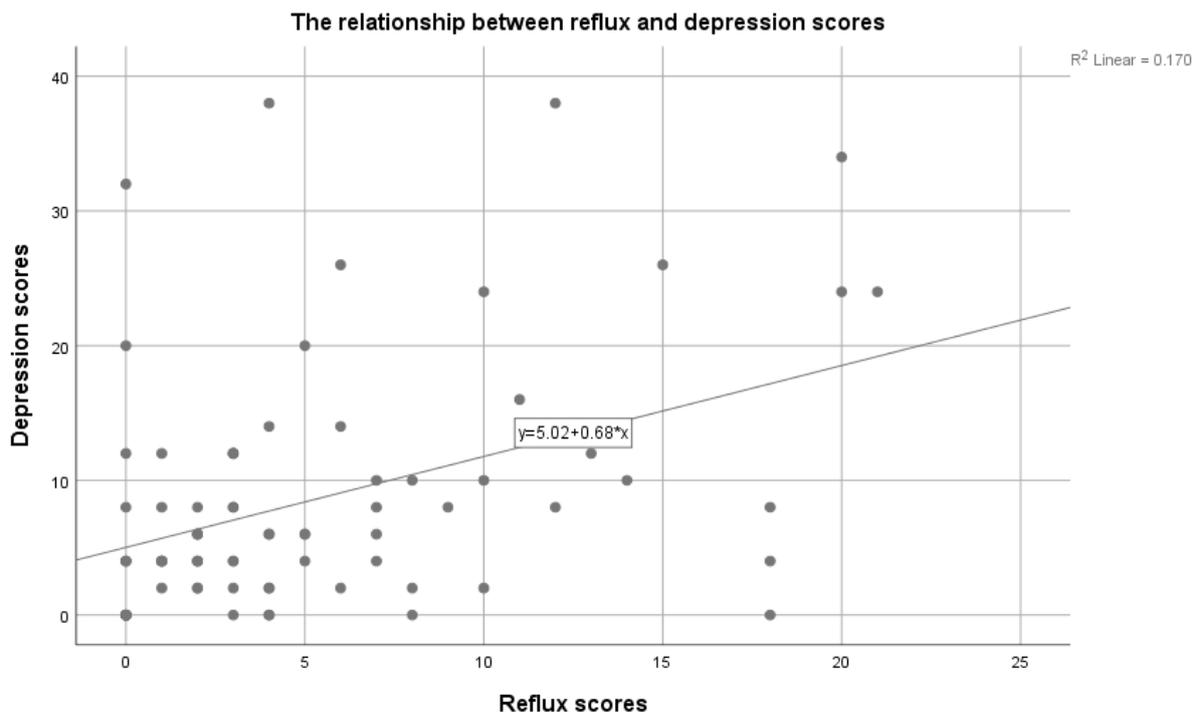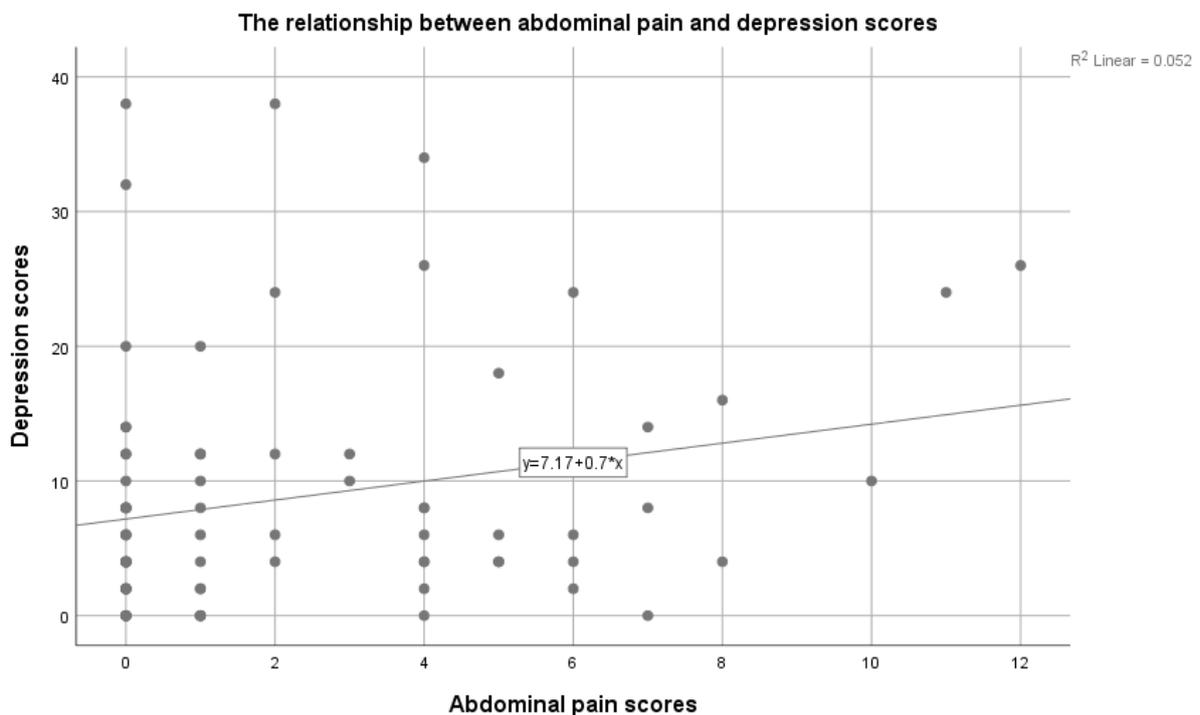

Figure 3 *Scatterplot Illustrating the Relationship Between Abdominal Pain and Depression Scores*

   Hypothesis 4. There will be lower levels of depression, anxiety and stress among those that take a daily probiotic in comparison with those that do not

   The assumptions for a one-way MANOVA were met. A between subjects MANOVA was run and it was found that there was no statistically significant difference in mental health scores between those that take a daily probiotic and those that do not (F(3, 74) = 0.73, p = .538, effect size = .03). The null hypothesis was accepted.

3.3 Thematic Analysis

    Research Question 1. Are the general public aware of the gastrointestinal experiences that may be associated with stress, anxiety and depression?

    Qualitative analysis of the research question was conducted using the six steps outlined by Braun and Clarke (2006). First the responses to the open-ended question were read to gain familiarisation with the data. Following this, initial codes were generated. These codes were then analysed for recurring themes and grouped into these themes. The themes were then reviewed and refined. Next the themes were given final names and defined. And finally, a report was produced. A model demonstrating the codes used to generate the themes and the hierarchy of these is represented in Figure 4. The codes that arose from the data related to physical experiences that often occur alongside experiences of stress, anxiety and depression. On analysis of the generated codes, themes relating to specific bodily experiences began to arise. See table 3 for the themes and their definitions. "Gastrointestinal experiences" alongside "Weight and appetite" were the two second most common themes to arise in the thematic analysis, both appearing in 27.06% of responses. Only one theme was more prevalent in the analysis, "Energy and sleep," appearing in 52.94% of responses. The prevalence of Gastrointestinal experiences as a theme answered the research question demonstrating knowledge of the link between gastrointestinal experiences and mental health among participants.

Table 3 *Themes Generated from Thematic Analysis*

Theme	Definition	Quote	% of references theme occurs in
Body temperature experiences	Experiences relating to changes in body temperature	"sweating"	10.58
Circulatory experiences	Experiences relating to the circulatory system	"palpitations"	23.53
Energy and sleep	Changes in energy and sleeping patterns	"tiredness"	52.94
Gastrointestinal experiences	Experiences relating to any point in the gastrointestinal tract	"upset stomach"	27.06
Hair loss	Loss of hair	"hair loss"	10.58
Head related experiences	Experiences that can be related to the head	"headaches"	25.88
Illness experiences	Experiences related to illness and the immune system	"weakened immune system"	12.94
Muscle pain	Pain in the muscular system	"aching muscles"	10.58
Panic related experiences	Experiences that can be related to panic attacks	"panic attacks"	11.90

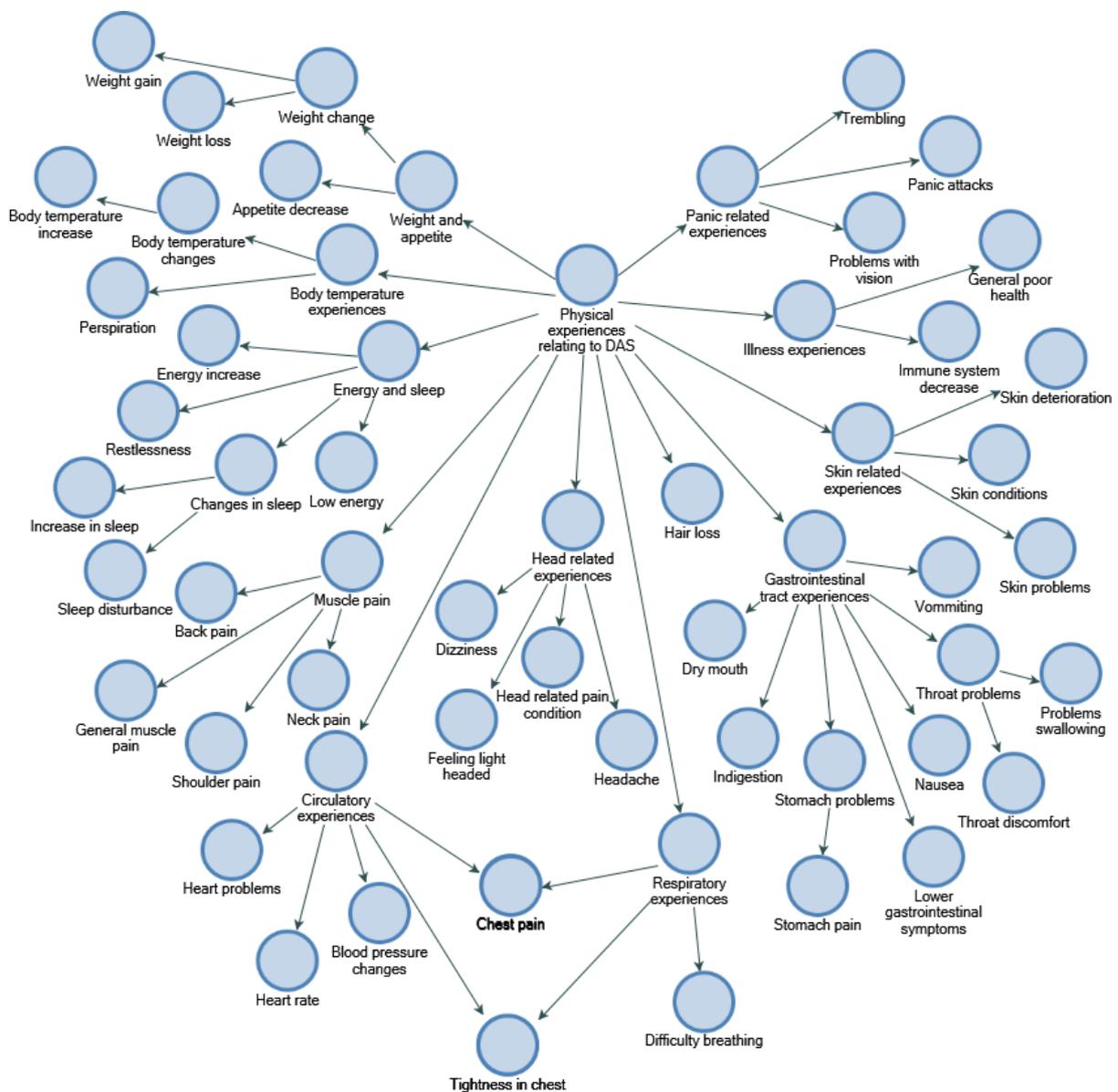|			
Respiratory experiences	Experiences related to breathing	"short of breath"	10.58
Skin related experiences	Experiences related to the skin and skin conditions	"rashes"	22.35
Weight and appetite	Changes in weight and in appetite	"fluctuation in weight"	27.06

Figure 4 *Model of Themes and Codes Generated from Thematic Analysis*

4. Discussion

This study aimed to examine the link between mental health and gastrointestinal health that has previously been demonstrated in literature. Often when examining this link, research has focused on clinical samples, looking at disorders of either the upper or lower gastrointestinal tract. Even in non-clinical studies the focus has often been on experiences of either the upper or the lower tract (Jansson et al., 2007; Walter et al., 2013). Recently, the brain-gut-microbiome axis has been used to explain the links between gastrointestinal and mental health, this axis includes the gastrointestinal tract as a whole. However, few psychological studies examining this axis currently exist (Aziz & Thompson, 1998). The current study examined this axis by looking at the relationship between experiences related to both the upper and lower gastrointestinal tract, and mental health variables. The study further aimed to examine this axis by testing the impact of probiotic use on mental health variables. If further support for the relationship between gastrointestinal and mental health experiences can be provided, knowledge of the link has the potential to have a positive impact among the general public, as positive mental health outcomes can be brought about through diet choices or probiotic use (Luna & Foster, 2015; Shi et al., 2016). The current study also aimed to test whether there is already an awareness of this link among the general public.

Several significant results were found. Abdominal pain and reflux were found to predict higher stress levels, supporting the research hypothesis that abdominal pain and reflux have a positive relationship with stress levels. Reflux on its own was found to significantly predict stress, however abdominal pain alone was not found to predict stress. Abdominal pain and reflux were also found to predict higher anxiety levels, supporting the research hypothesis that abdominal pain and reflux have a positive relationship with anxiety levels. Reflux on its own was found to significantly predict anxiety, however abdominal pain on its

own was not found to predict anxiety. Depression was found to have a moderate, positive relationship with reflux, supporting the post hoc research hypothesis that there is a positive relationship between depression and reflux. Depression was found to have a weak, positive relationship with abdominal pain, supporting the post hoc research hypothesis that there is a positive relationship between depression and abdominal pain. Given that the current study used a non-clinical sample these hypotheses support the idea that the link between gastrointestinal health and mental health does in fact extend to a non-clinical sample. This is an important finding as it contradicts the conclusion put forward by Drossman et el. (1988) that the link between mental and gastrointestinal health is due to the status of "patient." The lesser effect of abdominal pain alone in each of these findings suggests that it is the cumulative effect of reflux alongside abdominal pain that influences mental health. This cumulative effect provides evidence for dysfunction of the brain-gut axis, rather than dysfunction of solely the upper or lower tract, in the influence of mental health experiences. No significant difference was found in the mental health scores of those that took a daily probiotic and those that did not. This did not support the research hypothesis that there are lower levels of depression, anxiety and stress among those that take a daily probiotic in comparison with those that do not. The hypothesis is tentatively rejected as this finding conflicted with much previous research in the area (Benton et al., 2007; Clapp et al., 2017).

The results of the thematic analysis revealed gastrointestinal experiences as one of the second most prevalent themes in the study. This result answered the research question: Are the general public aware of the gastrointestinal experiences that may be associated with stress, anxiety and depression? A solid awareness of the link between gastrointestinal experiences and mental health was demonstrated. Codes relating to Cognition, Behaviour and Emotion were generated in the thematic analysis but were omitted from the final model (see Figure 4). The appearance of these codes was attributed to a misinterpretation of the question

asked. The current study was able to achieve a good analysis despite possible misinterpretations of the question. As a precaution, in future it is suggested that research with a similar research question should rephrase the open-ended question and run a pilot study to confirm that it is understood by participants.

The current study had several strengths. A good sample size overall meant that, even with unanswered questions and exclusion criteria, there were enough participants to meet requirements set out by Cohen (1992). The standardised questionnaires used demonstrated good reliability (see Tables 1 & 2). The use of standardised questionnaires also means that replication of the study in order to verify results will be straightforward. The study was also designed to adhere to professional codes of conduct (Psychological Society of Ireland, 2010) and was deemed ethically sound by a college filter committee. The hypotheses that were supported in the study can be accepted with a high degree of certainty given their strong basis in existing literature. The mixed qualitative and quantitative methods were also a strength in this study as they gave a comprehensive overview of the subject.

One limitation of the current study is the ambiguity of the questionnaire used to examine abdominal pain. The lesser effects of abdominal pain that were observed in the current study could potentially be explained by this ambiguity. The phrasing in the questions asks participants about their "belly pain" without explaining to participants what is meant by "belly pain" (see Appendix B.2.2). Abdominal pain has various possible origins, for example pain in the abdominal region is often observed during menstruation in women (Rosyida et al., 2017). It is suggested that future research uses a more specific scale in examining this experience. The non-experimental design of the study also acted as a limitation. This design meant that the group sizes in the examination of hypothesis 4, which looked at probiotic use and differences in mental health, were irregular. This could explain the contradiction of the

result of the current study with previous literature. Although the sample size in the analysis

overall was considered robust, a small number of participants were in the group that took

daily probiotics, less than the recommended 12 per group for a between-subjects MANOVA.

This imbalance in group sizes in represented graphically in Figure 1. The irregularity between

groups could have brought about the occurrence of a type II error. It is also possible that

external factors impacted results given the non-experimental nature, and lack of control, of

the study. For example, participants were not asked about the length of time that they had

been taking a daily probiotic. Participants may have begun consumption shortly before

participating in the study, studies often examine the effect of probiotics after several days of

consumption (Benton et al., 2007). Due to these limitations a speculative conclusion is

drawn. It is recommended that future research examines the same hypothesis using an

experimental design. An additional limitation of the study was the gender imbalance among

participants. The high rate of female participation in the study may have skewed results as it

has been demonstrated that higher rates of anxiety and depression occur in women than in

men (World Health Organization, 2017). In addition to this factor, certain gastrointestinal

disorders, for example IBS, have higher prevalence rates in women than in men (Lee et al.,

2007). A number of studies in the area of gastrointestinal health have looked exclusively at a

female sample for this reason (Hertig et al., 2007; Sanna et al., 2013). The observed gender

differences mean that the results of the current study cannot be assumed to be representative

of the whole population. Further research that examines an all male sample is necessary

before the results of the study can be applied with certainty to the entire population.

An interesting direction for future research includes nationality or country of

residence as an additional variable. It has been found that the gut microbiome of people

around the world varies based on the diet that is the cultural norm in their region (Senghor,

Sokhna, Ruimy, & Lagier, 2018). The examination of cross-cultural differences when it

comes to the brain-gut-microbiome axis, as well as diet trends, has potential to aid in the formation of diet plans that promote the health of the axis. However, it is important for researchers to note that globalisation may also be impacting upon the brain-gut-microbiome axis. The diet that is common in western cultures is quickly spreading to Asian cultures (Pingali, 2007). It has been suggested that a western diet, high in fat and carbohydrates, may have a detrimental effect on the microbiome and thus potentially on mental health (Allen et al., 2017). International travel also has the potential to impact diet and the gut microbiome, it has been found that changes in the microbiome often occur following travel (Conlon & Bird, 2014). It is important that future researchers keep these factors in mind when studying cross-cultural differences in the brain-gut-microbiome axis.

The connectedness within the brain-gut-microbiome axis that has been demonstrated in literature is supported by the relationships between gastrointestinal health and mental health demonstrated in this study. It is important that knowledge of this connectedness is established among the general public. The thematic analysis did reveal an awareness of the link between gastrointestinal health and mental health. While this theme was the second most prevalent to arise, awareness has the potential to be increased as the theme only arose in 27% of responses. The increase in awareness of this link has potential importance as unhealthy behaviours have been demonstrated to be associated with a lack of health related awareness (Steptoe & Wardle, 2001). Awareness of behaviours that promote a healthy microbiome, such as diet choice and probiotic use, have the potential to improve mental health among the general population (Luna & Foster, 2015; Shi et al., 2016). It is recommended that public legislatures consider a public health advertisement campaign in order to spread this information, campaigns have previously demonstrated an ability to increase health behaviours among the population (Yom-Tov, Shembekar, Barclay, & Muennig, 2018). It is in the best interest of governments to promote behaviours that improve mental health given that

negative mental health experiences are considered to be some of the greatest contributors to global disability (World Health Organization, 2017).

The connectedness in the brain-gut-microbiome axis is also important as it suggests that interventions that are aimed at one part of the axis may have an impact on other parts of the axis. This is an important finding for psychologists as interventions that account for both gastrointestinal health and mental health could be beneficial in terms of treating depression, anxiety and stress. It has previously been suggested that those presenting with gastrointestinal symptoms should be screened for anxiety and depression (Mussell et al., 2008). Given the apparent bidirectionality within the brain-gut-microbiome axis, it is suggested that those presenting with mental health issues be screened for gastrointestinal symptoms and vice versa. This will allow the selection of specific, targeted and more effective treatments. Treatment of gastrointestinal symptoms through diet or probiotic supplements may assist in the treatment of psychological problems. The inverse of this is also true; the treatment of psychological problems through typical psychological intervention could assist in the treatment of gastrointestinal issues. The potential of these types of interventions has been demonstrated in various research examples. A psychiatric review demonstrated that nutrition is an important factor in mental health (Sarris et al., 2015). A review by Kinsinger (2017) detailed the advantages of cognitive behavioural therapy as an intervention for the reduction of IBS symptoms. New interventions also show promise in the treatment of the brain-gut microbiome axis. A conference abstract published about a recent study that used transcranial magnetic stimulation (TMS) on a sample of over-weight people found that the stimulation both helped participants to lose weight and improved the composition of their gut microbiome, demonstrating the potential influence of the brain over the gut microbiome (Ferrulli et al., 2018). This is of particular interest given that TMS is also currently used in the treatment of major depressive disorder (Gellersen & Kedzior, 2018). As the full paper

examining the impact of TMS on the gut microbiome has not yet been published or verified, further research in the area is necessary before TMS is utilised as an intervention for dysfunction of the axis.

Despite the evidence of the effectiveness of these treatments, it is important that too strong an emphasis is not placed on the treatment of gastrointestinal symptoms. Although a relationship was seen between gastrointestinal experiences and mental health experiences in each of the research hypotheses, in each case less than half of the variance was explained by gastrointestinal symptoms. A complex combination of factors determine mental health (Sarris et al., 2015). The gastrointestinal tract and the gut microbiome cannot be relied upon as the sole determinants of mental health. Existing and verified psychological treatments should be relied upon as the main form of treatment for mental health problems. Even accounting for this fact, the potential impact of treatments of the brain-gut-microbiome axis should not be ignored. It is suggested that research is conducted into enhanced forms of psychological treatments that incorporate interventions targeting gastrointestinal symptoms. A treatment plan that incorporates the treatment of both mental and gastrointestinal symptoms has the greatest potential when it comes to improving overall quality of life for persons experiencing brain-gut-microbiome dysfunction.

It is important that psychologists understand the physical symptoms that often appear alongside poor mental health in order to properly treat those that suffer from depression, anxiety and stress. The high prevalence of gastrointestinal disorders in these cases makes them a key area of study. However there have been few studies looking at the occurrence of gastrointestinal experiences alongside mental health experiences in a non-clinical sample. The current study is important as it has clearly demonstrated the link between gastrointestinal experiences and mental health in a non-clinical sample, demonstrating strong support for the

brain-gut-microbiome axis and its impact on mental health. This axis has implications for psychologists in the way that the treatment of complaints such as depression, anxiety and stress are approached. Previous theory explaining the link between gastrointestinal experiences and mental health put forward an evolutionary explanation. This explanation did not give a comprehensive understanding of the multiple mental health factors that relate to gastrointestinal experiences. Thus, research into the brain-gut-microbiome axis acts as a more favourable explanation for the relationships observed in the current study. Although a link between probiotic use and mental health was not demonstrated in the current study, this appears to largely be due to the non-experimental nature of the study. Experimental research into the use of probiotics and diet plans has promising potential in the development of treatments for poor mental health, specifically experiences of depression, anxiety and stress. Further research is necessary before the findings of the current study can be applied in treatment. Knowledge of this axis also has potential in the promotion of general well-being among the public. Some public awareness of the relationship between mental health and gastrointestinal health does currently exist, however this awareness has the potential to be increased. Until specific interventions can be developed, the promotion of public awareness of this relationship, as well as the importance of a healthy gut microbiome, has the potential to improve the overall mental wellbeing of the general public.

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Appendices

Appendix A

Assessing mental and physical health experiences

My name is Amy Buckley and I am conducting research as part of my Higher Diploma in the Department of Psychology at Dublin Business School that explores mental health, specifically depression, anxiety and stress, and certain physical experiences. The physical experiences that the study focuses on will be revealed at the end of the study. This research is being conducted as part of my studies and will be submitted for examination, the study's results may be published in academic journals or presented at academic conferences. Answers to the open-ended question contained in the study may be included as quotations in the write up of results.

You are invited to take part in this study and participation involves completing the following online anonymous survey. While the survey asks some questions that may cause some minor negative feelings, it has been used widely in research. If any of the questions do raise difficult feelings for you, contact information for support services is included on the final page.
Participation is completely voluntary and so you are not obliged to take part.

Participation is ANONYMOUS and CONFIDENTIAL. Thus, responses cannot be attributed to any one participant. For this reason, it will not be possible to withdraw from participation after the questionnaire has been submitted. Before submission participants may withdraw at any time.

Responses will be stored anonymously in an electronic format on a password protected computer and data will be deleted after three years.

It is important that you understand that by completing and submitting the questionnaire that you are consenting to participate in the study.

Should you require any further information about the research, please contact Amy Buckley,   @mydbs.ie. My supervisor can be contacted at   @dbs.ie.
Thank you for taking the time to complete this survey.

Required
Do you consent to participate in this research? *

- ○ Yes
- ○ No

Appendix B - Questionnaire

Appendix B.1 Demographic and Qualitative Questions

What age are you?

What sex are you?

Male ☐

Female ☐

Prefer not to say ☐

Please list any physical health experiences that you associate with depression, anxiety or stress

Do you suffer from any diagnosed bowel disorder (eg. Inflammatory Bowel Disease, Crohn's Disease) or from Irritable Bowel Syndrome?

Yes ☐

No ☐

(If yes survey skips to debrief page)

Appendix B.2 Quantitative Questions

Do you currently take a daily probiotic (eg. oral supplement or probiotic yogurt)?

Yes ☐

No ☐

Appendix B.2.1 DASS-21

Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you *over the past week*. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

1	I found it hard to wind down	0	1	2	3
2	I was aware of dryness of my mouth	0	1	2	3
3	I couldn't seem to experience any positive feeling at all	0	1	2	3
4	I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
5	I found it difficult to work up the initiative to do things	0	1	2	3
6	I tended to over-react to situations	0	1	2	3
7	I experienced trembling (eg, in the hands)	0	1	2	3
8	I felt that I was using a lot of nervous energy	0	1	2	3
9	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
10	I felt that I had nothing to look forward to	0	1	2	3
11	I found myself getting agitated	0	1	2	3
12	I found it difficult to relax	0	1	2	3
13	I felt down-hearted and blue	0	1	2	3
14	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3
15	I felt I was close to panic	0	1	2	3
16	I was unable to become enthusiastic about anything	0	1	2	3
17	I felt I wasn't worth much as a person	0	1	2	3
18	I felt that I was rather touchy	0	1	2	3
19	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3
20	I felt scared without any good reason	0	1	2	3
21	I felt that life was meaningless	0	1	2	3

Appendix B.2.2 PROMIS Scale v1.0 – GI Belly Pain

Belly Pain

Please respond to each question or statement by marking one box.

1 GIS X78	In the past 7 days, how often did you have belly pain?

☐
1   Never   →   **If Never, go to #5**

☐
2   One day

☐
3   2-6 days

☐
4   Once a day

☐
5   More than once a day

2 GIS X79	In the past 7 days, at its worst, how would you rate your belly pain??

☐
1   Not bad at all

☐
2   A little bad

☐
3   Somewhat bad

☐
4   Quite bad

☐
5   Very bad

3 GIS X90	In the past 7 days, how much did belly pain interfere with your day-to-day activities?

☐ 1   Not at all

☐ 2   A little bit

☐ 3   Somewhat

☐ 4   Quite a bit

☐ 5   Very much

4 GIS X91	In the past 7 days, how much did belly pain bother you?

☐ 1   Not at all

☐ 2   A little bit

☐ 3   Somewhat

☐ 4   Quite a bit

☐ 5   Very much

5 GISX 92	In the past 7 days, how often did you have discomfort in your belly?

☐ 1   Never

☐ 2   Rarely

☐ 3   Sometimes

☐ 4   Often

☐ 5   Always

Appendix B.2.3 PROMIS Scale v1.0 – GI Reflux

Gastroesophageal Reflux

Please respond to each question or statement by marking one box.

1 GI SX 2	In the past 7 days, how often did you have regurgitation—that is, food or liquid coming back up into your throat or mouth without vomiting??

- ☐ 1 Never → **If Never, go to #3**
- ☐ 2 One day
- ☐ 3 2-6 days
- ☐ 4 Once a day
- ☐ 5 More than once a day

2 GI SX 3	In the past 7 days, what was the most food or liquid you had come back up into your mouth at one time?

- ☐ 1 None
- ☐ 2 Enough to fill a little of my mouth
- ☐ 3 Enough to fill some of my mouth
- ☐ 4 Enough to fill most of my mouth
- ☐ 5 So much that it filled my entire mouth

3 GIS X9	In the past 7 days, after eating a meal how often did food or liquid come back into your throat without vomiting?

- ☐ 1 Never → **If Never, go to #5**
- ☐ 2 Rarely
- ☐ 3 Sometimes
- ☐ 4 Often
- ☐ 5 Always

4 GI SX 10	In the past 7 days, how often did you re-swallow food that came back into your throat?

- ☐ 1   Never
- ☐ 2   Rarely
- ☐ 3   Sometimes
- ☐ 4   Often
- ☐ 5   Always

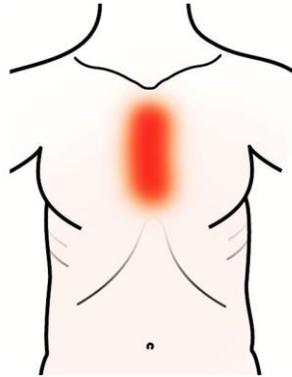| 5 GI SX 11	In the past 7 days, how often did you feel like you were going to burp, but food or liquid came up instead?

- ☐ 1   Never
- ☐ 2   One day
- ☐ 3   2-6 days
- ☐ 4   Once a day
- ☐ 5   More than once a day

6 GI SX 12	In the past 7 days, how often did you feel like there was too much saliva in your mouth?

- ☐ 1   Never
- ☐ 2   Rarely
- ☐ 3   Sometimes
- ☐ 4   Often
- ☐ 5   Always

7 GI SX 14	Look at the picture below. In the past 7 days, how often did you feel burning in the red area shown in the picture — that is, behind the breastbone?

☐ 1   Never

☐ 2   One day

☐ 3   2-6 days

☐ 4   Once a day

☐ 5   More than once a day

8 GI SX 21	In the past 7 days, how often did you feel burning in your throat?

☐ 1   Never

☐ 2   Rarely

☐ 3   Sometimes

☐ 4   Often

☐ 5   Always

9 GIS X22	In the past 7 days, how often did you burp?

☐ 1   Never → **If Never, go to #11**

☐ 2   One day

☐ 3   2-6 days

☐ 4   Once a day

☐ 5   More than once a day

10 GISX24	In the past 7 days, how much did burping bother you?

☐ 1   Not at all

☐ 2   A little bit

☐ 3   Somewhat

☐ 4   Quite a bit

☐ 5   Very much

11 GISX25	In the past 7 days, how often did you have hiccups?

☐ 1   Never

☐ 2   Rarely

☐ 3   Sometimes

☐ 4   Often

☐ 5   Always

12 GI SX 28	In the past 7 days, how often did you feel like there was a lump in your throat?

☐ 1   Never → **If Never, you are finished.**

☐ 2   Rarely

☐ 3   Sometimes

☐ 4   Often

☐ 5   Always

13 GI SX 30	In the past 7 days, how much did having a lump in your throat bother you?

☐ 1   Not at all

☐ 2   A little bit

☐ 3   Somewhat

☐ 4   Quite a bit

☐ 5   Very much

Appendix C

Debrief Sheet

Thank you for your answers. Your response has been recorded. This study has focused in particular on the experience of gastrointestinal health symptoms and mental health.

Any questions can be sent to me at   ₅@mydbs.ie.

If you feel that answering the mental health section of this survey has raised some issues for you, please consider contacting some of the support services listed below, or speak to a friend, family member or professional.

Aware:
The Aware Support Line 1890 303 302
Available Monday – Sunday, 10am to 10pm.
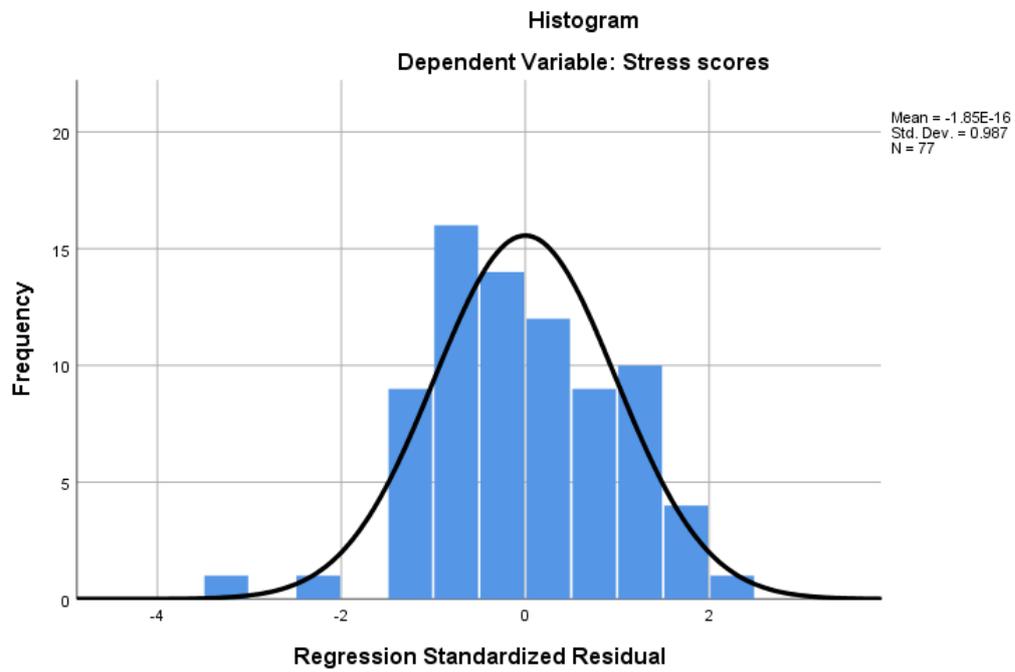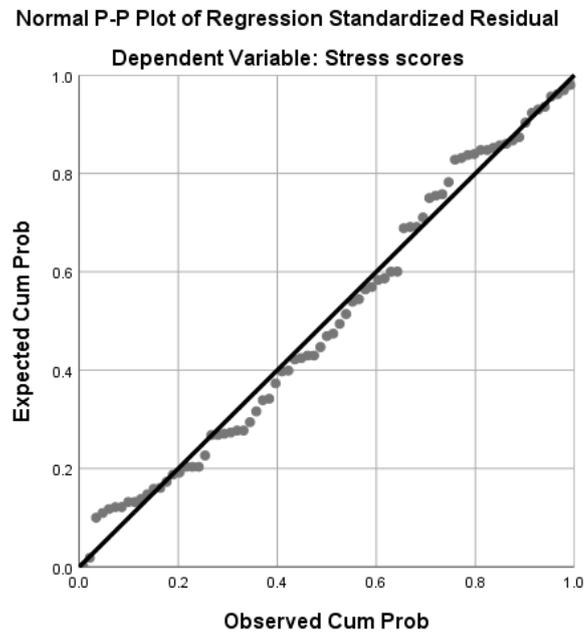Email for support at: supportmail@aware.ie

Samaritans
Call on: 116 123
Available 24hrs a day, 365 days a year. Free to call.
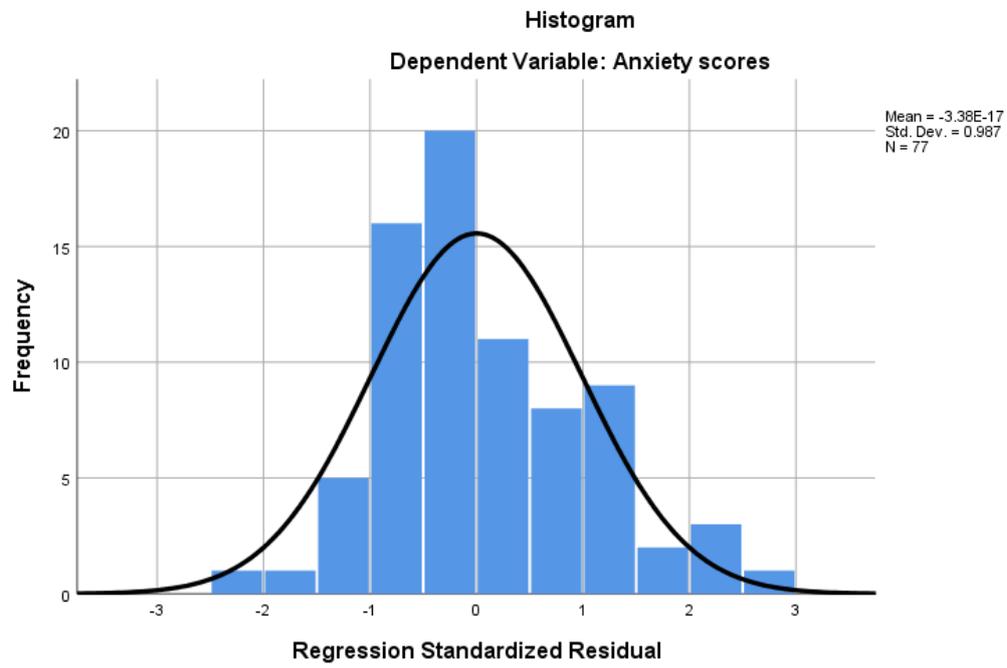Email: jo@samaritans.org

If you are concerned about your experience of any of the gastrointestinal symptoms brought up in this study the researcher recommends that you visit your general practitioner (GP).

Appendix D

Histogram

Dependent Variable: Stress scores

Appendix E

Normal P-P Plot of Regression Standardized Residual

Dependent Variable: Stress scores

Appendix F

Histogram

Dependent Variable: Anxiety scores

Appendix G

Normal P-P Plot of Regression Standardized Residual

Dependent Variable: Anxiety scores