An Exploration of The Nosology of Generalized Anxiety Disorder

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D.Clin.Psy. Thesis (Volume 1), 2021

University College London

UCL Doctorate in Clinical Psychology

Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Overview

This thesis explores the nosology of Generalized Anxiety Disorder (GAD) and features of the disorder.

The conceptual introduction in part 1 explores the literature related to different aspects of the nosology of GAD including the diagnostic and psychological conceptualisations of the disorder, epidemiology, evidence for the uniqueness of current features in the diagnostic criteria including the cardinal feature of worry and application of alternative frameworks to understand the presentation of the disorder. Overall, it suggests that GAD currently has no features unique to the disorder that can reliably distinguish it from other anxiety and depressive disorders. It seems that GAD continues its legacy as a residual disorder characterised by what it is not as opposed to what it is and there is limited research into options for alternative features that may help better understand presentations of the disorder.

The empirical study in part 2 explores the presence of subgroups within GAD and characterises their symptom profiles and stability using a latent transition analysis on sessional item-level data from a large sample of people receiving routine psychological treatment. Findings highlight the high levels of depression symptom endorsement in all GAD subgroups, the lack of distinguishing features between these groups and qualitative similarities with subgroups from a wider population of patients with anxiety and depressive disorders. Patterns in the transitions were found demonstrating the potential for GAD presentations to later emerge for some.

The critical appraisal in part 3 details reflections on the experience of working within and challenging the status quo of diagnostic-led service provision in mental health. It also includes reflections on the research process and experience of working with a large secondary dataset, and the importance of such approaches for psychologists.

Impact Statement

GAD is one of the most common mental health disorders but the current uncertainty surrounding the nosology of the disorder and difficulties in accurate recognition of the disorder by healthcare professionals mean that only around 13% of people receive a diagnosis resulting in most with the disorder being undiagnosed and untreated. Understanding the current evidence into the nosology and features of different subgroups of GAD is key to improving recognition of the disorder, what features are unique to the disorder and what typical profiles of symptoms look like in those with a likely diagnosis to potentially aid identification in clinical practice and improve the reliability of the diagnosis. This paper uses two approaches to exploring this, namely exploration of the current evidence into different areas related to the nosology of GAD in the conceptual introduction and using secondary data analysis on sessional data from patients in psychological treatment services to explore symptom profiles of subgroups and their stability in a clinical sample.

The findings from the conceptual introduction highlight the unclear nosology of GAD and poor specificity of the current diagnostic criteria which include no features unique to the disorder which instead overlap heavily with criteria for depressive and other anxiety disorders. There remains little research into exploring alternative potential cardinal features of GAD, with muscle tension proposed as one feature able to reliability distinguish GAD from depression, and therefore a key point to apply to clinical practice but also of note for future research into the disorder. This lack of research highlights why the current understanding of GAD which places worry as the cardinal feature has remained despite worry being featuring in the presentations of a range of other disorders. Additionally, alternative approaches to understanding GAD highlight the role of transdiagnostic factors in the presentation, in contrast to the categorical approach of diagnostic classification, and particularly the relationship with depression and highlight potential approaches to better understanding the presentation.

The empirical study uses a novel approach to exploring the presentations of GAD and their stability within a large sample of patients from psychological services. The findings highlight the norm of depressive symptomatology in all presentations of GAD, with severity ratings of depression symptoms to a similar level of the GAD symptoms in the majority of GAD subgroups and qualitatively similar patterns to those subgroups within the wider sample of anxiety and depressive disorders, demonstrating the high overlap within these groups. Importantly, the study demonstrates how a GAD presentation can emerge for a portion with the disorder, particular who initially present with mild depressive and anxiety symptoms, which may help identification of the disorder in practice and demonstrates quantitatively themes that have been discussed in previous research..

Evidence from both sections highlight the role of a transdiagnostic approaches in understanding nosology and treatment of GAD with the demonstrable overlap between GAD and depressive presentations, which contrasts disorder-specific approaches currently adopted in practice in many settings.

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Part 2

Acknowledgments

I would like to thank my supervisors Professor Steve Pilling and Dr Rob Saunders for their invaluable support and advice over the past two and half years. I would particularly like to thank Rob for his patience and dedication of time in supporting me through the whole research project and guidance and expertise in statistical approaches I was quite frankly scared to approach and did not envision myself being able to complete. I am very grateful for your help getting me over the final hurdle.

I also thank my friends and family for their support, compassion and encouragement throughout this process. Your positivity, laughter and kindness when faced with a person who at times could only talk about one topic and efforts to ensure I had a life outside the computer made this bumpy journey much more manageable.

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Part 1: Literature Review

Exploring the Nosology of Generalized Anxiety Disorder

Introduction

Generalized anxiety disorder (GAD) is a relatively new diagnostic entity that has been associated with controversy over its nosological status since its inception. While initially conceived as a residual disorder, characterised by what it was not rather than what it was, the diagnostic criteria have been substantially revised over time in attempt to reduce high rates of comorbidity, improve the reliability of the diagnosis and establish it as an independent disorder. Despite this, GAD remains a comorbid disorder with “pure” presentations rare (Bruce et al., 2001), associated with questions over the specificity of its diagnostic criteria (Faravelli et al., 2012) and poorly recognised in services and frequently misdiagnosed as a mood or other anxiety disorders (Bebbington et al., 2000; Brown et al., 2001a). As such, there still remains a level of uncertainty over the future of GAD, whether it is a valid entity in need of further research to better understand its presentation or if it is simply a redundant diagnosis with the syndrome better understood in another form.

This conceptual review aims to explore the presentation of GAD its current features and their specificity to the disorder to determine whether there any unique features which could improve understanding of what constitutes GAD and aid recognition of the disorder. This review explores the various conceptualisations of GAD within the different revisions of the diagnostic criteria since its inception and reasons for the alterations. It will then discuss the epidemiology of GAD worldwide and different factors associated with the course of the disorder. The main psychological models of GAD will be explored and their various proposed key features of the disorder. The features proposed to be key to GAD from the diagnostic criteria, psychological conceptualisation and researchers will be explored to determine whether there are any that are unique to the disorder or could help understand presentations of the disorder, particularly focusing on the role of worry in the disorder which has arguably over time has become the cardinal feature. Other proposals of ways to conceptualise GAD and their evidence base will also be discussed to consider whether alternative understandings better capture the presentation of GAD or could provide insights into the

nosological understanding of the disorder. Finally, the implications of this will be discussed in relation to the difficulties in the recognition and psychological treatment of GAD.

Changes in The Diagnostic Criteria of GAD

The diagnostic criteria of GAD have changed significantly since its initial conceptualisation. The term “generalised anxiety disorder” first appeared in the Research Diagnostic Criteria (Spitzer et al., 1978), distinguishing GAD and panic disorder following research that found differential effects of tricyclic antidepressants (TCAs) between generalised anxiety and anxiety associated with panic attacks (Klein, 1964; Klein & Fink, 1962; Zitrin et al., 1978), which also later informed the conceptualisation in the diagnostic manuals. Later research has since contradicted these findings with dual efficacy of TCAs demonstrated in both disorders (e.g., Casacalenda & Boulenger, 1998; Kahn et al., 1986; Zohar & Westenberg, 2000), questioning the validity of this split of into different disorders based on the presence or absence of panic attacks. But despite this opposing evidence, the distinction between the two disorders remains.

GAD first appeared as a diagnostic entity in the *Diagnostic and statistical manual of mental disorders* third edition (DSM-III) (American Psychiatric Association [APA], 1980) following the split of “Anxiety Neurosis” into GAD and panic disorder. It was conceptualised as a residual disorder of “generalized, persistent anxiety” with associated somatic symptoms and mild impairment for over one month. The residual status acknowledged that the symptoms of GAD were always present in other anxiety disorders and a diagnosis only given in the absence of specific features of other anxiety disorders. Yet, an implication of this hierarchical relationship was that few patients received a diagnosis (Barlow et al., 1986) and it was also associated with low reliability (Di Nardo et al., 1983) and high levels of comorbid depression (Crocq, 2017).

Worry was first established as a key feature following the substantial revisions for the DSM-III-R (APA, 1987), with GAD becoming a disorder of excessive, unrealistic worry and anxiety following research that found distinctions between anticipatory anxiety accompanying other anxiety disorders and generalised anxiety associated with chronic worry and apprehensive expectation about different life domains (Barlow et al., 1986). In efforts to reduce the high comorbidity with depression and based on research finding less comorbidity with increased duration of GAD (Breslau & Davis, 1985), the criteria were increased to six months. But despite these changes, the disorder continued to be plagued by poor reliability and almost led its exclusion from the DSM-IV (Brown et al., 1995).

During the development of the DSM-IV (APA, 1994) there were suggestions that GAD may be better classified as anxious temperament to capture what some viewed as the typical life-long nature of the anxiety in the disorder (Akiskal, 1998). While GAD inevitably remained in Axis I, the criteria were revised again in another effort to increase reliability with some reported success to a level comparable to that of depression (Brown et al., 2001a; Andrews et al., 2010). Worry in GAD was further specified to be uncontrollable based on evidence that this distinguished pathological from everyday worry (Abel & Borkovec, 1995) and the associated features were also revised requiring at least three of six symptoms of tension and vigilance as these were viewed as more specific to GAD as opposed to other anxiety disorders (Ruscio et al., 2007). Concerns were raised this could further blur the boundaries with depression due to the overlap in associated symptoms (Brown et al., 1991). The criteria also required that GAD symptoms were not confined to an episode of another disorder to provide diagnostic parsimony (Breslau & Davis, 1985).

GAD's status was again debated during the development of the DSM-5 (APA, 2013), with some proposing it be renamed as 'Generalized Worry Disorder' to emphasise the key role of worry in the presentation (Andrews et al., 2010) with others seeking to reclassify it as a distress disorder with depression and dysthymia due to their close, frequently comorbid relationships (Watson, 2005). However, in the end the DSM-5 criteria remained similar to

DSM-IV apart from the removal of the hierarchical relationship with other psychiatric disorders and requiring the disturbance not be better explained by another disorder, restoring GAD's residual status as it was viewed to inhibit diagnosis and treatment (Reed et al., 2019). However, this may have led to a reduction in reliability in the DSM-5 iteration (Chmielewski et al., 2015) although the quality of the field tests testing its reliability have been questioned (Jones, 2012).

This increasing focus on worry contrasted with the approach taken by the International Classification of Diseases (ICD). Prior to its inclusion, a GAD presentation would have been encompassed under the broad "Anxiety States" diagnosis in the ICD-9 (World Health Organisation [WHO], 1975). When introduced in the ICD-10 (WHO, 1992), GAD was a disorder of free-floating anxiety, not predominating to any particular circumstances, associated with prominent tension, worry and feelings of apprehension that did not meet criteria for mood or other anxiety disorders. For the ICD-11 (WHO, 2018) GAD was revised to specify the worry to be "excessive" lasting several months but with no requirement of uncontrollability and, for the same reasoning as with the DSM-5, removed the hierarchical rule with other psychiatric disorders. These more defined criteria were viewed to have improved diagnostic agreement by producing a more distinct diagnostic entity (Rebello et al., 2019). In contrast to the DSM, the ICD GAD focused more on associated somatic features with inclusion of a broader range of symptoms in the diagnostic criteria (WHO, 2018).

These developments brought the ICD-11 and DSM-5 closer in agreement than previous versions (Stein et al., 2020), with both classifying GAD as a disorder of excessive worry and anxiety about a number of life events with associated somatic symptoms of tension and sleep difficulties. Both classifications differ in specific required criteria, with general apprehension proposed as an alternative to excessive worry in the ICD and worry to be uncontrollable in the DSM. Despite sharing a name, these differences have led the ICD-

11 criteria to be more inclusive whereas DSM-5 GAD is associated with more a chronic presentation (Slade & Andrews, 2001).

Summary of The Changes in The Diagnostic Criteria

Both diagnostic criteria of GAD have received repeated refinements in an attempt to outline a more independent reliable entity and reduce the levels of comorbidity. However, these revisions have led to substantial changes to the cluster of symptoms that constitute the disorder, resulting in categorisation of very different syndromes both within and between the systems. These efforts to further define boundaries of GAD through revisions to criteria have led to some questioning the specificity of its symptoms (e.g., Ruscio, 2002) but others argue that GAD may represent the best current conceptualisation for organising and explaining the complex heterogeneous symptoms which require further refinement (e.g., Mennin et al., 2008). Through revisions worry has emerged as a cardinal feature of the disorder, supposedly reflecting advances of phenomenological understandings of GAD (Reed et al., 2019). The increasing focus on worry and specific associated symptoms of tension and vigilance have reportedly reduced the comorbidity with other anxiety disorders but have inadvertently created an increasingly blurred boundary with depression. While the reliability has reportedly improved from earliest versions, GAD continues to have unsatisfactory reliably and has one of the lowest in the mood and anxiety disorders (Reed et al., 2018; Regier et al., 2013). However, it remains that the evidential basis for the initial separation from panic disorder which led to GAD becoming a distinct diagnostic entity has since been contradicted.

Epidemiology

Lifetime Prevalence

GAD appears to be a common disorder with estimates of lifetime prevalence globally around 6.2% (Somers et al., 2006; Starcevic, 2006). While previously rates remained relatively stable despite the changes in diagnostic criteria (Wittchen, 2002), the removal of the hierarchy criteria in the DSM-5 estimates of lifetime prevalence have increased by between 37% and 90% from DSM-IV GAD (Fabiano & Haslam, 2020; Ruscio et al., 2017).

However, prevalence rates vary considerably between countries, with higher rates in predominantly Caucasian countries. For example, estimates of lifetime prevalence in the United States was 9% (Kessler et al., 2012), 6% in New Zealand (Oakley Browne et al., 2006), and 2.8% in European countries (Alonso et al., 2004). In contrast, other estimates have suggested lifetime prevalence of 0.1% in Nigeria (Ruscio et al., 2017), 1.9% in Saudi Arabia (Altwaijri et al., 2020), 0.9% in Singapore (Lee et al., 2016), and 0.3% in China (Huang et al., 2019). Within the United States, lifetime prevalence varies between different ethnic groups with higher rates in white Americans compared to African, Hispanic, or Asian Americans (Asnaani et al., 2010; Breslau et al., 2006) and only higher rates found in Native Americans (Grant et al., 2005). From general population survey data from 26 countries using DSM-5 GAD, the rates of lifetime prevalence varied between those of different economic status with average rates of 5% in high, 2.8% in middle, and 1.6% in low-income countries (Ruscio et al., 2017). Such findings suggest that the true prevalence may be considerably lower than predicted due to overestimations based on data from on high-income, developed countries.

Despite this global variation, GAD is consistently more common in women than men (e.g., Lieb et al., 2005; McLean et al., 2011). While typical pattern of anxiety disorders, this is the greatest disparity in prevalence between the genders for any anxiety disorder (Hoge et al., 2012).

Age of Onset

While GAD is traditionally viewed to have a relatively later onset in comparison to other anxiety disorders (e.g., Olino et al., 2010; Wittchen & Hoyer, 2001), findings into the estimated age of onset for the disorder are inconclusive beyond this. Studies have found the age of onset to be in late adolescence or early twenties (e.g., Kessler et al., 2001; Vaingankar et al., 2013), thirties (e.g., Grant et al., 2005; Kessler et al., 2005) or forties and fifties (e.g., Goncalves & Byrne, 2012; Legerstee et al., 2019) whereas others have suggested a bimodal population distribution of age of onset (e.g., Le Roux et al., 2005; Rhebergen et al., 2017).

Within these studies, some have investigated the unique demographic and clinical variables associated with early and late onset using different approaches to determine the cut-off between these groups. Some studies have used a top-down approach with researcher determined cut-offs in the 20s (Goncalves & Byrne, 2012; Hoehn-Saric et al., 1993; Ramsawh et al., 2011) or 50s or 60s (Chou, 2009; Le Roux et al., 2005; Lenze et al., 2005), whereas others used a bottom-up data-driven approach to determine a cut-off of 24 years between early and late onset (Rhebergen et al., 2017). The proposed factors associated with early onset included lower education levels (Chou, 2009) or higher educational levels (Rhebergen et al., 2017), childhood adversity (Chou, 2009; Goncalves & Byrne, 2012; Hoehn-Saric et al., 1993; Le Roux et al., 2005), increased negative life events (Rhebergen et al., 2017), higher rates of psychiatric comorbidity (Chou, 2009; Goncalves & Bryne, 2012; Hoehn-Saric et al., 1993; Le Roux et al., 2005), higher trait anxiety or neuroticism (Hoehn-Saric et al., 1993; Rhebergen et al., 2017), greater symptom severity (Le Roux et al., 2005), increased physical illness (Chou, 2009) or less physical illness (Rhebergen et al., 2017), and female gender (Rhebergen et al., 2017). However, researchers used arbitrary cut-offs most often and the majority of these studies focus on either treatment-seeking or older adult populations. In wider research, most studies have

found no difference in age of onset between men and women (e.g., De Lijster et al., 2017; Vesga-López et al., 2008).

Again, a reason for this disparity could be due to the wide variation in age of onset across countries (e.g., de Lijster et al., 2017; Kessler et al., 2007), yet despite onset being slightly earlier in high-income countries, the distributions of age of onset were found to not be significantly different across 26 countries (Ruscio et al., 2017).

However, one explanation for GAD's relatively later onset has been suggested to be biased by the shared diagnostic features with depression and mood disorders which also have a later onset (e.g., de Lijster et al., 2017; Gorwood, 2004; Zbozinek et al., 2012), therefore instead perhaps representative of an artefact of the current diagnostic criteria.

Course

The literature on the longitudinal course of GAD is very limited with few studies investigating the naturalistic longitudinal course through prospective cohorts. Instead, the majority of research implements retrospective designs, short-term follow-up in treatment efficacy trials, focuses only on specific populations or include only data from baseline and a follow-up. As a result, most of the understanding on the natural course comes from studies within the Harvard/Brown Anxiety Research Project (HARP) (Massion et al., 1993) which have tracked the course of DSM-III-R GAD at regular intervals over a 17-year span and shorter studies such as the Netherlands Study of Depression and Anxiety (NESDA) with less frequent follow-up (e.g., Penninx et al., 2008) or fewer follow-ups over longer span such as The Zurich Cohort Study (Angst et al., 2009).

GAD is associated with significant impairment across multiple life domains (Bruce et al., 2005; Wittchen, 2002). 'Pure' GAD has comparable social, occupational, and economic burden to that of 'pure' depression (Grant et al., 2005; Kessler, 2000; Tyrer & Baldwin, 2006). In both retrospective and prospective studies, GAD has been shown to have low

rates of recovery and high likelihood of relapse. Compared to other anxiety disorders, it has a much lower probability of recovery over a decade (Bruce et al., 2005). While there is agreement that GAD has a chronic course, definitions of this vary with studies classifying "chronic" as either unremitting episodes or waxing and waning in symptom severity (Weisberg, 2009; Wittchen, 2002). HARP findings suggest that a significant portion of individuals experience a chronic, unremitting course and even in those who do remit recurrence is common (Bruce et al., 2005). Remission appears to be most likely within the first 2 years when 80% of the HARP sample had received some form of treatment (Yonkers et al., 1996), with a cumulative probability of remission being 58% within 12 years and in those who had recovered the chance of recurrence was 45% over this period (Bruce et al., 2005). This chronicity also found in the Epidemiologic Catchment Area Study (ECA) with episodes lasting longer than 5 years in 40% individuals with DSM-III GAD (Blazer et al., 1991). In retrospective accounts, a large portion of participants also report a chronic, decades-long, unremitting course (Bruce et al., 2005; Le Roux et al., 2005; Lenze et al., 2005).

This picture contrasts with NESDA studies which found 69.7% remittance over 2 years (Hendriks et al., 2013), 79.7 % over 4 years (Hendriks et al., 2016) and 82.3% after 6 years (Hovenkamp-Hermelink et al., 2016). Most notably, over 6 years only 4.2% within NESDA had a chronic, unremitting course (Hovenkamp-Hermelink et al., 2016). Likewise, in the Zurich Cohort Study over a 20-year period, while over half of a community sample of young adults experienced a recurrent course with periods without symptoms only 7% experienced a chronic course (Angst et al., 2009). However, even in NESDA of those who were remitted at baseline, 19.7% experienced a relapse within 2 years (Scholten et al., 2013).

One reason for the varying accounts of chronicity may be due to the differences in samples and methodology. For example, NESDA used a sample with diagnoses of DSM-IV GAD from primary care, community and specialist services (Penninx et al., 2008) whereas

HARP used an outpatient sample with DSM-III-R GAD which was heavily biased being 97% Caucasian and mostly female.

It appears that while a portion of individuals remit over a period of years, for a large portion the symptoms remain chronic for years and even for those who remit relapse is very common. It seems GAD is characterized by remarkable persistence over time and notably far exceeding the duration required in both versions of diagnostic criteria. It has been argued that a far more chronic course may be masked by tracking diagnosis as opposed to symptoms as even when remitted most individuals still experience significant impairment over a decade despite not meeting diagnostic threshold (Ramsawh et al., 2009). Even when individuals were most likely to remit in the first 2 years of HARP, the probability of becoming asymptomatic in this period was only 8% (Yonkers et al., 1996).

Predictors of Course

Recurrence appears to be common regardless of whether a 'pure' or comorbid GAD course (Scholten et al., 2013), however research findings into the specific impact of comorbidity on the longitudinal course of GAD are equivocal.

In the short-term, in psychiatric follow-up studies over periods of 1 to 2 years found comorbidity reduced the chance of recovery (e.g., Durham et al., 1997; Mancuso et al., 1993). Similarly, over 2 years primary care patients that did not recover were more likely to have comorbid depression and significantly more anxiety disorders at intake than those who remitted or partially remitted (Rodriguez et al., 2006).

Within HARP, comorbidity with Axis I disorders at 5 years appeared to have no impact on chronicity (Yonkers et al., 2000) but at 8 years being in episode of comorbid depression or panic disorder with agoraphobia decreased the probability of remission from GAD (Bruce et al., 2001). Over a similar period, individuals with comorbid panic disorder or panic with agoraphobia were at increased the risk of recurrence when in remission

(Rodriguez et al., 2005). Over 12 years likelihood of recovery significantly lower when GAD was comorbid with panic disorder with agoraphobia or depression whereas comorbid alcohol or substance misuse was significantly decreased likelihood of recovery and increased the likelihood of recurrence in those who had remitted (Bruce et al., 2005). Whereas, in HARP comorbidity with Axis II disorders was associated with reduced remission over 5 years (Yonkers et al., 2000) with comorbid personality disorder reducing likelihood of remission from GAD by 30% and significantly related to particularly avoidant and dependent personality disorders over this period (Massion et al., 2002). Whereas in the Collaborative Longitudinal Personality Disorders Study over 7 years, only OCPD found to increase risk of relapse in GAD (Ansell et al., 2011).

However other studies have found differences of the impact of age of onset, in a study using modelling over a 14-year period, individuals with later onset had better prognosis than younger adults with a steeper decline in symptom severity (Ramsawh et al., 2009). While another study over 15 years found no significant difference in the course for those with earlier or later onset as calculated using modelling to be 24 years (Ramsawh et al., 2011). Within HARP, older age of onset was associated with better likelihood of recovery (Rodriguez et al., 2006) whereas there were no gender differences in overall rates of remission and relapse over the longitudinal course up to 8 years (Yonkers et al., 2003). However, in primary care setting being female significant reduced likelihood of a partial recovery (Rodriguez et al., 2006).

Over 12 years, a course with lower probability of remission and increased persistence was predicted by more severe symptoms, increased duration of anxiety and avoidance, and higher levels of disability at intake (Bruce et al., 2005). Greater severity of psychosocial impairment at intake significantly reduced likelihood of full or partial recovery from GAD (Rodriguez et al., 2006). Psychosocial factors such as lower life satisfaction, poorer relationships, and lower daily and social functioning were predictive of reduced

likelihood of remission over 5 years (Yonkers et al., 2000) and increased risk of recurrence in those who have remitted (Rodriguez et al., 2005).

Comorbidity

Comorbidity poses one of the biggest threats to the clinical validity for GAD and further complicates recognition of the disorder (Tyrer & Baldwin, 2006). ”Pure” GAD is rare, and it more frequently presents as comorbid with other mental health disorders, particularly mood or other anxiety disorders (e.g., Lieb et al., 2005; Kessler et al., 2002). There have been suggestions that “pure” GAD is common in primary care but poorly recognised (Allgulander, 2006; Wittchen et al., 2002) or that individuals with “pure” GAD are less likely to seek treatment (Kessler et al., 2001).

GAD and depression are the most comorbid mood-anxiety pairing with estimates varying in the literature between 53% to 89% (Lamers et al., 2011; Moffitt et al., 2007a; Ruscio et al., 2017) with similar rates found in both the general population and clinical samples (e.g., Bruce et al., 2001; Carter et al., 2001). Studies have estimated that approximately 60 to 70% of individuals with GAD receive a lifetime diagnosis of depression (Carter et al., 2001) with some suggesting that the two disorders occur together more often than either “pure” GAD or “pure” depression (Mineka et al., 1998). This pairing is associated with higher levels of impairment, reduced GAD remission, lower quality of life, and more disability than “pure” GAD (e.g., Kessler, 2000; Kessler et al., 1999, 2002; Zhou et al., 2017).

Studies have indicated that comorbid GAD whether the primary or secondary diagnosis, is similar in terms of prevalence, course, and levels of treatment and only those with secondary GAD were more likely to have current or past anxiety, alcohol use disorders or depression (Rogers et al., 1999). Similarly, in children no differences were found in severity, impairment, or patterns of comorbidity between primary and secondary GAD (Ollendick et al., 2016), suggesting its independence as a disorder whether occur primarily

or secondary. However, while the comorbid nature has challenged the view of GAD being a distinct clinical entity, the rates are not substantially greater than for most Axis I or II disorders (Grant et al., 2005; Stein et al., 2017).

Temporal Continuity

All disorders have some heterotypic continuity, where onset of one disorder leads to an increased risk of later onset of another disorder, but if GAD is to be a distinct entity it should have strong homotypic continuity, where the occurrence of a disorder predicts later continuation of the same disorder. While research suggests that GAD has strong homotypic continuity, it also appears to have strong heterotypic continuity particularly with other internalising disorders and sometimes at higher rates than homotypic continuity (e.g., Ferdinand et al., 2007; Lahey et al., 2014; Shevlin et al., 2017). Yet, this seems to follow the pattern of widespread heterotypic continuity particularly amongst mood and anxiety disorders even when controlling for homotypic continuity, sex and age (Lahey et al., 2014).

Longitudinal studies investigating the patterns of temporal onset of comorbid GAD and depression have produced mixed findings which support the possibility of a bi-directional connections between the disorders. It has been estimated that around half of those with GAD develop later depression (Essau, 2003). Some studies have found that GAD most often precedes depression (e.g., Mathew et al., 2011; Kaufman & Charney, 2000; Wittchen et al., 2000), others found depression precedes GAD (e.g., Brown et al., 2001b; Cramer et al., 2010; Moffitt et al., 2007a; Zavos et al., 2012), others similar rates of depression or GAD preceding one another (Moffitt et al., 2007a), and others a simultaneous onset (e.g., De Graaf et al., 2003; Lamers et al., 2011).

More broadly, research has suggested that anxiety disorders often precede the onset of depressive disorders (e.g., Wittchen et al., 2000; Parker et al., 1999), a pattern that GAD appears to somewhat follow with GAD increasing risk for later depression more than

depression increasing risk of later GAD (Blanco et al., 2014; Davies et al., 2016; Mathew et al., 2011; Merikangas et al., 2003). However, reciprocal temporal relationships have also been found specifically between depression and GAD over a three-year period (Grant et al., 2009) and baseline depression has been found to be predictive of onset of GAD whereas baseline GAD predictive of subsequent onset and persistence of depression (Kessler et al., 2008).

GAD has historically a close diagnostic relationship with panic disorder. Some studies have suggested that GAD may be a prodrome to panic disorder, with research finding GAD appears for years prior to the first panic attack in 28% of those with panic disorder (Garvey et al., 1988). However, longitudinal research has also found reciprocal temporal relationships panic disorder and GAD over three years (Grant et al., 2009). Similar levels of homotypic and heterotypic continuity have been found for GAD with other anxiety disorders (Ferdinand et al., 2007; Pine et al., 2001).

Research has suggested that GAD is the biggest risk factor for later onset of depression or other anxiety disorders (Bittner et al., 2004) but also conversely mood and anxiety disorders have been associated with an elevated risk of developing GAD (Kessler et al., 2002). In children, GAD in childhood was predictive of adolescent onset of depression or GAD whereas GAD in adolescence was predicted by specific phobia, social phobia, PTSD, GAD, or depression (Shevlin et al., 2017).

These heterotypic patterns could simply be more representative of the wider relationship between anxiety and mood disorders. Yet these temporal patterns give no indication of the connecting process and the relationships may be due to an artefact of overlapping symptoms, common underlying causes or shared diathesis, perhaps particularly for depression and GAD. Another reason may be the limited predictive value of anxiety disorder diagnoses which have low longitudinal stability, particularly in chronic courses, with around 70% of diagnoses transitioning and increasing transitions over time (Hovenkamp-Hermelink et al., 2016).

Summary of The Epidemiology of GAD

GAD is a common disorder although studies have provided mixed results regarding the rates of prevalence and age of onset, varying depending on sample. Research suggests that GAD has a similar age of onset to depression which is later to other anxiety disorders. Earlier onset of GAD appears to be associated with comorbidity or early life risk factors.

Despite variation between studies, the findings suggest that GAD has a chronic course in some form, with most individuals experiencing a chronic waxing and waning course but a large portion experiencing an unremitting course, sometimes lasting decades. Even in those who do remit, recurrence is common. Some suggest that a far more chronic course might be overlooked by the use of diagnostic threshold to track course as opposed to the presence of symptoms as many still experience symptoms which significantly impact their life despite not meeting threshold. Despite the differences in course, it is clear that GAD shows a persistent course, notably far higher than required for both diagnostic criteria. While comorbidity and psychosocial stressors appear to be associated with a worse prognosis, results vary on the impact of particular comorbid disorders and at different time points.

Comorbidity is the norm in GAD with “pure” presentations rare. The disorder is most often comorbid with depression but also frequently with mood and other anxiety disorders. GAD has both homotypic and heterotypic continuity with other internalising disorders, in some studies the latter more common, and seems to again highlight the close relationships amongst all the internalising disorders. The reasoning for this close relationship remains unclear but demonstrates the issues with temporal continuity for GAD also appear to apply other disorders.

However, the evidence base behind the current understanding of the epidemiology of GAD has issues, particularly longitudinally. Due to the repeated revisions of the diagnostic criteria it is difficult to develop a consistent understanding of GAD as the symptoms that constitute the disorder have changed over time and therefore limited the utility of older

studies. As a result, the understanding of GAD has lagged behind that of other anxiety disorders (Dugas et al., 2010). Also, with very few studies investigating longitudinally, what is currently known about the course of GAD comes from a few research projects, but mostly from HARP, which each have their own issues, perhaps resulting in the equivocal findings.

The understanding of the epidemiology of GAD is also limited by cross-cultural issues with most research conducted in Western countries. The current variation in findings in studies from non-Western countries may in part be due to the limited cross-cultural applicability of the diagnostic criteria. The current emphasis on worry and reduced focus on the somatic symptoms may mismatch with presentations typical of other cultures (Lewis-Fernández et al., 2011). GAD is less diagnosed in minority groups, for example White Americans consistently endorsed GAD symptoms more than minority ethnic groups (Asnaani et al., 2010; Hoffman & Hinton, 2014). This may relate to cultural differences in attitudes to anxiety (Lee et al., 2009b). It has also been argued that the requirement of *excessive* worry may discount those who are experiencing real life concerns due to their situation (Marques et al., 2011).

Theoretical Conceptualisations Relevant to GAD

Different psychological conceptualisations have been proposed to explain the key features and underlying processes in GAD. Some specifically focus on the disorder whereas other models relate to particular processes relevant to the current understanding of GAD, namely models of worry. While in the diagnostic criteria GAD is conceptualised as a disorder of excessive worry, general apprehension and somatic symptoms, the psychological models of the disorder vary in their conceptualisation and main processes. Below each of the main relevant conceptualisations are briefly detailed and shared features and key differences between models discussed.

Avoidance Model of Worry and GAD

With worry positioned as the cardinal feature in the current diagnostic criteria of GAD, the Avoidance Model of Worry (AMW, Borkovec & Inz, 1990, Borkovec et al., 2004) provides a theoretical perspective of the processes underlying this feature. The AMW proposes that worry is a form of cognitive avoidance as it is viewed as a verbal-linguistic, thought-based activity which inhibits the unpleasant imagery, associated somatic activation and negative affect triggered by a threat (Borkovec & Inz, 1990). Worry moves attention focus from the aversive imagery to the verbal activity, inhibiting the emotional processing of the threat-related material needed for habituation and extinction of the fear, therefore negatively reinforcing worry and maintaining anxious meanings associated with the threat. Worry also becomes positively reinforced as the lack of aversive outcome is attributed to worry, leading to positive beliefs about the utility of worry and the continued implementation of worry as an ineffective cognitive attempt to problem solve. The model has been revised since its original conception to include the role of attachment, trauma, and interpersonal relationships in the maintenance of worry and GAD (Borkovec et al., 2004).

Evidence for the central tenet of the model, that worry serves an avoidant function and decreases somatic arousal, has been mixed. Experimental studies using different tasks have demonstrated a greater inhibitory effect of verbal than imaginal mentalisation on reducing emotional arousal (e.g., Behar & Borkovec, 2020; Borkovec & Hu, 1990) and a reduction in somatic activation at rest following worry (e.g., Lyonfields et al., 1995; Thayer et al., 1996) and after the introduction of a threat (e.g., Behar & Borkovec, 2020; Peasley-Miklus & Vrana, 2000). A review on the topic also supports the inhibitory effects of worry on emotional arousal (Sibrava & Borkovec, 2006). However, a range of experimental studies suggest that the inverse is true, with worry viewed to instead create and maintain a negative emotional state and increase arousal, for example studies have shown worry to increase physiological activation and prolong stress-reflective autonomic responding (e.g., Brosschot et al., 2007; Llera & Newman, 2010; Stapinski et al., 2010) and individuals report

subjectively higher levels of negative emotional experiences when worrying (Andor et al., 2008; Llera & Newman, 2010, 2017).

In contrast, there seems to be unanimity among studies which evidence that people view worry as helpful and useful (e.g., Barahmand, 2009; Newman & Llera, 2011; Ruscio & Borkovec, 2004; Wells & Papageorgious, 1998).

Intolerance of Uncertainty Model of GAD

The Intolerance of Uncertainty (IOU) model of GAD (Dugas et al., 1995; Herbert & Dugas, 2019) suggests that individuals with the disorder find ambiguous situations to be particularly distressing in comparison to those without. The IOU triggers worry due to an individual's positive beliefs about worry, believing it will prevent an aversive outcome and help them to cope with the situation. Worry and anxiety are maintained by both the individual's negative problem orientation, having low confidence in their problem-solving ability and pessimism about the outcome, and cognitive avoidant function of worry to avoid aversive imagery and unpleasant arousal and affect (Koerner & Dugas, 2006).

The IOU model was later revised (Herbert & Dugas, 2019) in an acknowledgement of the increasingly transdiagnostic view of IOU, in the general population and other disorders, and influenced by models of obsessive-compulsive disorder (OCD; Salkovskis, 1999), that worry was instead triggered by a catastrophic misinterpretation of uncertainty as opposed to IOU directly, for example that it is dangerous.

There has been some evidence in support of the presence of the four key tenets of the model: IOU, positive beliefs about worry, negative problem orientation (NPO) and the cognitive avoidant function of worry. However, the amount of research and evidence in favour of each varies with some aspects with more researched than others.

There is a lot of evidence from experimental and clinical settings for the presence of IOU in GAD presentations, with most support for the model focusing on this element. Studies have demonstrated associations between IOU and GAD, for example finding that individuals with GAD report higher levels of IOU than those in a non-GAD, high worrier control group (Ladouceur et al., 1998) or IOU being predictive of GAD symptom severity (Dugas et al., 2007). Individuals in a high IOU group were found to display higher levels of worry in comparison to a low IOU group (Ladoucer et al., 2000a). Experimental studies have found a unidirectional relationship between worry and IOU with high IOU levels predictive of high worry but not the inverse (Dugas & Ladouceur, 2000), also that increases in IOU induces increases in worry and vice versa (Ladouceur et al., 2000b), and stronger associations between IOU and worry compared to other processes like perfectionism (Buhr & Dugas, 2006). However, while GAD analogue groups were found to score higher on scales of IOU than controls or those with only somatic GAD symptoms, stronger correlations were not found between IOU and worry than were with depression or anxiety ratings (Buhr & Dugas, 2002).

In contrast, there has been less research into the role of NPO in GAD. NPO has been found to be predictive of GAD symptom severity (Dugas et al., 2007) and individuals with GAD displayed higher levels of NPO than high worrier non-GAD controls (Ladouceur et al., 1998). However, one study found NPO was more associated with IOU levels than to worry (Clarke et al., 2017).

As discussed in the AMW section, there is a lot evidence to suggest that individuals view worry as helpful, but findings are mixed regarding the avoidant function of worry.

Overall, out of the four components, while all found to be predictive of GAD symptoms or worry studies have found that only IOU related to GAD (Dugas et al., 2005; Ladouceur et al., 1999) or found that either NPO or IOU had more robust relationships with GAD severity (Dugas et al., 2007). Other research has found that IOU was the strongest element in distinguishing those with GAD from controls (Dugas et al., 1998) and other

clinical groups (Dugas et al., 2005; Ladouceur et al., 1999). Currently here seems researching is lacking into NPO with findings suggesting it may more be a facet of IOU and limited evidence for the cognitive avoidant function of worry.

Metacognitive Model of GAD

The Metacognitive Model (MM; Wells, 1995, 1999) suggests that worry is motivated by metacognitive beliefs and not simply a part of anxiety. They distinguish two types of worry: type 1 worry relating to worry about external events or internal non-cognitive issues, such as physical symptoms, and is experienced by all individuals whereas type 2 worry (also called meta-worry) relates to worry about type 1 worry, for example that is it dangerous or uncontrollable. Type 2 worry is thought to distinguish individuals with GAD from non-clinical worriers (Wells, 2005). Again, such individuals have positive beliefs about worry leading them to select worry as a problem-solving strategy in response to a threat, however they also experience negative beliefs about worry which is triggered by type 1 worry and leads to type 2 worry. Worry in GAD is maintained by this type 2 worry as it leads to implementation of coping strategies with the aim to avoid this meta-worry such as behaviours or thought control strategies (Wells, 2004).

The authors position metacognitive beliefs and meta-worry (type 2 worry) as the key element and central to the maintenance of GAD (Wells, 2010) and this has some evidential basis. Individuals with GAD report experiencing negative beliefs about worry and meta-worry (e.g., Ruscio & Borkovec, 2004; Wells & Carter, 2001) and in some studies, they endorse these beliefs more than non-clinical control groups (e.g., Davis & Valentiner, 2000; Wells, 2005) or those with other anxiety (Davis & Valentiner, 2000; Wells & Carter, 2001) or mood disorders (Cartwright-Hatton & Wells, 1997). Studies also found meta-worry to be more associated with pathological worry than with type 1 worry (Wells & Carter, 1999, 2001) and that meta-worry and not type-1 worry predicted later development of GAD over a period of

12 to 15 weeks (Nassif, 1999). Significant associations have also been found between metacognitions and worry in GAD even when controlling for emotional dysregulation (Salguero et al., 2019). Those with GAD were distinguished from groups or non-anxious, high worriers or those presenting with somatic GAD symptoms by meta-worries related to beliefs around danger of worry (Wells, 2005). The relationship between meta-worry and pathological worrying as found by Wells and Carter (1999) has also been demonstrated in samples of individuals from different ethnic groups (e.g., Nassif, 1999; Nuevo et al., 2004). However, other studies suggest that these negative beliefs are just indicative of high worry with similar levels of metacognitive beliefs and meta-worry found in individuals with high levels of worry without GAD diagnoses (Cartwright-Hatton & Wells, 1997), OCD (Ruscio & Borkovec, 2004) and panic disorder (Wells & Carter, 2001).

Some of the key elements of the MM remain undefined and lack evidence, for example in the reliability of distinguishing between and demonstrating the temporal relationships between negative beliefs about worry and meta-worry with the model suggesting that negative metacognitive beliefs lead to meta-worry (Behar et al., 2009). It has also been highlighted that most studies into meta-worry utilise measures which focus on the uncontrollability of worry, including the Metacognitions Questionnaire (Cartwright-Hatton & Wells, 1997) or the Anxious Thoughts Inventory (Wells, 1994), which is a criterion for DSM GAD therefore those with GAD are likely to score higher as it is facet of the disorder (Behar et al., 2009). The model is also lacking in clinical studies and there are few longer-term studies into the elements.

Emotion Dysregulation Model of GAD

The Emotion Dysregulation Model (EDM; Mennin et al., 2002, 2005) suggests that individuals with GAD are very sensitive to emotions and have deficits in emotional regulation leading to a reliance on cognitive control strategies such as worry to avoid aversive affective

experiences. They propose that specifically individuals with GAD experience a heightened intensity of emotions (both positive and negative) and more negative reactivity to emotions (becoming overwhelmed or anxious), have limited understandings of emotions, and employ maladaptive coping strategies such as worry or suppression of emotions in efforts to minimize or over-control emotions (Mennin et al., 2005).

Studies into the four key elements to the EDM have provided mixed results with some parts receiving more support.

Research has found that individuals with GAD experience negative but not positive emotions more intensely than healthy controls (Mennin et al., 2005; Salters-Pedneault et al., 2006; Turk et al., 2005) and those with other disorders including depression (Mennin et al., 2007) and social anxiety disorder on retrospective self-report measures (Mennin et al., 2007; Turk et al., 2005). Additionally, emotional intensity and dysregulation levels have also been found to be more predictive of a GAD rather than social anxiety (Mennin et al., 2009) or panic disorder diagnosis (Tull et al., 2009).

While experimental induction of a negative mood was found to evoke a greater increase in negative affect in those with GAD compared to a non-GAD control group (Pruitt, 2011), this finding was not replicated using a different task (Hanley, 2014). Other studies have found those with more severe GAD symptoms display less variable and more rigid mood over different days in comparison to those with less severe symptoms (Fisher & Newman, 2016). Additionally, significant correlations between emotional dysregulation and worry in GAD became non-significant when accounting for individual's metacognitive beliefs (Salguero et al., 2019). While higher negative affect variability and high affect arousal variability was found to be uniquely predictive GAD status, this association also became non-significant when controlling for baseline affect level (Ranney et al., 2020).

As for individuals with GAD having a poorer understanding of their emotions, it appears that there are no clear differences from other groups. Studies using self-report

measures for capturing client reported levels of skill in identifying, describing, and understanding emotions and found individuals with GAD had more difficulties in comparison healthy undergraduate controls (Mennin et al., 2005, 2007; Turk et al., 2005). However, other studies have found no differences between controls and those with GAD on emotional differentiation with individuals with GAD actually found to use more emotional regulation strategies than controls with the researchers concluding that this may be due to biased interpretation leading to underestimation of their own skill and suggest the model may need reviewing (Decker et al., 2008). Additionally, when independent observers rated participants written descriptions of their emotional experiences, they found individuals with GAD displayed more nuanced descriptions of emotion in comparison to controls (Novick-Kline et al., 2005). There also does not appear to be a difference in identifying, describing, or understanding emotions between individuals with GAD and individuals with other forms of disorders including depression (Mennin et al., 2007) and social anxiety disorder (Mennin et al., 2007; Turk et al., 2005).

Regarding the proposal that individuals with GAD have greater negative attitudes about emotions, evidence appears mixed. There are some findings in favour, with individuals with GAD found to exhibit increased fear of intense emotions compared to healthy controls (Mennin et al., 2005; Salters-Pedneault et al., 2006; Turk et al., 2005). However, in some studies it seems that there are no significant differences between fear of intense emotions among individuals with GAD compared to those with depression (Mennin et al., 2007) or social anxiety (Mennin et al., 2007; Turk et al., 2005) although other studies have found that individuals with GAD experience emotions as more threatening and distressing than those with mood or other anxiety disorders (Newman & Llera, 2011).

The evidence for the use of maladaptive emotional regulation and management strategies in GAD is mixed. Individuals with GAD were found to engage in more emotional coping strategies (i.e., excessive worry, emotional outbursts, emotional suppression) compared to healthy controls (Mennin et al., 2007) and individuals with depression and

social anxiety (Mennin et al., 2007). Yet, other studies have found that individuals with GAD use adaptive strategies, such as cognitive reappraisal, more often than control groups (Kerns et al., 2014).

Overall, the evidence for various elements of the EDM appears mixed. A lot of the research utilises low severity cases or university samples which has implications for the applicability of the model to more severe GAD presentations (Behar et al., 2009). There is limited research implementing samples from clinical populations, instead most of the studies using experimental designs. Some aspects of the model are also under researched, for example into to affect variability and instability in GAD.

Acceptance-based Model of GAD

The Acceptance-Based Model (ABM; Roemer & Orsillo, 2002, 2005, 2007) proposes that individuals with GAD have problematic relationships with their internal experiences cognitions, emotions, or physical sensations) leading them to respond negatively to their own internal experiences and experience "fusion" with internal experiences, that these negative experiences are permanent and unchangeable. This leads individuals to use behavioural and cognitive strategies as a form of experiential avoidance to avoid these "threatening" internal experiences, which may include worry. A perceived external threat triggers an internal experience and leads to negative thoughts or meta-emotions, for example appraisals that a thought is dangerous or fear of their fear. The use of worry, or other avoidance, in response becomes negatively reinforced due to the reduction in distress associated with the internal experience and the individual restricts meaningful activities so completing less "valued" actions as a result. The "fusion" with internal experiences is unique to this approach amongst models of GAD and worry.

There has been some research into the various components of the model providing mixed support for the model, with some areas with a more limited evidence base than others.

There appears to be some evidence to suggest individuals with GAD response negatively to their internal experiences and display experiential avoidance. Individuals with GAD report higher levels of fear or negative reactions to their emotions than control groups (e.g., Mennin et al., 2005; Roemer et al., 2005), even when for controlling for depressive symptoms (Lee et al., 2010). Studies has also found significantly higher levels of experience avoidance and distress about emotions compared to non-clinical controls with GAD status predicted on measures of experiential avoidance and fear of emotions compared to control (Lee et al., 2010). In therapy, changes in experiential avoidance were predictive of reductions in worry and improvements in ratings of quality of life (Eustis et al., 2016). Also, a significantly greater endorsement of experiential avoidance and fear of emotions has also been found to be associated with more severe GAD symptoms in a non-clinical sample of women, however this was not replicated in a small clinical sample (Roemer et al., 2005). Individuals with GAD have been shown to engage in less in valued actions compared to a nonclinical control group (Michelson et al., 2008).

However, there has been little research into fusion with internal experiences, which is proposed as a key element of the model. However, one study found in therapy decentring, separating from one's experiences, was found to be most the indicative of changes in the GAD symptom of worry (Hayes-Skelton et al., 2015).

The evidence for all the aspects of the model is limited, highlighting the need for further research particularly into the presence of fusion in GAD. The current studies predominantly use small samples and some only focus on scores on measures of worry as opposed to GAD symptomology.

Contrast Avoidance Model of GAD

The Contrast Avoidance Model (CAM; Newman et al., 2014; Newman & Llera, 2011), places the main fear in GAD as one of a negative emotional contrast (shift), defining this as the process of changing from a relaxed or euthymic emotional state to intensively negative emotional state which typically accompanies negative events. They suggest worry acts as a method to avoid such sharp shifts in negative emotions by evoking and sustaining negative emotions, preventing relaxation, and remaining in a continual state of tension and alertness to prevent an unexpected shift to a negative state. According to the CAM, individuals with GAD do not avoid all positive emotions but prefer a negative emotional state to avoid a negative contrast (Llera & Newman, 2017). This perspective of worry creating and maintaining a negative state and the fear of a negative emotional contrast is unique among models.

As the CAM is a relatively new model, there has been limited research into the key elements of the model.

There is evidence in support of the main feature that individuals with GAD fear a sharp shift in negative emotions, with scores on measures of contrast avoidance being predictive of GAD classification with individuals with GAD more likely than controls to endorse worry to avoid a negative emotional contrast and a dislike of a negative emotional contrast (Llera & Newman, 2017). Also, when tracking individuals over an 8-week period, for individuals with more GAD symptoms their negative emotional contrasts lead to more negative emotions and they rated these as the worst parts of their week (Crouch et al., 2017). Worry is also predictive of less negative emotional contrast over an hour following worry (Newman et al., 2019b). In a naturalistic weekly diary study, while increased GAD symptoms were predictive of higher endorsement of negative contrast experiences following a negative event, higher baseline GAD symptoms and higher worry were reduced this relationship suggesting worry blunted the emotional effects of the contrast (Crouch et al., 2017).

The second feature of the model, that worry sustains negative emotion, has mixed supported with worry found to increase negative emotionality however other research has found the opposite, as previously discussed before in the AMW section. Worry also was found to boost emotionality from baseline and individuals with GAD reported finding worry more helpful than relaxation whereas control groups reported preferring relaxation (Llera & Newman, 2014).

The final tenet of the model, that worry increases the likelihood of a positive emotional contrast, has some support from experimental studies. For individuals with clinical levels of GAD symptoms, worry appeared to increase the probability of experiencing a positive emotional contrast (Llera & Newman, 2017). Additionally, in a study of university students a longer worry duration led to higher sustained anxious arousal over a subsequent hour and those in the analogue GAD group were less likely to experience a negative emotional contrast and had an increased likelihood of a positive emotional contrast (Newman et al., 2019b). Worriers were also found to have a larger subsequent positive contrast compared to those who were relaxed regardless of GAD status (Llera & Newman, 2014).

However, the current evidence remains limited with few studies researching the different aspects of the model. Many of the studies also utilise experimental designs with subclinical populations and small samples or implement retrospective designs requiring individuals to recall their behaviours over the previous day or week. Further research with treatment seeking or GAD clinical population is needed and questions remain whether the current model is generalizable to clinical population.

Conceptual Similarities and Differences Between Models

The different models give insight into the potential processes occurring in the aetiology and maintenance of GAD and highlighting possible key features. However, while

there is some overlap in models to varying degrees between approaches, there is no agreement of which factors are unique or cardinal to GAD and each differ in particular aspects.

The models contrast in their different conceptualisations of the key processes in the disorder. Behar and colleagues (2009) have suggested the models can be grouped according to overall theoretical approach into cognitive, emotional or behavioural, and integrative models with each group sharing conceptual key drivers of the disorder but diverging in their specific elements. The cognitive models (IOU and MM) emphasise cognitions as the key feature driving the development and maintenance of GAD, with a lesser focus on emotions or behaviours in the disorder. Specifically, in the IOU model the cognitions relate to IOU and NPO whereas for the MM it is meta-worry, worry about worry. In contrast, other models focus more on emotions and behaviour as the drivers of the disorder as opposed to cognitions (EBM, ABM, and CAM) but also differ on the particular aspect of emotions. The EDM model places regulation of emotions as the key feature, whereas the ABM highlights the role of experiential avoidance of distressing internal experiences and CAM it is specifically a fear of sharp negative shifts in emotions. Finally, the AMW, a model of worry, integrates both cognitions and emotions and positions as important drivers of worry and GAD.

However, all models are unanimous that avoidance to internal experiences is at least one of the key processes in the maintenance and aetiology of GAD, but the models differ in the particular internal experience that is avoided and so the central fear underlying GAD. Specifically, the AMW focuses on the avoidance of aversive imagery, affect and somatic activation, the IOU model on aversive imagery, arousal and affect which accompanies a catastrophic misinterpretation of uncertainty, for the MM it is meta-worry, EDM aversive affective experiences, ABM any distressing internal experiences, and in the CAM it is negative emotional contrasts. Clearly, there is some overlap in these with some agreement in the AMW, IOU, EDM and ABM of the avoidance of negative affect experiences in GAD

however for some of these models, their avoided features also include other internal experiences in addition to affect such as somatic activation and distressing imagery in AMW or cognitions or physical sensations in ABM. In contrast, the MM and CAM identify unique specific avoided internal experiences amongst GAD models, namely meta-worry and negative emotional contrasts respectively. Notably amongst these models, the CAM unique as it views worry as maintaining negative emotional state, as opposed to avoiding negative emotions which features in most other models despite evidence to the contradicting this perceived role.

Additionally, while all the models highlight the role of worry as a method of avoidance, its centrality to the disorder varies between models. For some it is placed as the sole avoidant processes that maintains GAD or worry (AMW and IOU) and in others it is but one type of wider experiential avoidance as opposed to solely cognitive avoidance (MM, EDM, ABM, and CAM).

Summary of Psychological Models

Different research groups have proposed several theoretical conceptualisations of GAD. There is some agreement on the processes that maintain the disorder between some of the models, however there is no consensus on what constitutes GAD or which elements are unique or even central to GAD. All models propose that a key process within GAD is a reactivity to specific internal experiences, but the particular internal experience varies between models. Also, while included in all models, the centrality of worry to each varies substantially despite currently being a purported diagnosis of pathological worry. Some models place worry as a central tenet as a form of cognitive avoidance but with different triggers and focuses of the avoidance whereas for other models worry plays a less central role with different elements viewed as key to GAD.

The evidence for each of these models is not equivalent, with stronger evidence base for some of the older, more established models and their component's role in GAD and limited in the newer approaches. Some of the research also measures the association of model components with worry rather than all GAD features and much of the evidence base for each remains within the same research groups which developed the models. The newer models are particularly limited by studies with small samples or those using only experimental designs with university student samples.

Is Worry the Cardinal Feature of GAD?

Despite being a disorder of generalised anxiety, the diagnostic criteria in both classification systems place excessive worry as the key feature of GAD and worry features in all psychological models with varying centrality. For some, the disorder has become synonymous with pathological worry and the increasing importance of worry in the diagnostic criteria have led some to argue that the disorder is better conceptualised as "Generalised Worry Disorder" (Andrews et al., 2010). These shifts seem to occur despite the presence of the associated symptoms which themselves have also been revised according to research to those specific to GAD anxiety. With the elevation of excessive worry to perhaps the cardinal feature, it poses the question whether there is a quality to the worry in GAD that is unique to the disorder and can differentiate it from that in other disorders.

Excessive Worry

While pathological or excessive worry is synonymous with GAD to some, research has contradicted this and the perception it is unique to GAD. While the focus or content of the worry differs according to the specific disorder, similar levels of worry have been found in other anxiety disorders including social anxiety disorder (e.g., Olatunji et al., 2010a; Starcevic et al., 2007), health anxiety (Noyes, 1999) and panic disorder (e.g., Gladstone et

al., 2005; Mohlman et al., 2004). Similar levels have also been found in depression (e.g., Kertz et al., 2012; Muris et al., 2005), obsessive-compulsive disorder (Gladstone et al., 2005; Olatunji et al., 2010a), bipolar affective disorder (Kertz et al., 2012), psychosis (e.g., Morrison & Wells, 2007; Startup et al., 2007, 2016), eating disorders (e.g., Sassaroli et al., 2005; Sternheim et al., 2012), and PTSD (Molina & Borkovec, 1994). Additionally, most pathological worriers do not meet criteria for GAD (Ruscio, 2002) and those who meet all criteria except the excessive requirement present with similar syndromes, albeit slightly milder presentations, to those who meet all criteria (Lee et al., 2009a; Ruscio et al., 2005).

However, such findings are not unanimous as pathological worriers have been found to worry for longer than normal worriers (Craske et al., 1989). Also, higher levels of worry have been found in GAD compared to depression, social anxiety disorder, panic disorder, specific phobias, and post-traumatic stress disorder (Becker et al., 2003; Chelminski & Zimmerman, 2003; Fresco et al., 2003; Gladstone et al., 2005; Hoyer et al., 2001) and the levels of worry are significantly higher in depression when comorbid with an anxiety disorder than “pure” depression (Chelminski & Zimmerman, 2003; Gladstone et al., 2005).

Yet, the excessive criterion also poses issues for objective recognition as the boundary between GAD and normal worry is too porous and subjective (Frances & Nardo, 2013) and individuals with GAD are more likely report that others consider their worry excessive than report it themselves making it harder to diagnose using this criterion (Shear, 2012). Many with GAD also view themselves as worriers and it being part of their personality so do not seek help (Bland et al., 1997).

Such findings cast doubt on the specificity of excessive worry to GAD, instead suggesting that it is perhaps more a common transdiagnostic feature of psychopathology. Yet, if worry is truly common in disorders, it raises the question of if there are any other qualities of GAD worry that can distinguish it from worry in other disorders and everyday worry.

Content of Worry

One possibility relates to the content or domains of GAD worry. Unsurprisingly, worry in GAD is associated with a greater range of worry topics than those with panic disorder and social phobia (Hirsch et al., 2013; Hoyer et al., 2001). Studies also suggest that GAD worry encompasses more minor worries (Craske et al., 1989; Hoyer et al., 2001; Roemer et al., 1997) and domains (Hirsch et al., 2013; Roemer et al., 1997) than control groups. However, other research has found no difference in content between GAD and non-GAD worry (Borkovec et al., 1991; Ruscio et al., 2001) and it has been argued that any difference in worry content or domains may be an artefact of the excessive worry criteria in GAD (Olatunji et al., 2010b).

Appraisal of Worry

With many excessive worriers not meeting criteria for GAD (Ruscio, 2002), some have proposed that it is how someone worries and views their worry that matters. Such appraisals of worry are key to several models and the DSM diagnostic criteria of GAD. The appraisal of the uncontrollability of worry are highly intercorrelated with those that worry is excessive (Brown et al., 2001a; Hallion & Ruscio, 2013; Rutter & Brown, 2015). It has been suggested that the excessive criteria could encompass the uncontrollable criteria required by the DSM-5 (Andrews et al., 2010), however far more individuals with GAD view their worry as uncontrollable but not excessive (31.5%) than those who view their worry as excessive but still controllable (4.4%) (Beesdo-Baum et al., 2011). It has been suggested that the uncontrollability of worry explains significantly more of the variance of GAD severity than that explained by excessiveness of worry and therefore should instead be a core feature of GAD (Hallion & Ruscio, 2013).

GAD worriers have been found to view their worry as more uncontrollable and dangerous than non-patients and non-GAD high worriers (Craske et al., 1989; Hirsch et al.,

2013; Hoyer et al., 2001; Ruscio & Borkovec, 2004; Wells & Carter, 2001). Regression studies have found that such views also predict GAD symptoms and mediate the relationship between trait worrying and GAD symptoms (Penney et al., 2013).

However, when compared to other disorders, few studies look at appraisals of worry outside GAD and OCD. Despite similar levels of worry, some studies suggest individuals with GAD have more negative appraisals about uncontrollability or danger of worry than individuals with panic disorder (Hirsch et al., 2013; Wells & Carter, 2001) or social phobia (Hoyer et al., 2001; Wells & Carter, 2001). Similar levels of appraisals that worry is dangerous or uncontrollable have been found between GAD and depression (Cartwright-Hatton & Wells, 1997; Wells & Carter, 2001). Those who are currently depressed endorse this view more than those never depressed (Halvorsen et al., 2015). Beliefs that worry is dangerous and uncontrollable were also higher in individuals with depression (Barahmand, 2009; Sarisoy et al., 2014), bipolar disorder (Sarisoy et al., 2014) and OCD (Barahmand, 2009; Hermans et al., 2003; Myers & Wells, 2005) than controls. Such negative appraisals are also associated with the psychological distress in individuals with a range of chronic health conditions (Lenzo et al., 2019) and in psychosis where worry can relate to a lack of control over delusional thoughts (Morrison & Wells, 2007). Hypochondriasis also best predicted by worries about lack of control over thoughts about illness (Bouman & Meijer, 1999). It appears that these negative appraisals of worry and need to control thoughts may not be unique to GAD and are implicated in a range of disorders (Sun et al., 2017). Within the general population, self-report studies comparing non-GAD high worriers with GAD worriers found similar levels of excessive and uncontrollable worry suggesting these may be characteristic of high levels of worry (Ruscio, 2002).

In contrast, there are unanimous findings related to positive beliefs about worry which are endorsed by individuals with high levels of worry regardless of whether they have a GAD diagnosis (Davey et al., 1996; Ladouceur et al., 1998; Newman & Llera, 2011; Ruscio & Borkovec, 2004). Likewise, there was no difference in endorsement of positive beliefs about

worry in individuals with GAD, social anxiety disorder, depression, panic disorder, or in controls (Wells & Carter, 2001). It has been proposed that positive appraisals are shared by all that worry (Barahmand, 2009; Wells, 1995; Wells & Papageorgious, 1998). Ratings of positive beliefs were also unable to distinguish categories of GAD severity (Dugas et al., 2007).

Cross-Cultural Applicability of Worry

The conceptualisation of GAD as a "worry disorder" also potentially poses cross-cultural issues (Shear, 2012). As highlighted previously, worry is more typical of a western presentation of GAD with somatic presentations more prevalent in some other countries (e.g., Hoge et al., 2006; Ruscio, et al., 2017). In such cases the excessive criterion could discount those experience worry relating real life concerns which may not be considered excessive in context (Marques et al., 2011). However, some studies have found worry as the typical presentation in some non-western countries (e.g., Lee et al., 2009a).

Summary of the Specificity of Worry to GAD

This evidence suggests that excessive worry does not constitute GAD any more than it does a range of other psychiatric disorders and it is instead a transdiagnostic construct featured in psychopathology. In line with this view is the growing evidence that suggests worry is a dimensional construct (Kertz et al., 2014; Olatunji et al., 2010b; Ruscio et al., 2001), on a continuum with normal everyday worry and "pathological" on opposite ends in all people (Olatunji et al., 2010b; Ruscio et al., 2001). Some have suggested that GAD falls at the extreme end of this worry continuum with other anxiety disorders following with some uncertainty where depression lies (Olatunji et al., 2010b). While it seems that negative and positive appraisals of worry are potentially endorsed by all that worry, the paucity of research outside of GAD and OCD limits any conclusions.

It seems that GAD has been understood as a disorder of pathological worry despite a lack of evidence for this specificity. This overemphasis on worry, perhaps at the cost of other features of the disorder, arguably perpetuated the view that GAD is a residual disorder with no unique features (Starcevic et al., 2012) and perhaps erroneously equating worry with anxiety. The separation of worry and anxiety is also controversial, some argue that worry is an integral part of anxiety and reflective of the basic processes (O'Neill, 1985) and others distinguish worry as the separate cognitive process (Borkovec, 1985). Their assumed combination in GAD has led some to question whether GAD can ever be diagnosed in the absence of worry despite it not in theory required for a diagnosis under the ICD criteria (e.g., Starcevic et al., 2012). There also may be cross-cultural issues with the relevance of worry in the presentation of GAD outside western settings, where most of the current research is conducted, suggesting that a focus on worry may lead to some with the disorder not being recognised.

If worry is truly the cardinal feature of GAD, a unique quality to GAD worry needs to be identified to aid differentiation from worry in other disorders and everyday worry while accounting for different presentations of the disorder. As the current evidence stands, it seems that worry is not unique to GAD and prompts the question as to whether there are other unique aspects to the disorder.

Alternative Key Features in GAD

The revisions to the diagnostic criteria have increasingly positioned worry as the cardinal feature of GAD, despite it being only one element of the diagnostic criteria. The different conceptualisations of the disorder have implicated various transdiagnostic processes that may better explain presentations of GAD. Even within the diagnostic criteria the associated symptoms have been refined to those supposedly specific to the disorder but remain simply additional symptoms behind worry despite their purported uniqueness to GAD

anxiety. These features present possible alternative cardinal symptoms that may be unique to GAD, which if true then greater emphasis in the diagnostic criteria may aid the operationalisation of the disorder, or at least offer possible transdiagnostic processes that may better explain the variety of presentations associated with the disorder. Each of these potential features are explored below.

Apprehensive Expectation

Despite the prevailing view of worry being the cardinal symptom of GAD, the DSM criteria actually lists “apprehensive expectation” as the key symptom for GAD, defining this as excessive anxiety and worry. While sometimes used synonymously with worry, Rickels and Rynn (2001) propose that an emphasis on the overall severity of anxious symptomology to capture this apprehensive expectation may be a more appropriate key feature as opposed to a focus only on one element of it. Such a focus may help overcome the issue of recognition of GAD in groups where excessive worry is not part of the typical presentation, for example in individuals who experience dread without a specific focus of worry or those with somatic presentations more common to certain groups (Lewis-Fernández et al., 2011; Rickels & Rynn, 2001; Roy-Byrne & Wagner, 2004). However, there remains a lack of actual research into this proposal, therefore it remains theoretical and its potential utility and the overlap particularly with other anxiety disorders this may cause not explored.

Somatic Symptoms and Muscle Tension

The increasing emphasis on worry, particularly in diagnostic criteria, has overshadowed the role of somatic and autonomic arousal symptoms in the GAD presentation (Roth et al., 2008; Starcevic et al., 2012). This is in spite of strong evidence that somatic-based presentations of GAD are more common in certain groups such as older adults (Alwahhabi, 2003), primary care presentations (Davidson et al., 2010), those from

some non-Western cultures (Lewis-Fernández et al., 2011), or GAD presentations of non-specific dread (Rickels & Rynn, 2001). However, the somatic symptoms of GAD also have poor specificity and account for the large overlap in symptoms in the diagnostic criteria with depressive and other anxiety disorders with only muscle tension being the unique somatic symptom to GAD (Faravelli et al., 2012; Mennin et al., 2008; Rickels & Rynn, 2001), resulting in worry and muscle tension the only unique symptoms to the disorder.

In community studies, the only symptom able to distinguish those patients with GAD from those without was muscle tension (Faravelli et al., 2012), suggesting that a greater emphasis on muscle tension may be a key symptom in discriminating GAD from other disorders and healthy controls. Further support comes from studies that have also found differences between GAD and health controls in physiological measures of muscle tension (Hoehn-Saric et al., 1989), correlations uniquely relating muscle tension to worry and negatively to depression (Joormann & Stöber, 1999) and in twin studies where muscle tension was only unique DSM-IV GAD symptom in factor analyses (Kubarych et al., 2005). As a result, emphasising the role of muscle tension as a key feature, while also reducing emphasis on concentration difficulties, has been proposed as a way to clarify the blurred boundary between depression and GAD (Mennin et al., 2008). Based on such findings, some have proposed that GAD may be better conceptualised as a tension disorder with a greater focus on the mental and somatic symptoms of tension as opposed to just worry (Stein, 2005). However, the causal relationship between muscle tension and anxiety remains poorly understood (Pluess et al., 2009) so further research into this possibility is required. Additionally, there have been suggestions that increasing the focus on somatic symptoms could lead to a greater overlap with somatic distress disorders (Shear, 2012), again highlighting the need for further research.

Avoidance

Covert avoidance, such as cognitive or experiential avoidance, involves behaviours including thought suppression or worry itself to avoid distressing emotional or somatic experiences. Different covert behaviours feature heavily in the pathology and maintenance of GAD in the various psychological conceptualisations of the disorder. Research has supported the role of such avoidance in GAD presentations (e.g., Portman et al., 2011). Studies have found covert behaviours correlate and make a greater contribution to GAD symptoms and emotional processes in comparison to overt behaviours (Marcotte-Beaumier et al., 2021), highlighting their role in the maintenance of GAD symptoms. However, covert behavioural features are believed to be a transdiagnostic phenomenon observed in a range of psychopathology (e.g., Barlow et al., 2004; Chawla & Ostafin, 2007). Additionally, such behaviours may also be challenging to operationalise.

While less featured in models, overt avoidance has been implicated in the presentation of the disorder and there appears to be growing interest in understanding their role in GAD symptomatology and pathology. The inclusion of overt behavioural features including checking, reassurance-seeking, procrastination, and avoidance of potentially negative events in the DSM-5 criteria was recommended during its development by some (e.g., Andrews et al., 2010), however these were not included in the final version. Some have argued that compared to other anxiety disorders, the presentation of GAD is less associated with motoric avoidance and instead relates more with covert behaviours (Beesdo-Baum et al., 2012), however studies have found associations between increased use of both types of avoidance and increased GAD symptoms albeit a stronger correlation related to covert strategies (Marcotte-Beaumier et al., 2021).

Studies have demonstrated these overt behaviours occurring in GAD to a greater extent than in controls (e.g., Beesdo-Baum et al., 2012; Coleman et al., 2011; Mahoney et al., 2016). But some argue that there is a lack of evidence for the specificity of such behaviours (Starcevic et al., 2012) with these behaviours again occurring frequently across

disorders, for example in depression (e.g., Ferster, 1973; Ottenbreit & Dobson, 2004), OCD (e.g., Foa et al., 2005), and other anxiety disorders (e.g., Hoffman & Hay, 2018). Also, as GAD is frequently comorbid these disorders, these behaviours cannot be conclusively attributed to GAD and therefore their proposed addition to the criteria has questionable validity and utility (Starcevic et al., 2012). However, there is evidence to suggest that some particular overt behaviours, including making additional plans "just in case" or delaying making decisions, demonstrate some specificity and sensitivity to GAD in comparison to depression, social anxiety disorder and panic disorder (Mahoney et al., 2016, 2018).

Overall, evidence therefore seems mixed as to whether such behavioural avoidance covert or overt aid understanding of the presentation due to their transdiagnostic nature. Associations with GAD symptoms and covert avoidance appear to be stronger and such covert behaviours feature heavily in psychological models. However, there also appears to be some initial evidence that suggests that perhaps focus on particular overt behaviours which have demonstrated specificity to GAD symptoms may aid understanding of presentations within the disorder. Clearly, further research is required into the role of both covert and overt behavioural features in the disorder.

Intolerance of Uncertainty

IOU has been proposed by some as a key cognitive process in GAD pathology and suggest it relates to worry as individuals attempt to gain control over this uncertainty through the use of worry (Dugas et al., 2004). Initial research had suggested some specificity of IOU to GAD with evidence in favour of this specificity coming from studies which have found individuals with GAD having higher levels of IOU than those with other anxiety disorders (Ladouceur et al., 1999), IOU correlates positively with worry (Dugas et al., 2004), reductions in IOU precede reductions in worry (Bomyea et al., 2015; Dugas & Ladouceur, 2000) and increases in IOU precede increases in worry (Ladouceur et al., 2000a) and ratings of IOU

can distinguish different levels of GAD severity (Dugas et al., 2007). However since, an increasing body of evidence suggests that IOU is better understood as a transdiagnostic construct presenting across range of disorders. In the initial paper, Dugas and colleagues (2004) found no significant differences in correlations between IOU and either worry or depression despite concluding that there was a clinically meaningful difference due to the effect size. Research has implicated IOU in depression (Gentes & Ruscio, 2011; Mahoney & McEvoy, 2012; McEvoy & Mahoney, 2012; Yook et al., 2010;), other anxiety disorders (Carleton et al., 2012; Mahoney & McEvoy, 2012; McEvoy & Mahoney, 2012), and OCD (Gentes & Ruscio, 2011; Mahoney & McEvoy, 2012). Some have proposed that IOU instead relates to a general correlate of disorders characterised by negative affect in which individuals engage in repetitive negative thoughts to control feelings of uncertainty and anxiety about the future (Gentes & Ruscio, 2011). It therefore seems that while the cognitive process of IOU may feature in GAD presentations, it also is implicated across a range of mood and anxiety disorders, and better understood as a transdiagnostic concept as opposed to being unique to GAD.

Negative Problem Orientation

Negative problem orientation (NPO) is a psychological construct which relates to an individual's belief in their inability to solve problems and pessimism about the outcome. It was initially proposed to be one of the key processes occurring in GAD according to the IOU model (Dugas et al., 1998). Research has shown NPO to have strong associations with both worry and GAD somatic symptoms (Dugas et al., 2007), however NPO has a stronger correlation with IOU (Clarke et al., 2017). Also, while NPO has been shown to have a greater specificity to worry than to depression, this was only after controlling for personality variables (neuroticism, pessimism, and mastery) which were themselves more strongly associated with NPO (Robinchaud & Dugas, 2005). NPO is also associated with both depression and social anxiety (D'Zurilla et al., 1998; Fergus et al., 2015) and has comparable relationship

with symptoms of GAD to those of OCD (Fergus & Wu, 2010). Thus, it seems that NPO is a cognitive process implicated in a range of disorders and perhaps more so a facet of IOU, and therefore a transdiagnostic construct than a feature unique to GAD presentations.

Emotional Dysregulation

While emotional regulation deficits are implicated in a range of disorders (Sloan et al., 2017), it has been suggested that those with GAD experience a heightened intensity and fear particularly of negative emotions which lead them to use unhelpful coping strategies (Mennin et al., 2002). This has been supported by evidence that suggests that those with GAD experience specifically negative emotions more intensely and employ more unhelpful emotional coping strategies than healthy controls (e.g., Mennin et al., 2005; Salters-Pedneault et al., 2006) and those with depression or social anxiety disorder (Mennin et al., 2007). However, this has been challenged by a meta-analysis which found that internalising symptoms are strongly correlated with the maladaptive emotional regulation strategies of rumination, reappraisal and avoidance (Aldao et al., 2010), suggesting emotion-related deficits and maladaptive strategies were more a feature of internalising psychopathology. Research also found no differences in the fear of negative emotions between individuals with GAD, social anxiety or depression (Mennin et al., 2007). Further research is therefore required as the evidence is currently limited, but again it seems that this is again a transdiagnostic process occurring in GAD.

Fear of Negative Emotional Contrast

The Contrast Avoidance model (Newman & Llera, 2011) proposes that the central tenet of GAD is a fear of a negative emotional shift which is avoided through worry which maintains a negative state. Worry has been found to increase and sustain negative emotional states in those with and without GAD (Llera & Newman, 2010, 2014) but

individuals with GAD more likely to report discomfort and sensitivity to the negative emotional contrast than controls (Llera & Newman, 2014). Individuals with GAD are also more likely to report preferring to be in a negative mood over feeling positive (Llera & Newman, 2017). Studies have also found that individuals with GAD experience anxiety and depression as more distressing than those with social anxiety disorder (e.g., Roemer et al., 2005). However, this avoidance of negative emotional contrasts again may not be unique to GAD with studies suggesting it may also be a key process in depression (Crouch et al., 2017; Jamil & Llera, 2021; Kim & Newman, 2019). Studies have demonstrated that rumination can maintain a depressive state (Kuehner et al., 2009) which perhaps functions similar to the proposed role of worry in this model and some research has found similar reductions in emotional contrast in experimental tasks for both rumination and worry (Jamil & Llera, 2021). Yet with few studies have focused on this process limiting the conclusions, but current evidence suggests that the fear of negative emotional shift may be a transdiagnostic feature as opposed to unique to a GAD presentation.

Summary Alternative Key Features in GAD

Research suggests that many elements of the diagnostic criteria and psychological models are not unique to GAD and are instead better understood as transdiagnostic constructs featured across many disorders, with particular overlap with other internalising disorders. The current evidence seems to suggest that the only unique symptom in GAD's current form that can distinguish GAD from other anxiety and depressive disorders is muscle tension, suggesting that for discriminative purposes GAD may be better conceptualised as a tension disorder. However, an increased focus on these elements of tension risk increasing the overlap with somatization disorders. Previous authors have highlighted the need for further research particularly into the role of somatic symptoms in GAD pathology (Starcevic & Portman, 2013). Others have suggested a broader focus on anxious symptomatology in apprehensive expectation to account for different presentations of GAD may provide a better

conceptualisation as opposed to the current focus on worry, yet research is lacking into this option. Such discussions however highlight the role of features other than worry in the presentation of the disorder, something highlighted by some who argue that even the name GAD is misleading as it only focuses on the cognitive element of the disorder (Allgulander, 2006). The evidence presented here suggests that an alternative name, perhaps emphasising to tension, may highlight the specific symptoms unique to the disorder and aid recognition, but further research is required into this and other options which may better capture the range of presentations associated with the disorder.

Many of the other key processes implicated in GAD in the psychological models are transdiagnostic constructs, featuring particularly in depressive and other anxiety disorders. However, there remains a distinct lack of research into these processes and how they may relate and aid understanding of presentations of GAD. Some initial research highlights potential areas for further research such as particular covert and overt behavioural features.

Alternative Conceptualisations of GAD

Due to the lack of evidence for a cardinal feature, heterogeneity of presentations of and overlapping diagnostic criteria with other disorders, some argue that GAD may be a redundant diagnosis that is better understood in another format or in need of reconceptualization. As such there have been proposals of alternative ways to better conceptualise GAD, within the disorder or combined with other disorders. In addition to these, more broadly, there have been proposed alternatives to the current classification systems method to psychopathology which take different approaches to understanding the symptoms associated with GAD which also provide different conceptualisations of the disorder.

Addition of Subtypes To GAD

Worry has a central role in the current form of GAD; however, it does not play a defining role in all presentations (Portman et al., 2011). As previously discussed, certain groups are less likely to express fear and anxiety in cognitive terms and instead present with predominantly somatic presentations for example in primary care (Roy-Byrne & Wagner, 2004) or in some cultures (Lewis-Fernández et al., 2011). To capture this diversity in presentation, some have proposed the addition of subtypes to the diagnosis. Roth and colleagues (2008) suggest the addition of somatic subtype of "Generalized Tension Disorder" for those without worry with traditional GAD remaining the main presentation. Murphy and Leighton (2009) suggest classification of two types of general anxiety, one dominated by excessive worry and stress being the traditional GAD and another focused on autonomic fear. There is currently little research into these subtypes beyond proposed conceptualisations, but the recognition of subtypes in GAD would be akin to depression which also has a heterogeneous presentation and different subtypes are widely accepted (e.g., Goldberg, 2011; Lamers et al., 2016).

Combined with Depression

While historically associated with other anxiety disorders, the efforts to reduce this comorbidity with anxiety disorders through refinement of the associated somatic symptoms to those with specificity to GAD anxiety appear to have had some success, however these revisions have also increased the diagnostic overlap with depression resulting in a diagnosis that now appears more closely related to depression. Perspectives differ on how to understand this close relationship, some argue that the disorders should remain as separate entities that share similar features (e.g., Sunderland et al., 2010) whereas others suggest that they are better conceptualised as one with varying views on how this should occur. Such proposals have included GAD being better understood as a prodrome, residual, or

severity marker of depression (e.g., Brown et al., 1998; Cloninger et al., 1990), both subsumed under “Distress Disorders” (e.g., Watson, 2005; Watson et al., 2008), GAD be recategorized as a mood disorder (Vollebergh et al., 2001) or GAD becoming a subtype of depression (Kendler et al., 1996; Mennin et al., 2008). Arguments for these proposals are based on the similarity and differences between GAD and depression on many levels beyond diagnostic features.

While GAD and depression have similarities on a phenotypic level (e.g., Watson, 2005; Watson et al., 2008), there also appears to be some shared genetic vulnerability (e.g., Hettema et al., 2006; Kendler et al., 2007; Watson, 2005; Watson et al., 2008) and both have a reciprocal predictive temporal relationship over a three-year period (Grant et al., 2009). Structural modelling studies have also supported this close relationship, linking GAD more closely to an internalising anxious-misery dimension shared with depression than to internalising fear dimension which relates more to other anxiety disorders (e.g., Krueger, 1999; Krueger et al., 1998; Vollebergh et al., 2001) and with both loading onto the underlying construct of negative affectivity or general distress (e.g., Brown et al., 1998; Slade & Watson, 2006). If both disorders loaded onto such higher-order factors it could explain their shared features (Zbozinek et al., 2012). The symptoms of GAD and depression, mediated by worry and rumination respectively, are also found to be related to neuroticism (Merino et al., 2016).

However other studies have challenged the view that they are similar. Diagnoses of GAD and depression have been found to differ in environmental (e.g., Kendler, 1996; Kessler, 2000; Roy et al., 1995) and familial risk factors (e.g., Kessler et al., 2008; Moffitt et al., 2007b), temporal course (Kessler, 2000; Wittchen et al., 2000), and temperament (Brown, 2007) suggesting partly different aetiological pathways. Longitudinal symptom trajectories have associated GAD more with other anxiety rather than depressive disorders (Beesdo et al., 2010) and shown that the disorders differ in inter-temporal stability of symptoms due to disorder-specific variance rather than shared underlying factors

(Fergusson et al., 2006). Likewise, factor analyses have also indicated that DSM-IV GAD and depression are closely related but have distinct latent structures, clinical manifestations, and patterns of comorbidity best represented by a bifactor model with a general factor underlying criteria for both disorders (Blanco et al., 2014). It has also been suggested that grouping GAD and depression by the shared cross-sectional features and comorbidity patterns loses the differences longitudinally and in symptom trajectories (Beesdo et al., 2010). It seems that the relationship between GAD, depression and higher-order internalizing dimension may just be representative of a wider relationship between internalizing factors and all mood and anxiety disorders (e.g., Krueger, 1999; Krueger & Markon, 2006; McGlinchey & Zimmerman, 2007). All have close ties to neuroticism, the trait disposition to experience negative affect, which appears to be the core to all internalising disorders (Griffith et al., 2010; Hettema et al., 2006).

Another possible explanation for their close relationship may be an artefactual comorbidity due to the overlapping criteria rather than true relationship. While GAD criteria appear to have poor specificity in general, there is a particular overlap with depression due to the shared symptoms of fatigue, poor concentration, psychomotor agitation, and difficulty sleeping (Mennin et al., 2008; Sunderland et al., 2010; Zbozinek et al., 2012). In studies of community samples, these symptoms were found to be more prevalent in those diagnosed with depression than those with GAD (Faravelli et al., 2012) and the DSM-IV criteria was unable to reliably differentiate individuals with GAD from those with depression or dysthymia (Brown et al., 2001a). This similarity in cross-sectional features has been shown to differ longitudinally (Beesdo et al., 2010).

It is uncertain where this relationship is merely an artefact of inadequately constructed diagnostic criteria with poor boundaries between two distinct entities or that they should remain distinct clinical entities with shared features or whether it is more representative of a shared psychopathology or associated with shared higher-order factors. The non-specific findings suggest that while there are links between GAD and depression

particularly in presentation and some shared genetics, there also appear to be areas of difference longitudinally. However, the ongoing lack of clear separation between GAD and depression has undermined the utility of the categorical nosologies (Curtiss & Klemanski, 2016). Also, the particular focus on the GAD-depression association in the literature has also been questioned as there may be similar relationships between GAD and other anxiety disorders, particularly panic disorder (Hettema, 2008; Grant et al., 2009), with this just perhaps representative of wider relationships among mood and anxiety disorders rather than specific to these disorders.

GAD as a Personality Trait

Some have proposed that the chronic nature of generalised anxiety instead represents trait anxiety or an anxious temperament which has become disordered at the extreme end of the spectrum or onto which state anxiety symptoms are added to at times of stress (Akiskal, 1998; Rapee, 1991). This perspective would account for the similarity in content between GAD and everyday worry (Borkovec et al., 1991; Ruscio et al., 2001) and the increasing evidence for lifelong, chronic nature of the disorder (Keller, 2002). More so, many with GAD view worry as being part of their personality and state they have always been a worrier and so are a low treatment-seeking population (Bland et al., 1997). However, if GAD is equivalent to a stable disorder of high trait anxiety, it would not explain the heterotypic continuity associated with the disorder. Likewise, GAD is rarely seen in childhood, making it unlikely to be a just personality trait or disorder or anxious temperament (Wittchen & Hoyer, 2001).

Similarly, some have suggested that high neuroticism and GAD seem to refer to similar constructs (Hettema et al., 2004) and that high neuroticism is very similar to chronic worry (e.g., Kotov et al., 2007; Watson et al., 2005). Twin data suggests their underlying genetic risk factors are nearly indistinguishable, but they differ in environmental risk factors

(Hettema et al., 2004). There also appears to be etiological interrelatedness on dimensional measures of trait anxiety, pathological worry, fear of uncertainty, or neuroticism (Hettema et al., 2004). Yet, this close relationship is not unique to GAD, for example with neuroticism closely related to all internalising disorders (e.g., Griffith et al., 2010; Hettema et al., 2006).

Two possibilities have been suggested for GAD in relation to personality traits. Either with GAD remaining an Axis I syndrome that develops from same liability as neuroticism but different disposing life events or that it is better characterised as a generalized anxious temperament or disorder under Axis II (Akiskal, 1998; Hettema et al., 2004). Currently most symptoms of GAD are intrapersonal (e.g., worry, anxiety, muscle tension) and there has been a lack of consideration of personality dimensions in the disorder (Newman & Erickson, 2010) or the boundary between GAD and personality traits (Crocq, 2017). The lack of research into such factors limits the understanding of their role in the conceptualisation of GAD, whether personality elements are merely risk factors for generalized anxiety symptoms, a prerequisite for developing the disorder or the disorder better conceptualised within a personality dimension.

GAD Within the Research Domain Criteria

The Research Domain Criteria (RDoC, Insel et al., 2010) set out to be an alternative to the traditional nosological approaches to classifying mental health disorders by adopting a dimensional approach to psychopathology. RDoC aims to enhance validation of mental health disorder classification through incorporation of research into the neurobiological understanding of disorders and identifying etiological factors and views mental health disorders as brain disorders resulting from issues of brain circuits (Cuthbert & Insel, 2010, 2013). Within RDoC disorders are conceptualised with constructs from five basic domains of functioning: negative valence systems, positive valence systems, cognitive systems, social processes and arousal and regulatory systems.

Of relevance to the understanding of GAD within this framework would be the "Negative Valence System" which contain several constructs applicable to GAD, however anxious apprehension would be a more valid study in RDoC than GAD itself (Crocq, 2017). Firstly, "Potential threat (anxiety)" in which the brain system initiates pattern of neural responses such as "Enhanced risk assessment (Vigilance)" to remain on edge for an ambiguous but low, uncertain probability harm may occur (Watson et al., 2017) and "Sustained threat" which focuses on aversive emotional state prolonged for weeks or months and is adapted to escape or avoid an actual or anticipated threat (Patriquin & Mathew, 2017). The behaviour of worry is an element in RDoC under "Negative Valence System", but under this system it is part of wider transdiagnostic processes that cut across traditional diagnostic categories and so not viewed as unique to one disorder (Kozak & Cuthbert, 2016) and the overlap with depression could be understood from both disorders having constructs within this negative valence system. In RDoC, comorbidity is not an issue as it focuses on complex overlapping multidimensionality of mental health disorders (Insel et al., 2010). While still a work in progress, the researchers aim to identify both transdiagnostic and disorder-specific mechanisms which may in future help determine a more valid understanding of GAD based in neurobiology.

GAD Within Network Theory of Psychopathology

An alternative approach to understanding psychopathology is network analysis which views disorders as resulting from interplay between a complex network of symptoms which remain stable over time and correlate and cause each other rather than caused by a single latent disorder (Borsboom & Cramer, 2013). The connections between symptoms can lead to bridge symptoms which connect disorders through shared symptoms such as sleep problems in GAD and depression (Cramer et al., 2010). Proponents for this approach argue that it provides a better understanding to the high rates of comorbidity and heterogeneity in presentations within traditional approaches to psychopathology (Castro et al., 2019).

Network analysis studies allow for the exploration of the centrality of certain symptoms to other symptoms within a disorder and identification of “bridge” symptoms that connect comorbid disorders which may help understand nosology of GAD particularly with its close relationship with depression. Such studies have found symptoms of depression and GAD form one cluster within a network (e.g., Bekhuis et al., 2016; Cramer et al., 2010) and share close interconnectedness in their symptoms (Beard et al., 2016; Price et al., 2019), questioning the validity the current distinction between the disorders. However, while Price and colleagues (2019) found that any symptoms of depression or GAD were of comparable distance from any another symptom, Beard et al. (2016) found that the symptoms of GAD and depression more related to symptoms within their own disorder, with two worry symptoms measured among the most strongly connected within GAD although this strong connection may relate to overlapping measuring of the same constructs. Some of the strongest cross-diagnostic “bridge” symptoms identified in one study were between chronic worry and depressed mood and depressed mood and inability to relax (Price et al., 2019). Particularly focused on the somatic symptoms in the disorders, studies have found unique clusters of somatic symptoms for depression and GAD (Bekhuis et al., 2016; Boschloo et al., 2016) but in one study that these somatic symptoms were separate to both GAD and depression domains in network, suggesting not part of either disorder, however this study crucially did not include muscle tension in their analysis (Bekhuis et al., 2016).

Crucially for the nosology of GAD, when exploring the centrality of symptoms in GAD and depression, in one study the most potent drivers of symptomology were found to be positive mood, hopelessness, anger, and irritability, and crucially not the supposed cardinal symptoms of either disorder with worry interestingly being one of the least influential nodes (Fisher et al., 2017). The authors also highlighted the key role of anger in symptomology in these disorders despite not considered core in criteria in either which has also been evidenced in other studies and may be a feature of anxiety and mood disorders (e.g., Deschênes et al., 2012; Fava et al., 2010).

Such studies raise concerns for the continued emphasis of worry in GAD and highlight the close relationship with depression symptoms. However, there are very few studies into GAD alone and few focused on the GAD-depression relationship with limited studies beyond this, therefore more studies focused on these areas and particularly GAD's interconnectedness with other anxiety disorders are needed to understand this more clearly.

GAD and the P Factor

Another approach to understanding mental health disorders comes from bifactor modelling and the p factor (Caspi et al., 2014). This proposes that there is a transdiagnostic higher-order dimension, a latent general psychopathology factor called p factor, that underlies all psychopathology (Kotov et al., 2017; Krueger et al., 2018). In addition to this factor, there are two specific factors of externalising and internalizing that are correlated to one another but relate to different groups of disorders which share more variance, with internalising dimension consisting of mood and anxiety disorders and the externalising dimension including disorders such as substance misuse, anti-social, oppositional defiant and hyperactive-impulsive disorders (Caspi et al., 2014).

In this framework, GAD would be encompassed under the internalising dimension, having its own specific variance but also sharing a lot of variance with other internalising disorders, in addition to that shared by all disorders under the p factor. While influenced by p factor, perhaps more clinically useful for GAD would be considering the disorder within the internalising dimension indicating a shared liability to experience mood and anxiety disorders as well as some overlap in presentation. As discussed earlier, these disorders are frequently comorbid, share many features and longitudinally heterogenous continuity within this group is the norm. As such, one could argue for diagnosing solely by an internalising factor to capture these factors as opposed to a specific diagnosis or multiple diagnoses (Caspi &

Moffitt, 2018) or at least consideration of this may increase awareness of the close relationship GAD shares with other disorders in this dimension and so likely in presentation.

Summary of Alternative Conceptualisations of GAD

GAD appears has close relationships with depression and high trait anxiety, sharing genetic risk factors and similar features with both constructs but also with areas of difference. There again seem to be no specific findings to suggest GAD may be better conceptualised in a different format and the close ties to depression and personality factors may also represent the wider inter-relatedness between mood and anxiety disorders and their core relationship with neuroticism. However, there is limited research into the personality elements that may play a key role in GAD.

The alternative approaches to understanding psychopathology provide some research which may help better understand GAD. The RDoC provides some evidence for the underlying neurobiology under some of the processes relevant to GAD which may aid validity of the features, network analysis provides understanding of the centrality of features in a disorder, questioning the role of worry, and an alternative to understanding comorbid symptoms, and p factor provides some suggestions relevant to the close relationship with other disorders under the internalising dimension. However, the research from these different approaches is limited currently but potentially providing key evidence to understanding the nosology of GAD in the future.

The Implications for Assessment and Psychological Treatment of GAD

GAD is under recognised and under treated in the general population (Bebbington et al., 2000). The lack of clarity about what constitutes the disorder, the absence of unique features, an arguably incorrect overemphasis on worry, and frequent overlapping diagnostic

criteria and comorbid presentation likely play a role in some of the difficulties in the recognition and treatment of GAD.

Assessment of GAD

Recognition is key to proper treatment and management (Culpepper, 2002). While thought to be the most common anxiety disorder in primary care (Wittchen, 2002), studies have estimated that recognition rates for GAD in this setting are poor, ranging from 34.4% to 72.5% (Wittchen et al., 2002). This may in part be due to the increasing emphasis on the role of worry and lessening of somatic symptoms in the diagnostic criteria which is at odds with the more somatic-type GAD presentations in this population with many instead referred for physical health investigations (Roy-Byrne & Wagner, 2004). In one study only 13% of GAD presentations to primary care reported anxiety as their main complaint with the majority instead reporting issues with pain, insomnia, and other somatic symptoms (Wittchen et al., 2002). In addition, recognition of GAD is difficult due to the fluctuating severity of symptoms and comorbid presentations individuals experience making it difficult to recognise a distinct entity (Ballenger et al., 2001; Culpepper, 2002; Lydiard, 2000). Individuals with pure GAD are also far less likely to seek treatment than those with comorbid GAD (e.g., Bland et al., 1997; Kessler et al., 2001; Mojtabai et al., 2002; Newman et al., 2010). They are also unlikely to seek help with worry, viewing their worry positively or as part of their personality as a “worrier” (Bland et al., 1997) and unaware that their somatic symptoms are part of anxiety (Wittchen, 2002).

Psychological Treatment of GAD

The lack of interest in GAD until recent years and changing diagnostic criteria have limited the research into psychological treatments for GAD, leaving the efficacy of treatments lagging far behind that of mood and other anxiety disorders (Newman et al., 2013). It has

been argued that one of the reasons GAD remains difficult to treat is due to the continuing uncertainty of the causes and factors that maintain the disorder (Newman et al., 2011).

Cognitive behavioural therapy (CBT) has been established as the most empirically supported psychological therapy for GAD (e.g., Carpenter et al., 2018; Cuijpers et al., 2014). However, a significant portion of individuals, some estimates suggesting around a third (Durham et al., 2003), show little to no benefit from psychological treatment and remain symptomatic (Springer et al., 2018). Only around 50% individuals achieve a high level of functioning following therapy (Erickson & Newman, 2005) and review of meta-analyses found only half respond to treatment (Hofmann et al., 2012). The long-term benefits of CBT are also questionable with an RCT finding no evidence that CBT influenced the course and likelihood of recovery over an 8-14 year follow up period with those experiencing the most severe symptoms or levels of disability showing no substantial improvement (Durham et al., 2003). Psychiatric treatment, including psychotherapy, was also found not associated with time to full or partial recovery over two years in primary care (Rodriguez et al., 2006), although the authors of this study suggest this result is due to a treatment-biasing effect.

However due to the scarcity of pure GAD, the condition is not treated in isolation. When considering psychological approaches, the comorbid nature of GAD needs to be accounted for (Stein et al., 2017) which does not explicitly occur in disorder-specific CBT for GAD but, given the transdiagnostic features of some CBT approaches, may be occurring implicitly. Research into the impact of comorbidity on therapy outcomes for GAD provides mixed findings. Some studies found worse outcomes (e.g., Bruce et al., 2005; Rodriguez et al., 2006) but others have found more treatment gains in both GAD and comorbid disorder symptomatology in both individual (Carl et al., 2020; Newman et al., 2010; Provencher et al., 2006) and group CBT (Wetherell et al., 2005). Few studies look at the impact longer-term, but in one study gains in depressive symptomology were not maintained at 2-year follow up (Newman et al., 2010) and in another CBT for GAD was found to reduce comorbid diagnoses at 1-year follow up although the study excluded those with comorbid depression

or panic disorder and only focused on dysthymia, social and simple phobia (Borkovec et al., 1995), suggesting some generalization to other disorders. However, there remains a lack of studies in general and particularly in the longer-term.

While not occurring within the course of treatment, there is some evidence that suggests that psychological and pharmacological interventions can prevent onset of future comorbid disorders, for example in randomised control trials interventions for depression were found to reduce anxiety symptoms and those for GAD reduced depressive symptoms (Gorman, 2002, Leichsenring et al., 2009, Newman et al., 2011, Rivas-Vazquez, 2001). Targeting particularly depressive symptoms has been suggested to play a prominent role in the process of change in both depression and GAD psychological and pharmacological interventions and result in better outcomes with changes in depressive symptoms temporally preceding changes in GAD symptoms to a greater extent than vice versa and changes in depressive symptoms better predicting change in anxiety symptoms then vice versa (Aderka et al., 2015). Similar results were also found for counselling of college students with changes in depression symptoms mediating changes in generalized anxiety symptoms using GAD measures that focused on physiological and somatic symptoms (Niileksela et al., 2020). Both suggest that it is perhaps best to target symptoms of depression than GAD, which remains against the current guidance to treatment the primary disorder or more severe disorder first (National Institute for Health and Care Excellence [NICE], 2011). Comorbid depression has also been found to respond better to CBT than applied relaxation, another recommended CBT approach in the treatment of GAD, with the authors suggesting this is due to the focus on worry in CBT for GAD generalising to rumination with both being forms of repetitive negative thinking (Newman et al., 2019a).

With comorbidity being the norm in GAD and perhaps the wider relationship among internalising disorders, one approach to therapy could be to explicitly target the common transdiagnostic factors underlying the frequently comorbid disorders through Transdiagnostic CBT. Transdiagnostic CBT has demonstrated efficacy (e.g., Farchione et al., 2012; Newby

et al., 2015; Norton, 2012; Norton & Barrera, 2012; Titov et al., 2010). Particularly relevant to GAD, with its frequent comorbid with mood and anxiety disorders, it that is it associated with significant reductions in both depressive and anxiety symptoms and diagnoses regardless of primary or secondary diagnosis (Norton & Paulus, 2017).

However, there remains a lack of research on depression and GAD temporal relationship during course of empirically supported therapy. Another approach as highlighted by Curtiss and Klemanski (2016) is the need for application of techniques as growth mixture modelling to longitudinal data to aid identification of different subgroups in the symptom trajectories of GAD and depression in response to therapy to identify those who may benefit most from therapy. Such research is important as disorder-specific CBT for GAD is the recommended psychological approach to treatment in the IAPT services (NICE, 2011). This poses a challenge for GAD in IAPT as they are associated with comorbidity and heterogeneity in presentation (Rickels & Rynn, 2001) which are not explicitly accounted for by the worry-focused CBT approaches implemented within IAPT. Research in these areas could identify the differential treatment responses of different symptom profiles in GAD.

Summary of the Approaches to Assessment and Psychological Treatment of GAD

GAD remains poorly recognised and treated. Issues in the conceptualisation in GAD perhaps play a role in the issues with clinicians finding it hard to recognise pure GAD as well as individuals themselves recognising their difficulty as an anxiety disorder or even viewing it as a problem. It seems particularly in primary care, where GAD is thought to be most common, there is a clear disparity between the increased emphasis on the cognitive symptoms of worry within diagnostic criteria and the more typical somatic GAD presentation in this setting which may make it more difficult to recognise and therefore many individuals do not receive the correct treatment.

However, even when receiving treatment, the vast majority of individuals do not improve and, in the few studies available, it seems there are poor outcomes in the longer-term for the disorder-specific CBT. CBT for GAD may have some generalisability to comorbid depression but findings into the impact of comorbidity on outcomes appear equivocal. There are suggestions that a focus on the depression symptoms could potentially improve outcomes as studies have shown the changes on the symptom level depression changes mediate those of generalised anxiety. However, again findings are limited by the lack of research into overall outcomes as well as identifying which presentations benefit from treatments. Overall, it seems GAD hard to detect and difficult to treat successfully. Clarifying what constitutes GAD may aid detection and understanding of who may benefit from therapy.

Conclusion

In its current form, GAD remains a residual diagnosis characterised by predominantly transdiagnostic features shared with a range of mood and anxiety disorders, a quality that the disorder has had since its inception. The evidence presented here suggests that GAD is no more a disorder of worry than are mood or other anxiety disorders despite its current position as a disorder of pathological worry as it seems no qualities of worry are unique to GAD. Other features and processes suggested to be key in pathology and maintenance of the disorder according to researchers or psychological models also appear to be transdiagnostic, although research into most is limited. However there is some evidence to suggest that muscle tension could be a feature unique to the disorder, but this possibility requires further research to clarify its relationship to GAD symptomatology and other disorders.

Given transdiagnostic processes, overlap in diagnostic criteria with other disorders and high levels of associated comorbidity, particularly with mood and other anxiety

disorders, another possibility is that GAD is a redundant diagnosis. If true, the disorder may be better grouped with other disorders or the categorisation changed to acknowledge the large overlap among these internalising disorders. Such revisions have been proposed by some as a better way of capturing the presentation of the disorder (e.g., Tyrer, 2018, Watson, 2005) and were even considered in development of the DSM-5.

However, until recent years there has been limited research into GAD. As a result, the understanding of the disorder has lagged behind that of other anxiety disorders and so there is a limited evidence base from which to understand the presentation of the disorder. It is therefore clear that in order to better understand GAD presentations, further research is required to determine which features are integral to the disorder to aid continued refinement of the diagnostic criteria. If GAD is considered an independent nosological entity with clinical utility, a view of some (e.g., Hallion et al., 2018; Shear 2012), a crucial area of research is in the identification of any potential unique or cardinal symptoms associated with different presentations of the disorder. Such research has the potential to improve the reliability and aid identification of the diagnosis. Without such research, GAD will continue to remain a diagnosis surrounded by uncertainty with continued questions regarding its validity as an independent diagnostic entity resulting in consequences for the identification and treatment of the disorder in practice.

References

Abel, J. L., & Borkovec, T. D. (1995). Generalizability of DSM-III-R generalized anxiety disorders to proposed DSM-IV criteria and cross-validation of proposed changes. *Journal of Anxiety Disorders*, *9*(4), 303-315.

Aderka, I. M., Beard, C., Lee, J., Weiss, R. B., & Björgvinsson, T. (2015). The relationship between depression and generalized anxiety during intensive psychological and pharmacological treatment. *Journal of affective disorders*, *184*, 261-268.

Akiskal, H. S. (1998). Toward a definition of generalized anxiety disorder as an anxious temperament type. *Acta Psychiatrica Scandinavica*, *98*, 66-73.

Aldao, A., Nolen-Hoeksema, S., & Schweizer, S. (2010). Emotion-regulation strategies across psychopathology: A meta-analytic review. *Clinical psychology review*, *30*(2), 217-237.

Allgulander, C. (2006). Generalized anxiety disorder: What are we missing?. *European Neuropsychopharmacology*, *16*, S101-S108.

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S., Bryson, H., ... & Haro, J. M. (2004). ESEMeD/MHEDEA 2000 Investigators, European Study of the Epidemiology of Mental Disorders (ESEMeD) Project. Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatr Scand Suppl*, *420*, 21-27.

Altwaijri, Y. A., Al-Subaie, A. S., Al-Habeeb, A., Bilal, L., Al-Desouki, M., Aradati, M., ... & Kessler, R. C. (2020). Lifetime prevalence and age-of-onset distributions of mental disorders in the Saudi National Mental Health Survey. *International Journal of Methods in Psychiatric Research*, *29*(3), e1836.

Alwahhabi, F. (2003). Anxiety symptoms and generalized anxiety disorder in the elderly: a review. *Harvard review of psychiatry*, *11*(4), 180-193.

American Psychiatric Association. (1980). *Diagnostic and statistical manual of mental disorders* (3rd ed.). American Psychiatric Association.

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., rev.). American Psychiatric Association.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). American Psychiatric Association.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). American Psychiatric Association.

Andor, T., Gerlach, A. L., & Rist, F. (2008). Superior perception of phasic physiological arousal and the detrimental consequences of the conviction to be aroused on worrying and metacognitions in GAD. *Journal of Abnormal Psychology, 117*(1), 193–205.

Andrews, G., Hobbs, M. J., Borkovec, T. D., Beesdo, K., Craske, M. G., Heimberg, R. G., ... & Stanley, M. A. (2010). Generalized worry disorder: a review of DSM-IV generalized anxiety disorder and options for DSM-V. *Depression and anxiety*, *27*(2), 134-147.

Angst, J., Gamma, A., Baldwin, D. S., Ajdacic-Gross, V., & Rössler, W. (2009). The generalized anxiety spectrum: prevalence, onset, course and outcome. *European archives of psychiatry and clinical neuroscience*, *259*(1), 37-45.

Ansell, E. B., Pinto, A., Edelen, M. O., Markowitz, J. C., Sanislow, C. A., Yen, S., ... & Grilo, C. M. (2011). The association of personality disorders with the prospective 7-year course of anxiety disorders. *Psychological Medicine*, *41*(5), 1019-1028.

Asnaani, A., Richey, J. A., Dimaite, R., Hinton, D. E., & Hofmann, S. G. (2010). A cross-ethnic comparison of lifetime prevalence rates of anxiety disorders. *The Journal of nervous and mental disease*, *198*(8), 551-555.

Ballenger, J. C., Davidson, J. R., Lecrubier, Y., Nutt, D. J., Borkovec, T. D., Rickels, K., ... & Wittchen, H. U. (2001). Consensus statement on generalized anxiety disorder from the International Consensus Group on Depression and Anxiety. *The Journal of clinical psychiatry*, *62*(suppl 11), 53-58.

Barahmand, U. (2009). Meta-cognitive profiles in anxiety disorders. *Psychiatry Research*, *169*(3), 240-243.

Barlow, D. H., Allen, L. B., & Choate, M. L. (2004). Toward a unified theory for emotional disorders. *Behavior Therapy, 35*, 205–230.

Barlow, D. H., Blanchard, E. B., Vermilyea, J. A., Vermilyea, B. B., & DiNardo, P. A. (1986). Generalized anxiety and generalized anxiety disorder: description and reconceptualization. *The American journal of psychiatry*, 143(1), 40-44.

Beard, C., Millner, A. J., Forgeard, M. J., Fried, E. I., Hsu, K. J., Treadway, M. T., ... & Björgvinsson, T. (2016). Network analysis of depression and anxiety symptom relationships in a psychiatric sample. *Psychological medicine*, *46*(16), 3359-3369.

Bebbington, P. E., Brugha, T. S., Meltzer, H., Jenkins, R., Ceresa, C., Farrell, M., & Lewis, G. (2000). Neurotic disorders and the receipt of psychiatric treatment. *Psychol Med*, *30*(6), 1369-1376.

Becker, E. S., Goodwin, R., Hölting, C., Hoyer, J., & Margraf, J. (2003). Content of worry in the community: what do people with generalized anxiety disorder or other disorders worry about?. *The Journal of nervous and mental disease*, *191*(10), 688-691.

Beesdo, K., Pine, D. S., Lieb, R., & Wittchen, H. U. (2010). Incidence and risk patterns of anxiety and depressive disorders and categorization of generalized anxiety disorder. *Archives of general psychiatry*, *67*(1), 47-57.

Beesdo-Baum, K., Jenjahn, E., Höfler, M., Lueken, U., Becker, E. S., & Hoyer, J. (2012). Avoidance, safety behavior, and reassurance seeking in generalized anxiety disorder. *Depression and Anxiety*, *29*(11), 948-957.

Beesdo-Baum, K., Winkel, S., Pine, D. S., Hoyer, J., Höfler, M., Lieb, R., & Wittchen, H. U. (2011). The diagnostic threshold of generalized anxiety disorder in the community: a developmental perspective. *Journal of psychiatric research*, *45*(7), 962-972.

Behar, E., & Borkovec, T. D. (2020). The effects of verbal and imaginal worry on panic symptoms during an interoceptive exposure task. *Behaviour Research and Therapy*, *135*, 103748.

Behar, E., DiMarco, I. D., Hekler, E. B., Mohlman, J., & Staples, A. M. (2009). Current theoretical models of generalized anxiety disorder (GAD): Conceptual review and treatment implications. *Journal of anxiety disorders*, *23*(8), 1011-1023.

Bekhuis, E., Schoevers, R. A., Van Borkulo, C. D., Rosmalen, J. G., & Boschloo, L. (2016). The network structure of major depressive disorder, generalized anxiety disorder and somatic symptomatology. *Psychological medicine*, *46*(14), 2989-2998.

Bittner, A., Goodwin, R. D., Wittchen, H. U., Beesdo, K., Höfler, M., & Lieb, R. (2004). What characteristics of primary anxiety disorders predict subsequent major depressive disorder?. *The Journal of clinical psychiatry*, *65*(5), 618-626.

Blanco, C., Rubio, J. M., Wall, M., Secades-Villa, R., Beesdo-Baum, K., & Wang, S. (2014). The latent structure and comorbidity patterns of generalized anxiety disorder and major depressive disorder: a national study. *Depression and anxiety*, *31*(3), 214–222.

Bland, R. C., Newman, S. C., & Orn, H. (1997). Help-seeking for psychiatric disorders. *The Canadian Journal of Psychiatry*, *42*(9), 935-942.

Blazer, D. G., Hughes, D., George, L. K., Swartz, M. & Boyer, R. (1991). Generalized anxiety disorder. In L. N. Robins & D. A. Regier (Eds.), *Psychiatric Disorders in America: The Epidemiologic Catchment Area Study.* The Free Press. (1st ed., pp. 180-203).

Bomyea, J., Ramsawh, H., Ball, T. M., Taylor, C. T., Paulus, M. P., Lang, A. J., & Stein, M. B. (2015). Intolerance of uncertainty as a mediator of reductions in worry in a cognitive behavioral treatment program for generalized anxiety disorder. *Journal of anxiety disorders*, *33*, 90-94.

Borkovec, T. D. (1985). Worry: A potentially valuable concept. *Behaviour Research and Therapy, 23*(4), 481–482.

Borkovec, T. D., & Hu, S. (1990). The effect of worry on cardiovascular response to phobic imagery. *Behaviour research and therapy*, *28*(1), 69-73.

Borkovec, T. D., & Inz, J. (1990). The nature of worry in generalized anxiety disorder: A predominance of thought activity. *Behaviour Research and Therapy, 31*, 153–158.

Borkovec, T. D., Abel, J. L., & Newman, H. (1995). Effects of psychotherapy on comorbid conditions in generalized anxiety disorder. *Journal of Consulting and Clinical Psychology*, *63*(3), 479-483.

Borkovec, T. D., Alcaine, O., & Behar, E. S. (2004). Avoidance theory of worry and generalized anxiety disorder. In: R. G. Heimberg, C. L. Turk, & D. S. Mennin (Eds.), *Generalized anxiety disorder: Advances in research and practice*. Guilford Press. (1st ed., pp. 77-108).

Borkovec, T. D., Shadick, R. N., & Hopkins, M. (1991). *The nature of normal and pathological worry.* In R. M. Rapee & D. H. Barlow (Eds.), *Chronic anxiety: Generalized anxiety disorder and mixed anxiety-depression* (p. 29–51). Guilford Press.

Borsboom, D., & Cramer, A. O. (2013). Network analysis: an integrative approach to the structure of psychopathology. *Annual review of clinical psychology*, *9*, 91-121.

Boschloo, L., Schoevers, R. A., van Borkulo, C. D., Borsboom, D., & Oldehinkel, A. J. (2016). The network structure of psychopathology in a community sample of preadolescents. *Journal of Abnormal Psychology*, *125*(4), 599-606.

Breslau, J., Aguilar-Gaxiola, S., Kendler, K. S., Su, M., Williams, D., & Kessler, R. C. (2006). Specifying race-ethnic differences in risk for psychiatric disorder in a US national sample. *Psychological medicine*, *36*(1), 57-68.

Breslau, N., & Davis, G. C. (1985). DSM-III generalized anxiety disorder: an empirical investigation of more stringent criteria. *Psychiatry Research*, *15*(3), 231-238.

Brosschot, J. F., Van Dijk, E., & Thayer, J. F. (2007). Daily worry is related to low heart rate variability during waking and the subsequent nocturnal sleep period. *International journal of psychophysiology*, *63*(1), 39-47.

Brown, T. A. (2007). Temporal course and structural relationships among dimensions of temperament and DSM-IV anxiety and mood disorder constructs. *Journal of Abnormal Psychology*, *116*(2), 313-328.

Brown, T. A., & Barlow, D. H. (2009). A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: Implications for assessment and treatment. *Psychological assessment*, *21*(3), 256-271.

Brown, T. A., Campbell, L. A., Lehman, C. L., Grisham, J. R., & Mancill, R. B. (2001a). Current and lifetime comorbidity of the DSM-IV anxiety and mood disorders in a large clinical sample. *Journal of abnormal psychology*, *110*(4), 585-599.

Brown, T. A., Chorpita, B. F., & Barlow, D. H. (1998). Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative

affect, positive affect, and autonomic arousal. *Journal of abnormal psychology*, *107*(2), 179.

Brown, T. A., Di Nardo, P. A., Lehman, C. L., & Campbell, L. A. (2001b). Reliability of DSM-IV anxiety and mood disorders: implications for the classification of emotional disorders. *Journal of abnormal psychology*, *110*(1), 49-58.

Brown, T. A., Marten, P. A., & Barlow, D. H. (1995). Discriminant validity of the symptoms constituting the DSM-III-R and DSM-IV associated symptom criterion of generalized anxiety disorder. *Journal of Anxiety Disorders*, *9*(4), 317-328.

Bruce, S. E., Machan, J. T., Dyck, I., & Keller, M. B. (2001). Infrequency of “pure” GAD: impact of psychiatric comorbidity on clinical course. *Depression and Anxiety*, *14*(4), 219-225.

Bruce, S. E., Yonkers, K. A., Otto, M. W., Eisen, J. L., Weisberg, R. B., Pagano, M., ... & Keller, M. B. (2005). Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: a 12-year prospective study. *American Journal of psychiatry*, *162*(6), 1179-1187.

Buhr, K., & Dugas, M. J. (2002). The intolerance of uncertainty scale: Psychometric properties of the English version. *Behaviour research and therapy*, *40*(8), 931-945.

Buhr, K., & Dugas, M. J. (2006). Investigating the construct validity of intolerance of uncertainty and its unique relationship with worry. *Journal of anxiety disorders*, *20*(2), 222-236.

Carleton, R. N., Mulvogue, M. K., Thibodeau, M. A., McCabe, R. E., Antony, M. M., & Asmundson, G. J. (2012). Increasingly certain about uncertainty: Intolerance of uncertainty across anxiety and depression. *Journal of anxiety disorders*, *26*(3), 468-479.

Carpenter, J. K., Andrews, L. A., Witcraft, S. M., Powers, M. B., Smits, J. A., & Hofmann, S. G. (2018). Cognitive behavioral therapy for anxiety and related disorders: A meta-analysis of randomized placebo-controlled trials. *Depression and anxiety*, *35*(6), 502-514.

Carter, R. M., Wittchen, H. U., Pfister, H., & Kessler, R. C. (2001). One-year prevalence of subthreshold and threshold DSM-IV generalized anxiety disorder in a nationally representative sample. *Depression and anxiety*, *13*(2), 78-88.

Cartwright-Hatton, S., & Wells, A. (1997). Beliefs about worry and intrusions: The Meta-Cognitions Questionnaire and its correlates. *Journal of anxiety disorders*, *11*(3), 279-296.

Casacalenda, N., & Boulenger, J. P. (1998). Pharmacologic treatments effective in both generalized anxiety disorder and major depressive disorder: clinical and theoretical implications. *The Canadian Journal of Psychiatry*, *43*(7), 722-730.

Caspi, A., & Moffitt, T. E. (2018). All for one and one for all: Mental disorders in one dimension. *American Journal of Psychiatry*, *175*(9), 831-844.

Caspi, A., Houts, R. M., Belsky, D. W., Goldman-Mellor, S. J., Harrington, H., Israel, S., ... & Moffitt, T. E. (2014). The p factor: one general psychopathology factor in the structure of psychiatric disorders?. *Clinical psychological science*, *2*(2), 119-137.

Castro, D., Ferreira, F., de Castro, I., Rodrigues, A. R., Correia, M., Ribeiro, J., & Ferreira, T. B. (2019). The Differential Role of Central and Bridge Symptoms in Deactivating Psychopathological Networks. *Frontiers in psychology*, *10*, 2448.

Chawla, N., & Ostafin, B. (2007). Experiential avoidance as a functional dimensional approach to psychopathology: An empirical review. *Journal of Clinical Psychology, 63*, 871–890.

Chelminski, I., & Zimmerman, M. (2003). Pathological worry in depressed and anxious patients. *Journal of Anxiety Disorders*, *17*(5), 533-546.

Chmielewski, M., Clark, L. A., Bagby, R. M., & Watson, D. (2015). Method matters: Understanding diagnostic reliability in DSM-IV and DSM-5. *Journal of abnormal psychology*, *124*(3), 764.

Chou, K. L. (2009). Age at onset of generalized anxiety disorder in older adults. *The American Journal of Geriatric Psychiatry*, *17*(6), 455-464.

Clarke, J. B., Ford, M., Heary, S., Rodgers, J., & Freeston, M. H. (2017). The relationship between negative problem orientation and worry: a meta-analytic review. *Psychopathology Review*, *4*(3), 319-340.

Cloninger, C. R., Martin, R. L., Guze, S. B., & Clayton, P. J. (1990). The empirical structure of psychiatric comorbidity and its theoretical significance. In J. D. Maser & C. R. Cloninger (Eds.), *Comorbidity of Mood and Anxiety Disorders*. (1st ed., pp. 439–462). American Psychiatric Press.

Coleman, S. L., Pieterefesa, A. S., Holaway, R. M., Coles, M. E., & Heimberg, R. G. (2011). Content and correlates of checking related to symptoms of obsessive compulsive disorder and generalized anxiety disorder. *Journal of anxiety disorders*, *25*(2), 293-301.

Cramer, A. O., Waldorp, L. J., Van Der Maas, H. L., & Borsboom, D. (2010). Comorbidity: A network perspective. *Behavioral and brain sciences*, *33*(2-3), 137-150.

Craske, M. G., Rapee, R. M., Jackel, L., & Barlow, D. H. (1989). Qualitative dimensions of worry in DSM-III-R generalized anxiety disorder subjects and nonanxious controls. *Behaviour research and therapy*, *27*(4), 397-402.

Crocq, M. A. (2017). The history of generalized anxiety disorder as a diagnostic category. *Dialogues in clinical neuroscience*, *19*(2), 107-116.

Crouch, T. A., Lewis, J. A., Erickson, T. M., & Newman, M. G. (2017). Prospective investigation of the contrast avoidance model of generalized anxiety and worry. *Behavior therapy*, *48*(4), 544-556.

Cuijpers, P., Sijbrandij, M., Koole, S., Huibers, M., Berking, M., & Andersson, G. (2014). Psychological treatment of generalized anxiety disorder: a meta-analysis. *Clinical psychology review*, *34*(2), 130-140.

Curtiss, J., & Klemanski, D. H. (2016). Taxonicity and network structure of generalized anxiety disorder and major depressive disorder: An admixture analysis and complex network analysis. *Journal of Affective Disorders*, *199*, 99-105.

Cuthbert, B. N., & Insel, T. R. (2010). Toward new approaches to psychotic disorders: The NIMH research domain criteria project. *Schizophrenia Bulletin*, *36*(6), 1061–1062.

Cuthbert, B. N., & Insel, T. R. (2013). Toward the future of psychiatric diagnosis: the seven pillars of RDoC. *BMC Medicine*, *11*(1), 126.

Davey, G. C., Tallis, F., & Capuzzo, N. (1996). Beliefs about the consequences of worrying. *Cognitive Therapy and Research*, *20*(5), 499-520.

Davidson, J. R., Feltner, D. E., & Dugar, A. (2010). Management of generalized anxiety disorder in primary care: identifying the challenges and unmet needs. *Primary care companion to the Journal of clinical psychiatry*, *12*(2), PCC.09r00772.

Davies, S. J., Pearson, R. M., Stapinski, L., Bould, H., Christmas, D. M., Button, K. S., ... & Evans, J. (2016). Symptoms of generalized anxiety disorder but not panic disorder at age 15 years increase the risk of depression at 18 years in the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort study. *Psychological medicine*, *46*(1), 73-85.

Davis, R. N., & Valentiner, D. P. (2000). Does meta-cognitive theory enhance our understanding of pathological worry and anxiety?. *Personality and Individual Differences*, *29*(3), 513-526.

De Graaf, R., Bijl, R. V., Spijker, J., Beekman, A. T. F., & Vollebergh, W. A. M. (2003). Temporal sequencing of lifetime mood disorders in relation to comorbid anxiety and substance use disorders. *Social psychiatry and psychiatric epidemiology*, *38*(1), 1-11.

de Lijster, J. M., Dierckx, B., Utens, E. M., Verhulst, F. C., Zieldorff, C., Dieleman, G. C., & Legerstee, J. S. (2017). The age of onset of anxiety disorders: a meta-analysis. *Canadian journal of psychiatry. Revue canadienne de psychiatrie*, *62*(4), 237.

Decker, M. L., Turk, C. L., Hess, B., & Murray, C. E. (2008). Emotion regulation among individuals classified with and without generalized anxiety disorder. *Journal of Anxiety Disorders*, *22*(3), 485-494.

Deschênes, S. S., Dugas, M. J., Fracalanza, K., & Koerner, N. (2012). The role of anger in generalized anxiety disorder. *Cognitive Behaviour Therapy*, *41*(3), 261-271.

Di Nardo, P. A., O'Brien, G. T., Barlow, D. H., Waddell, M. T., & Blanchard, E. B. (1983). Reliability of DSM-III anxiety disorder categories using a new structured interview. *Archives of General psychiatry*, *40*(10), 1070-1074.

Dugas, M. J., & Ladouceur, R. (2000). Treatment of GAD: Targeting intolerance of uncertainty in two types of worry. *Behavior modification*, *24*(5), 635-657.

Dugas, M. J., Anderson, K. G., Deschênes, S. S., & Donegan, E. (2010). Generalized anxiety disorder publications: Where do we stand a decade later?. *Journal of Anxiety Disorders*, *24*(7), 780-784.

Dugas, M. J., Letarte, H., Rhéaume, J., Freeston, M. H., & Ladouceur, R. (1995). Worry and problem solving: Evidence of a specific relationship. *Cognitive Therapy and Research*, *19*(1), 109-120.

Dugas, M. J., Marchand, A., & Ladouceur, R. (2005). Further validation of a cognitive behavioral model of generalized anxiety disorder: diagnostic and symptom specificity. Journal of Anxiety Disorders, 19, 329–343.

Dugas, M. J., Savard, P., Gaudet, A., Turcotte, J., Laugesen, N., Robichaud, M., ... & Koerner, N. (2007). Can the components of a cognitive model predict the severity of generalized anxiety disorder?. *Behavior therapy*, *38*(2), 169-178.

Dugas, M. J., Schwartz, A., & Francis, K. (2004). Brief report: Intolerance of uncertainty, worry, and depression. *Cognitive Therapy and Research*, *28*(6), 835-842.

Dugas, M., Gagnon, F., Ladouceur, R., & Freeston, M. (1998). Generalized anxiety disorder: A preliminary test of a conceptual model. *Behaviour Research and Therapy*, *36*(2), 215-226.

Durham, R. C., Allan, T., & Hackett, C. A. (1997). On predicting improvement and relapse in generalized anxiety disorder following psychotherapy. *British Journal of Clinical Psychology*, *36*(1), 101-119.

Durham, R. C., Chambers, J. A., Macdonald, R. R., Power, K. G., & Major, K. (2003). Does cognitive-behavioural therapy influence the long-term outcome of generalized anxiety disorder? An 8–14 year follow-up of two clinical trials. *Psychological Medicine*, *33*(3), 499-509.

D'Zurilla, T. J., Chang, E. C., Nottingham IV, E. J., & Faccini, L. (1998). Social problem-solving deficits and hopelessness, depression, and suicidal risk in college students and psychiatric inpatients. *Journal of clinical psychology*, *54*(8), 1091-1107.

Eustis, E. H., Hayes-Skelton, S. A., Roemer, L., & Orsillo, S. M. (2016). Reductions in experiential avoidance as a mediator of change in symptom outcome and quality of life in acceptance-based behavior therapy and applied relaxation for generalized anxiety disorder. *Behaviour research and therapy*, *87*, 188-195.

Fabiano, F., & Haslam, N. (2020). Diagnostic inflation in the DSM: A meta-analysis of changes in the stringency of psychiatric diagnosis from DSM-III to DSM-5. *Clinical Psychology Review*, 101889.

Faravelli, C., Castellini, G., Benni, L., Brugnera, A., Landi, M., Sauro, C. L., ... & Ricca, V. (2012). Generalized anxiety disorder: is there any specific symptom?. *Comprehensive psychiatry*, *53*(8), 1056-1062.

Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Thompson-Hollands, J., Carl, J. R., ... & Barlow, D. H. (2012). Unified protocol for transdiagnostic treatment of emotional disorders: a randomized controlled trial. *Behavior therapy*, *43*(3), 666-678.

Fava, M., Hwang, I., Rush, A. J., Sampson, N., Walters, E. E., & Kessler, R. C. (2010). The importance of irritability as a symptom of major depressive disorder: results from the National Comorbidity Survey Replication. *Molecular psychiatry*, *15*(8), 856-867.

Ferdinand, R. F., Dieleman, G., Ormel, J., & Verhulst, F. C. (2007). Homotypic versus heterotypic continuity of anxiety symptoms in young adolescents: evidence for distinctions between DSM-IV subtypes. *Journal of abnormal child psychology*, *35*(3), 325-333.

Fergus, T. A., & Wu, K. D. (2010). Do symptoms of generalized anxiety and obsessive-compulsive disorder share cognitive processes?. *Cognitive Therapy and Research*, *34*(2), 168-176.

Fergus, T. A., Valentiner, D. P., Wu, K. D., & McGrath, P. B. (2015). Examining the symptom-level specificity of negative problem orientation in a clinical sample. *Cognitive Behaviour Therapy*, *44*(2), 153-161.

Fergusson, D. M., Horwood, L. J., & Boden, J. M. (2006). Structure of internalising symptoms in early adulthood. *The British Journal of Psychiatry*, *189*(6), 540-546.

Ferster, C. B. (1973). A functional analysis of depression. *American psychologist*, *28*(10), 857-870.

Fisher, A. J., & Newman, M. G. (2016). Reductions in the diurnal rigidity of anxiety predict treatment outcome in cognitive behavioral therapy for generalized anxiety disorder. *Behaviour research and therapy*, *79*, 46-55.

Fisher, A. J., Reeves, J. W., Lawyer, G., Medaglia, J. D., & Rubel, J. A. (2017). Exploring the idiographic dynamics of mood and anxiety via network analysis. *Journal of abnormal psychology*, *126*(8), 1044-1056.

Foa, E. B., Liebowitz, M. R., Kozak, M. J., Davies, S., Campeas, R., Franklin, M. E., ... & Simpson, H. B. (2005). Randomized, placebo-controlled trial of exposure and ritual prevention, clomipramine, and their combination in the treatment of obsessive-compulsive disorder. *American Journal of psychiatry*, *162*(1), 151-161.

Frances, A. J., & Nardo, J. M. (2013). ICD-11 should not repeat the mistakes made by DSM-5. *The British Journal of Psychiatry*, *203*(1), 1-2.

Fresco, D. M., Mennin, D. S., Heimberg, R. G., & Turk, C. L. (2003). Using the Penn State Worry Questionnaire to identify individuals with generalized anxiety disorder: A receiver operating characteristic analysis. *Journal of behavior therapy and experimental psychiatry*, *34*(3-4), 283-291.

Garvey, M. J., Cook, B., & Noyes Jr, R. (1988). The occurrence of a prodrome of generalized anxiety in panic disorder. *Comprehensive psychiatry*, *29*(5), 445-449.

Gentes, E. L., & Ruscio, A. M. (2011). A meta-analysis of the relation of intolerance of uncertainty to symptoms of generalized anxiety disorder, major depressive disorder, and obsessive–compulsive disorder. *Clinical psychology review*, *31*(6), 923-933.

Gladstone, G. L., Parker, G. B., Mitchell, P. B., Malhi, G. S., Wilhelm, K. A., & Austin, M. P. (2005). A Brief Measure of Worry Severity (BMWS): Personality and clinical correlates of severe worriers. *Journal of Anxiety Disorders*, *19*(8), 877-892.

Goldberg, D. (2011). The heterogeneity of “major depression”. *World Psychiatry*, *10*(3), 226-228.

Goncalves, D. C., & Byrne, G. J. (2012). Sooner or later: age at onset of generalized anxiety disorder in older adults. *Depression and Anxiety*, *29*(1), 39-46.

Gorman, J. M. (2002). Treatment of generalized anxiety disorder. The Journal of clinical psychiatry, 17-23.

Gorwood, P. (2004). Generalized anxiety disorder and major depressive disorder comorbidity: an example of genetic pleiotropy?. *European Psychiatry*, *19*(1), 27-33.

Grant, B. F., Goldstein, R. B., Chou, S. P., Huang, B., Stinson, F. S., Dawson, D. A., ... & Ruan, W. J. (2009). Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *Molecular psychiatry*, *14*(11), 1051-1066.

Grant, B. F., Hasin, D. S., Stinson, F. S., Dawson, D. A., Ruan, W. J., Goldstein, R. B., ... & Huang, B. (2005). Prevalence, correlates, co-morbidity, and comparative disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychological medicine*, *35*(12), 1747-1759.

Griffith, J. W., Zinbarg, R. E., Craske, M. G., Mineka, S., Rose, R. D., Waters, A. M., & Sutton, J. M. (2010). Neuroticism as a common dimension in the internalizing disorders. *Psychological medicine*, *40*(7), 1125.

Hallion, L. S., & Ruscio, A. M. (2013). Should uncontrollable worry be removed from the definition of GAD? A test of incremental validity. *Journal of abnormal psychology*, *122*(2), 369-375.

Hallion, L. S., Steinman, S. A., & Kusmierski, S. N. (2018). Difficulty concentrating in generalized anxiety disorder: An evaluation of incremental utility and relationship to worry. *Journal of anxiety disorders*, *53*, 39-45.

Halvorsen, M., Hagen, R., Hjemdal, O., Eriksen, M. S., Sørli, Å. J., Eisemann, M., & Wang, C. E. (2015). Metacognitions and thought control strategies in unipolar major depression: a comparison of currently depressed, previously depressed, and never-depressed individuals. *Cognitive Therapy and Research*, *39*(1), 31-40.

Hanley, K. E. (2013). *The ability to shift emotions in individuals with generalized anxiety disorder*. (Unpublished doctoral thesis). The Pennsylvania State University.

Hayes-Skelton, S. A., Calloway, A., Roemer, L., & Orsillo, S. M. (2015). Decentering as a potential common mechanism across two therapies for generalized anxiety disorder. *Journal of Consulting and Clinical Psychology, 83*(2), 395–404.

Hendriks, S. M., Spijker, J., Licht, C. M., Beekman, A. T., & Penninx, B. W. (2013). Two-year course of anxiety disorders: different across disorders or dimensions?. *Acta psychiatrica scandinavica*, *128*(3), 212-221.

Hendriks, S. M., Spijker, J., Licht, C. M., Hardeveld, F., de Graaf, R., Batelaan, N. M., ... & Beekman, A. T. (2016). Long-term disability in anxiety disorders. *BMC psychiatry*, *16*(1), 1-8.

Herbert, E. A., & Dugas, M. J. (2019). Behavioral experiments for intolerance of uncertainty: Challenging the unknown in the treatment of generalized anxiety disorder. *Cognitive and Behavioral Practice*, *26*(2), 421-436.

Hermans, D., Martens, K., De Cort, K., Pieters, G., & Eelen, P. (2003). Reality monitoring and metacognitive beliefs related to cognitive confidence in obsessive–compulsive disorder. *Behaviour Research and Therapy*, *41*(4), 383-401.

Hettema, J. M. (2008). The nosologic relationship between generalized anxiety disorder and major depression. *Depression and Anxiety*, *25*(4), 300-316.

Hettema, J. M., Neale, M. C., Myers, J. M., Prescott, C. A., & Kendler, K. S. (2006). A population-based twin study of the relationship between neuroticism and internalizing disorders. *American journal of Psychiatry*, *163*(5), 857-864.

Hettema, J. M., Prescott, C. A., & Kendler, K. S. (2004). Genetic and environmental sources of covariation between generalized anxiety disorder and neuroticism. *American Journal of Psychiatry*, *161*(9), 1581-1587.

Hirsch, C. R., Mathews, A., Lequertier, B., Perman, G., & Hayes, S. (2013). Characteristics of worry in generalized anxiety disorder. *Journal of Behavior Therapy and Experimental Psychiatry*, *44*(4), 388-395.

Hoehn-Saric, R., Hazlett, R. L., & McLeod, D. R. (1993). Generalized anxiety disorder with early and late onset of anxiety symptoms. *Comprehensive Psychiatry*, *34*(5), 291-298.

Hoehn-Saric, R., McLeod, D. R., & Zimmerli, W. D. (1989). Somatic manifestations in women with generalized anxiety disorder: Psychophysiological responses to psychological stress. *Archives of general psychiatry*, *46*(12), 1113-1119.

Hoffman, S. G., & Hinton, D. E. (2014). Cross-Cultural Aspects of Anxiety Disorders. Current Psychiatry Reports, *16*(6), 450.

Hofmann, S. G., & Hay, A. C. (2018). Rethinking avoidance: Toward a balanced approach to avoidance in treating anxiety disorders. *Journal of anxiety disorders*, *55*, 14-21.

Hofmann, S. G., Asnaani, A., Vonk, I. J., Sawyer, A. T., & Fang, A. (2012). The efficacy of cognitive behavioral therapy: A review of meta-analyses. *Cognitive therapy and research*, *36*(5), 427-440.

Hoge, E. A., Ivkovic, A., & Fricchione, G. L. (2012). Generalized anxiety disorder: diagnosis and treatment. *BMJ*, *345*, e7500.

Hoge, E. A., Tamrakar, S. M., Christian, K. M., Mahara, N., Nepal, M. K., Pollack, M. H., & Simon, N. M. (2006). Cross-cultural differences in somatic presentation in patients with generalized anxiety disorder. *The Journal of nervous and mental disease*, *194*(12), 962-966.

Hovenkamp-Hermelink, J. H., Riese, H., Batelaan, N. M., Penninx, B. W., & Schoevers, R. A. (2016). Low stability of diagnostic classifications of anxiety disorders over time: A six-year follow-up of the NESDA study. *Journal of affective disorders*, *190*, 310-315.

Hoyer, J., Becker, E. S., & Roth, W. T. (2001). Characteristics of worry in GAD patients, social phobics, and controls. *Depression and Anxiety*, *13*(2), 89-96.

Huang, Y., Wang, Y., Wang, H., Liu, Z., Yu, X., Yan, J., ... & Wang, Z. (2019). Prevalence of mental disorders in China: a cross-sectional epidemiological study. *The Lancet Psychiatry*, *6*(3), 211-224.

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., ... & Wang, P. (2010). Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. The American Journal of Psychiatry, *167*(7), 748-751.

Jamil, N., & Llera, S. J. (2021). A Transdiagnostic Application of the Contrast-Avoidance Model: The Effects of Worry and Rumination in a Personal-Failure Paradigm. *Clinical Psychological Science*, 2167702621991797.

Jones, K. D. (2012). A critique of the DSM-5 field trials. *The Journal of nervous and mental disease*, *200*(6), 517-519.

Joormann, J., & Stöber, J. (1999). Somatic symptoms of generalized anxiety disorder from the DSM-IV: associations with pathological worry and depression symptoms in a nonclinical sample. *Journal of anxiety disorders*, *13*(5), 491-503.

Kahn, R. J., McNair, D. M., Lipman, R. S., Covi, L., Rickels, K., Downing, R., ... & Frankenthaler, L. M. (1986). Imipramine and chlordiazepoxide in depressive and anxiety disorders: II. Efficacy in anxious outpatients. *Archives of General Psychiatry*, *43*(1), 79-85.

Kaufman, J., & Charney, D. (2000). Comorbidity of mood and anxiety disorders. *Depression and anxiety*, *12*(S1), 69-76.

Keller, M. B. (2002). The long-term clinical course of generalized anxiety disorder. *The Journal of clinical psychiatry*, *63*(suppl 8), 11-16.

Kendler, K. S. (1996). Major depression and generalised anxiety disorder: same genes, (partly) different environments – revisited. *The British Journal of Psychiatry*, *168*(S30), 68-75.

Kendler, K. S., Eaves, L. J., Walters, E. E., Neale, M. C., Heath, A. C., & Kessler, R. C. (1996). The identification and validation of distinct depressive syndromes in a population-based sample of female twins. *Archives of general psychiatry*, *53*(5), 391-399.

Kendler, K. S., Gardner, C. O., Gatz, M., & Pedersen, N. L. (2007). The sources of co-morbidity between major depression and generalized anxiety disorder in a Swedish national twin sample. *Psychological medicine*, *37*(3), 453-462.

Kerns, C. E., Mennin, D. S., Farach, F. J., & Nocera, C. C. (2014). Utilizing an ability-based measure to detect emotion regulation deficits in generalized anxiety disorder. *Journal of Psychopathology and Behavioral Assessment*, *36*(1), 115-123.

Kertz, S. J., Bigda-Peyton, J. S., Rosmarin, D. H., & Björgvinsson, T. (2012). The importance of worry across diagnostic presentations: Prevalence, severity and associated symptoms in a partial hospital setting. *Journal of Anxiety Disorders*, *26*(1), 126–133.

Kertz, S. J., McHugh, R. K., Lee, J., & Björgvinsson, T. (2014). Examining the latent structure of worry and generalized anxiety in a clinical sample. *Journal of anxiety disorders*, *28*(1), 8-15.

Kessler, R. C. (2000). The epidemiology of pure and comorbid generalized anxiety disorder: a review and evaluation of recent research. *Acta Psychiatrica Scandinavica*, *102*, 7-13.

Kessler, R. C., Andrade, L. H., Bijl, R. V., Offord, D. R., Demler, O. V., & Stein, D. J. (2002). The effects of co-morbidity on the onset and persistence of generalized anxiety disorder in the ICPE surveys. *Psychological Medicine*, *32*(7), 1213-1225.

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), 168-176.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry, 62, 593–602.

Kessler, R. C., DuPont, R. L., Berglund, P., & Wittchen, H. U. (1999). Impairment in pure and comorbid generalized anxiety disorder and major depression at 12 months in two national surveys. *American journal of psychiatry*, *156*(12), 1915-1923.

Kessler, R. C., Gruber, M., Hettema, J. M., Hwang, I., Sampson, N., & Yonkers, K. A. (2008). Co-morbid major depression and generalized anxiety disorders in the National Comorbidity Survey follow-up. *Psychological medicine*, *38*(3), 365-374.

Kessler, R. C., Keller, M. B., & Wittchen, H. U. (2001). The epidemiology of generalized anxiety disorder. *Psychiatric Clinics of North America*, *24*(1), 19-39.

Kessler, R. C., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Wittchen, H. U. (2012). Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *International journal of methods in psychiatric research*, *21*(3), 169-184.

Kim, H., & Newman, M. G. (2019). The paradox of relaxation training: Relaxation induced anxiety and mediation effects of negative contrast sensitivity in generalized anxiety disorder and major depressive disorder. *Journal of affective disorders*, *259*, 271-278.

Klein, D. F. (1964). Delineation of two drug-responsive anxiety syndromes. *Psychopharmacologia*, *5*(6), 397-408.

Klein, D. F., & Fink, M. (1962). Psychiatric reaction patterns to imipramine. *American Journal of Psychiatry*, *119*(5), 432-438.

Koerner, N., & Dugas, M. J. (2006). *A Cognitive Model of Generalized Anxiety Disorder: The Role of Intolerance of Uncertainty.* In G. C. L. Davey & A. Wells (Eds.), *Worry and its psychological disorders: Theory, assessment and treatment* (p. 201–216). Wiley Publishing.

Kotov, R., Krueger, R. F., Watson, D., Achenbach, T. M., Althoff, R. R., Bagby, R. M., ... & Zimmerman, M. (2017). The Hierarchical Taxonomy of Psychopathology (HiTOP): A dimensional alternative to traditional nosologies. *Journal of abnormal psychology*, *126*(4), 454–477.

Kotov, R., Watson, D., Robles, J. P., & Schmidt, N. B. (2007). Personality traits and anxiety symptoms: The multilevel trait predictor model. *Behaviour research and therapy*, *45*(7), 1485-1503.

Kozak, M. J., & Cuthbert, B. N. (2016). The NIMH research domain criteria initiative: background, issues, and pragmatics. *Psychophysiology*, *53*(3), 286-297.

Krueger, R. F. (1999). The structure of common mental disorders. *Archives of general psychiatry*, *56*(10), 921-926.

Krueger, R. F., & Markon, K. E. (2006). Reinterpreting comorbidity: A model-based approach to understanding and classifying psychopathology. *Annu. Rev. Clin. Psychol.*, *2*, 111-133.

Krueger, R. F., Caspi, A., Moffitt, T. E., & Silva, P. A. (1998). The structure and stability of common mental disorders (DSM-III-R): a longitudinal-epidemiological study. *Journal of abnormal psychology*, *107*(2), 216-227.

Krueger, R. F., Kotov, R., Watson, D., Forbes, M. K., Eaton, N. R., Ruggero, C. J., ... & Zimmermann, J. (2018). Progress in achieving quantitative classification of psychopathology. *World Psychiatry*, *17*(3), 282-293.

Kubarych, T. S., Aggen, S. H., Hettema, J. M., Kendler, K. S., & Neale, M. C. (2005). Endorsement frequencies and factor structure of DSM-III-R and DSM-IV Generalized Anxiety Disorder symptoms in women: implications for future research, classification, clinical practice and comorbidity. *International Journal of Methods in Psychiatric Research*, *14*(2), 69-81.

Kuehner, C., Huffziger, S., & Liebsch, K. (2009). Rumination, distraction and mindful self-focus: Effects on mood, dysfunctional attitudes and cortisol stress response. *Psychological Medicine*, *39*(2), 219-228.

Ladouceur, R., Blais, F., Freeston, M. H., & Dugas, M. J. (1998). Problem solving and problem orientation in generalized anxiety disorder. *Journal of anxiety disorders*, *12*(2), 139-152.

Ladouceur, R., Dugas, M. J., Freeston, M. H., Léger, E., Gagnon, F., & Thibodeau,, N. (2000b). Efficacy of a cognitive–behavioral treatment for generalized anxiety disorder: Evaluation in a controlled clinical trial. *Journal of consulting and clinical psychology*, *68*(6), 957-964.

Ladouceur, R., Dugas, M. J., Freeston, M. H., Rhéaume, J., Blais, F., Boisvert, J. M., ... & Thibodeau, N. (1999). Specificity of generalized anxiety disorder symptoms and processes. *Behavior Therapy*, *30*(2), 191-207.

Ladouceur, R., Gosselin, P., & Dugas, M. J. (2000a). Experimental manipulation of intolerance of uncertainty: A study of a theoretical model of worry. *Behaviour research and therapy*, *38*(9), 933-941.

Lahey, B. B., Zald, D. H., Hakes, J. K., Krueger, R. F., & Rathouz, P. J. (2014). Patterns of heterotypic continuity associated with the cross-sectional correlational structure of prevalent mental disorders in adults. *JAMA psychiatry*, *71*(9), 989-996.

Lamers, F., Beekman, A. T. F., Van Hemert, A. M., Schoevers, R. A., & Penninx, B. W. J. H. (2016). Six-year longitudinal course and outcomes of subtypes of depression. *The British Journal of Psychiatry*, *208*(1), 62-68.

Lamers, F., Comijs, H. C., Smit, J. H., Spinhoven, P., Nolen, W. A., Zitman, F. G., ... & Penninx, B. W. (2011). Comorbidity patterns of anxiety and depressive disorders in a large cohort study: the Netherlands Study of Depression and Anxiety (NESDA). *The Journal of clinical psychiatry*, *72*(3), 341-348.

Le Roux, H., Gatz, M., & Wetherell, J. L. (2005). Age at onset of generalized anxiety disorder in older adults. *The American Journal of Geriatric Psychiatry*, *13*(1), 23-30.

Lee, J. K., Orsillo, S. M., Roemer, L., & Allen, L. B. (2010). Distress and avoidance in generalized anxiety disorder: Exploring the relationships with intolerance of uncertainty and worry. *Cognitive behaviour therapy*, *39*(2), 126-136.

Lee, S. P., Sagayadevan, V., Abdin, E., Vaingankar, J. A., Chong, S. A., & Subramaniam, M. (2016). Prevalence, correlates, comorbidity and severity of generalized anxiety disorder in Singapore. *Asian journal of psychiatry*, *23*, 32-38.

Lee, S., Ma, Y. L., Tsang, A., & Kwok, K. (2009a). Generalized anxiety disorder with and without excessive worry in Hong Kong. *Depression and anxiety*, *26*(10), 956-961.

Lee, S., Tsang, A., Ruscio, A. M., Haro, J. M., Stein, D., Alonso, J., ... & De Graaf, R. (2009b). Implications of modifying the duration requirement of generalized anxiety disorder in developed and developing countries. *Psychological Medicine*, *39*(7), 1163-1176.

Legerstee, J. S., Dierckx, B., Utens, E. M. W. J., Verhulst, F. C., Zieldorff, C., Dieleman, G. C., & de Lijster, J. M. (2019) Age of onset of anxiety disorders. In G. de Girolamo, P. D. McGorry and N. Sartoris, *Age of Onset of Mental Disorders: Etiopathogenetic and Treatment Implications* (pp. 125-147). Springer International Publishing AG.

Leichsenring D Sc, F., Salzer, S., Jaeger, U., Kächele, H., Kreische, R., Leweke, F., ... & Leibing D Sc, E. (2009). Short-term psychodynamic psychotherapy and cognitive-behavioral therapy in generalized anxiety disorder: a randomized, controlled trial. *American Journal of Psychiatry*, *166*(8), 875-881.

Lenze, E. J., Mulsant, B. H., Mohlman, J., Shear, M. K., Dew, M. A., Schulz, R., ... & Reynolds III, C. F. (2005). Generalized anxiety disorder in late life: lifetime course and comorbidity with major depressive disorder. *The American journal of geriatric psychiatry*, *13*(1), 77-80.

Lenzo, V., Sardella, A., Martino, G., & Quattropani, M. C. (2019). A systematic review of metacognitive beliefs in chronic medical conditions. *Frontiers in Psychology*, *10*, 2875.

Lewis-Fernández, R., Hinton, D. E., Laria, A. J., Patterson, E. H., Hofmann, S. G., Craske, M. G., ... & Liao, B. (2011). Culture and the anxiety disorders: recommendations for DSM-V. *Focus*, *9*(3), 351-368.

Lieb, R., Becker, E., & Altamura, C. (2005). The epidemiology of generalized anxiety disorder in Europe. *European Neuropsychopharmacology*, *15*(4), 445-452.

Llera, S. J., & Newman, M. G. (2010). Effects of worry on physiological and subjective reactivity to emotional stimuli in generalized anxiety disorder and nonanxious control participants. *Emotion*, *10*(5), 640-650.

Llera, S. J., & Newman, M. G. (2014). Rethinking the role of worry in generalized anxiety disorder: Evidence supporting a model of emotional contrast avoidance. *Behavior Therapy*, *45*(3), 283-299.

Llera, S. J., & Newman, M. G. (2017). Development and validation of two measures of emotional contrast avoidance: The contrast avoidance questionnaires. *Journal of Anxiety Disorders*, *49*, 114-127.

Lydiard, R. B. (2000). An overview of generalized anxiety disorder: disease state—appropriate therapy. *Clinical therapeutics*, *22*, A3-A24.

Lyonfields, J. D., Borkovec, T. D., & Thayer, J. F. (1995). Vagal tone in generalized anxiety disorder and the effects of aversive imagery and worrisome thinking. *Behavior Therapy*, *26*(3), 457-466.

Mahoney, A. E., & McEvoy, P. M. (2012). A transdiagnostic examination of intolerance of uncertainty across anxiety and depressive disorders. *Cognitive Behaviour Therapy*, *41*(3), 212-222.

Mahoney, A. E., Hobbs, M. J., Newby, J. M., Williams, A. D., & Andrews, G. (2018). Psychometric properties of the Worry Behaviors Inventory: replication and extension in a large clinical and community sample. *Behavioural and cognitive psychotherapy*, *46*(1), 84-100.

Mahoney, A. E., Hobbs, M. J., Newby, J. M., Williams, A. D., Sunderland, M., & Andrews, G. (2016). The Worry Behaviors Inventory: Assessing the behavioral avoidance associated with generalized anxiety disorder. *Journal of Affective Disorders*, *203*, 256-264.

Mancuso, D. M., Townsend, M. H., & Mercante, D. E. (1993). Long-term follow-up of generalized anxiety disorder. *Comprehensive Psychiatry*, *34*(6), 441-446.

Marcotte-Beaumier, G., Malivoire, B. L., Koerner, N., & Ovanessian, M. M. (2021). The Role of Overt and Covert Avoidance Strategies in Generalized Anxiety Disorder Symptoms and Fear of Emotion. *Journal of Psychopathology and Behavioral Assessment*, 1-9.

Marques, L., Robinaugh, D. J., LeBlanc, N. J., & Hinton, D. (2011). Cross-cultural variations in the prevalence and presentation of anxiety disorders. *Expert Review of Neurotherapeutics*, *11*(2), 313-322.

Massion, A. O., Dyck, I. R., Shea, M. T., Phillips, K. A., Warshaw, M. G., & Keller, M. B. (2002). Personality disorders and time to remission in generalized anxiety disorder, social phobia, and panic disorder. *Archives of General Psychiatry*, *59*(5), 434-440.

Massion, A. O., Warshaw, M. G., & Keller, M. B. (1993). Quality of life and psychiatric morbidity in panic disorder and generalized anxiety disorder. *The American Journal of Psychiatry, 150*(4), 600–607.

Mathew, A. R., Pettit, J. W., Lewinsohn, P. M., Seeley, J. R., & Roberts, R. E. (2011). Co-morbidity between major depressive disorder and anxiety disorders: shared etiology or direct causation?. *Psychological medicine*, *41*(10), 2023-2034.

McEvoy, P. M., & Mahoney, A. E. (2012). To be sure, to be sure: Intolerance of uncertainty mediates symptoms of various anxiety disorders and depression. *Behavior therapy*, *43*(3), 533-545.

McEvoy, P. M., & Mahoney, A. E. (2013). Intolerance of uncertainty and negative metacognitive beliefs as transdiagnostic mediators of repetitive negative thinking in a clinical sample with anxiety disorders. *Journal of Anxiety Disorders*, *27*(2), 216-224.

McGlinchey, J. B., & Zimmerman, M. (2007). Examining a dimensional representation of depression and anxiety disorders' comorbidity in psychiatric outpatients with item response modeling. *Journal of Abnormal Psychology*, *116*(3), 464-474.

McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. *Journal of psychiatric research*, *45*(8), 1027–1035.

Mennin, D. S., Heimberg, R. G., Fresco, D. M., & Ritter, M. R. (2008). Is generalized anxiety disorder an anxiety or mood disorder? Considering multiple factors as we ponder the fate of GAD. *Depression and Anxiety*, *25*(4), 289-299.

Mennin, D. S., Heimberg, R. G., Turk, C. L., & Fresco, D. M. (2002). Applying an emotion regulation framework to integrative approaches to generalized anxiety disorder. *Clinical Psychology: Science and Practice*, *9*(1), 85-90.

Mennin, D. S., Heimberg, R. G., Turk, C. L., & Fresco, D. M. (2005). Preliminary evidence for an emotion dysregulation model of generalized anxiety disorder. *Behaviour research and therapy*, *43*(10), 1281-1310.

Mennin, D. S., Holaway, R. M., Fresco, D. M., Moore, M. T., & Heimberg, R. G. (2007). Delineating components of emotion and its dysregulation in anxiety and mood psychopathology. *Behavior therapy*, *38*(3), 284-302.

Mennin, D. S., McLaughlin, K. A., & Flanagan, T. J. (2009). Emotion regulation deficits in generalized anxiety disorder, social anxiety disorder, and their co-occurrence. *Journal of anxiety disorders*, *23*(7), 866-871.

Merikangas, K. R., Zhang, H., Avenevoli, S., Acharyya, S., Neuenschwander, M., & Angst, J. (2003). Longitudinal trajectories of depression and anxiety in a prospective community study: the Zurich Cohort Study. *Archives of general psychiatry*, *60*(10), 993-1000.

Merino, H., Senra, C., & Ferreiro, F. (2016). Are worry and rumination specific pathways linking neuroticism and symptoms of anxiety and depression in patients with generalized anxiety disorder, major depressive disorder and mixed anxiety-depressive disorder?. *PloS one*, *11*(5), e0156169.

Michelson, S. E., Lee, J. K., Orsillo, S. M., & Roemer, L. (2011). The role of values-consistent behavior in generalized anxiety disorder. *Depression and Anxiety*, *28*(5), 358-366.

Mineka, S., Watson, D., & Clark, L. A. (1998). Comorbidity of anxiety and unipolar mood disorders. *Annual review of psychology*, *49*(1), 377-412.

Moffitt, T. E., Caspi, A., Harrington, H., Milne, B. J., Melchior, M., Goldberg, D., & Poulton, R. (2007b). Generalized anxiety disorder and depression: childhood risk factors in a birth cohort followed to age 32. *Psychological medicine*, *37*(3), 441-452.

Moffitt, T. E., Harrington, H., Caspi, A., Kim-Cohen, J., Goldberg, D., Gregory, A. M., & Poulton, R. (2007a). Depression and generalized anxiety disorder: cumulative and

sequential comorbidity in a birth cohort followed prospectively to age 32 years. *Archives of general psychiatry*, *64*(6), 651-660.

Mohlman, J., de Jesus, M., Gorenstein, E. E., Kleber, M., Gorman, J. M., & Papp, L. A. (2004). Distinguishing generalized anxiety disorder, panic disorder, and mixed anxiety states in older treatment-seeking adults. *Journal of anxiety disorders*, *18*(3), 275-290.

Mojtabai, R., Olfson, M., & Mechanic, D. (2002). Perceived need and help-seeking in adults with mood, anxiety, or substance use disorders. *Archives of general psychiatry*, *59*(1), 77-84.

Molina, S., & Borkovec, T. D. (1994). *The Penn State Worry Questionnaire: Psychometric properties and associated characteristics.* In G. C. L. Davey & F. Tallis (Eds.), *Wiley series in clinical psychology. Worrying: Perspectives on theory, assessment and treatment* (p. 265–283). John Wiley & Sons.

Morrison, A. P., & Wells, A. (2007). Relationships between worry, psychotic experiences and emotional distress in patients with schizophrenia spectrum diagnoses and comparisons with anxious and non-patient groups. *Behaviour research and therapy*, *45*(7), 1593-1600.

Muris, P., Roelofs, J., Rassin, E., Franken, I., & Mayer, B. (2005). Mediating effects of rumination and worry on the links between neuroticism, anxiety and depression. *Personality and Individual Differences*, *39*(6), 1105-1111.

Myers, S. G., & Wells, A. (2005). Obsessive-compulsive symptoms: the contribution of metacognitions and responsibility. *Journal of Anxiety Disorders*, *19*(7), 806-817.

Nassif, Y. (1999). *Predictors of pathological worry*. (Unpublished M. Phil. Thesis). University of Manchester.

Newby, J. M., McKinnon, A., Kuyken, W., Gilbody, S., & Dalgleish, T. (2015). Systematic review and meta-analysis of transdiagnostic psychological treatments for anxiety and depressive disorders in adulthood. *Clinical psychology review*, *40*, 91-110.

Newman, M. G., & Erickson, T. M. (2010). *Generalized anxiety disorder.* In J. G. Beck (Ed.), *Interpersonal processes in the anxiety disorders: Implications for understanding psychopathology and treatment* (p. 235–259). American Psychological Association.

Newman, M. G., & Llera, S. J. (2011). A novel theory of experiential avoidance in generalized anxiety disorder: A review and synthesis of research supporting a contrast avoidance model of worry. *Clinical psychology review*, *31*(3), 371-382.

Newman, M. G., Castonguay, L. G., Borkovec, T. D., Fisher, A. J., Boswell, J. F., Szkodny, L. E., & Nordberg, S. S. (2011). A randomized controlled trial of cognitive-behavioral therapy for generalized anxiety disorder with integrated techniques from emotion-focused and interpersonal therapies. *Journal of consulting and clinical psychology*, *79*(2), 171-181.

Newman, M. G., Llera, S. J., Erickson, T. M., & Przeworski, A. (2014). Basic science and clinical application of the Contrast Avoidance model in generalized anxiety disorder. *Journal of Psychotherapy Integration*, *24*(3), 155-167.

Newman, M. G., Llera, S. J., Erickson, T. M., Przeworski, A., & Castonguay, L. G. (2013). Worry and generalized anxiety disorder: a review and theoretical synthesis of evidence on nature, etiology, mechanisms, and treatment. *Annual review of clinical psychology*, *9*, 275-297.

Newman, M. G., Przeworski, A., Fisher, A. J., & Borkovec, T. D. (2010). Diagnostic comorbidity in adults with generalized anxiety disorder: Impact of comorbidity on psychotherapy outcome and impact of psychotherapy on comorbid diagnoses. *Behavior Therapy*, *41*(1), 59-72.

Newman, M. G., Shin, K. E., & Lanza, S. T. (2019a). Time-varying moderation of treatment outcomes by illness duration and comorbid depression in generalized anxiety disorder. *Journal of consulting and clinical psychology*, *87*(3), 282-293.

Newman, M. G., Jacobson, N. C., Zainal, N. H., Shin, K. E., Szkodny, L. E., & Sliwinski, M. J. (2019b). The effects of worry in daily life: An ecological momentary assessment study supporting the tenets of the contrast avoidance model. *Clinical Psychological Science*, *7*(4), 794-810.

National Institute for Health and Care Excellence. (2019). *Generalised anxiety disorder and panic disorder in adults: management* [NICE Guideline No. 113]. https://www.nice.org.uk/guidance/cg113

Niileksela, C. R., Ghosh, A., & Janis, R. A. (2020). Dynamic changes in generalized anxiety and depression during counseling. *Journal of counseling psychology*, 68 (1), 112–124.

Norton, P. J. (2012). A randomized clinical trial of transdiagnostic cognitive-behavioral treatments for anxiety disorders by comparison to relaxation training. *Behavior Therapy*, *43*(3), 506-517.

Norton, P. J., & Barrera, T. L. (2012). Transdiagnostic versus diagnosis-specific CBT for anxiety disorders: A preliminary randomized controlled noninferiority trial. *Depression and Anxiety*, *29*(10), 874-882.

Norton, P. J., & Paulus, D. J. (2017). Transdiagnostic models of anxiety disorder: Theoretical and empirical underpinnings. *Clinical Psychology Review*, *56*, 122-137.

Novick-Kline, P., Turk, C. L., Mennin, D. S., Hoyt, E. A., & Gallagher, C. L. (2005). Level of emotional awareness as a differentiating variable between individuals with and without generalized anxiety disorder. Journal of Anxiety Disorders, 19, 557–572.

Noyes Jr, R. (1999). The relationship of hypochondriasis to anxiety disorders. *General Hospital Psychiatry*, *21*(1), 8-17.

Nuevo, R., Montorio, I., & Borkovec, T. D. (2004). A test of the role of metaworry in the prediction of worry severity in an elderly sample. *Journal of Behavior Therapy and Experimental Psychiatry*, *35*(3), 209-218.

Oakley Browne, M. A., Elisabeth Wells, J., Scott, K. M., Mcgee, M. A., & New Zealand Mental Health Survey Research Team. (2006). Lifetime prevalence and projected lifetime risk of DSM-IV disorders in Te Rau Hinengaro: the New Zealand Mental Health Survey. *Australian & New Zealand Journal of Psychiatry*, *40*(10), 865-874.

Olatunji, B. O., Broman-Fulks, J. J., Bergman, S. M., Green, B. A., & Zlomke, K. R. (2010b). A taxometric investigation of the latent structure of worry: dimensionality and associations with depression, anxiety, and stress. *Behavior Therapy*, *41*(2), 212-228.

Olatunji, B. O., Wolitzky-Taylor, K. B., Sawchuk, C. N., & Ciesielski, B. G. (2010a). Worry and the anxiety disorders: A meta-analytic synthesis of specificity to GAD. *Applied and Preventive Psychology*, *14*(1-4), 1-24.

Olino, T. M., Klein, D. N., Lewinsohn, P. M., Rohde, P., & Seeley, J. R. (2010). Latent trajectory classes of depressive and anxiety disorders from adolescence to adulthood: descriptions of classes and associations with risk factors. *Comprehensive psychiatry*, *51*(3), 224-235.

Ollendick, T. H., Jarrett, M. A., White, B. A., White, S. W., & Grills, A. E. (2016). Primary Versus Secondary Diagnosis of Generalized Anxiety Disorder in Youth: Is the Distinction an Important One?. *Child Psychiatry & Human Development*, *47*(4), 548-553.

O'Neill, G. W. (1985). Is worry a valuable concept? *Behaviour Research and Therapy, 23*(4), 479–480.

Ottenbreit, N. D., & Dobson, K. S. (2004). Avoidance and depression: the construction of the Cognitive–Behavioral Avoidance Scale. *Behaviour research and therapy*, *42*(3), 293-313.

Parker, G., Wilhelm, K., Mitchell, P., Austin, M. P., Roussos, J., & Gladstone, G. (1999). The influence of anxiety as a risk to early onset major depression. *Journal of affective disorders*, *52*(1-3), 11-17.

Patriquin, M. A., & Mathew, S. J. (2017). The neurobiological mechanisms of generalized anxiety disorder and chronic stress. *Chronic Stress*, *1*, 1-10.

Peasley-Miklus, C., & Vrana, S. R. (2000). Effect of worrisome and relaxing thinking on fearful emotional processing. *Behaviour Research and Therapy*, *38*(2), 129-144.

Penney, A. M., Mazmanian, D., & Rudanycz, C. (2013). Comparing positive and negative beliefs about worry in predicting generalized anxiety disorder symptoms. *Canadian Journal of Behavioural Science/Revue canadienne des sciences du comportement*, *45*(1), 34-41.

Penninx, B. W., Beekman, A. T., Smit, J. H., Zitman, F. G., Nolen, W. A., Spinhoven, P., ... & Van Dyck, R. (2008). The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. *International journal of methods in psychiatric research*, *17*(3), 121-140.

Pine, D. S., Cohen, P., & Brook, J. (2001). Adolescent fears as predictors of depression. *Biological Psychiatry*, *50*(9), 721-724.

Pluess, M., Conrad, A., & Wilhelm, F. H. (2009). Muscle tension in generalized anxiety disorder: a critical review of the literature. *Journal of anxiety disorders*, *23*(1), 1-11.

Portman, M. E., Starcevic, V., & Beck, A. T. (2011). Challenges in assessment and diagnosis of generalized anxiety disorder. *Psychiatric Annals*, *41*(2), 79-85.

Price, M., Legrand, A. C., Brier, Z. M., & Hébert-Dufresne, L. (2019). The symptoms at the center: examining the comorbidity of posttraumatic stress disorder, generalized anxiety disorder, and depression with network analysis. *Journal of psychiatric research*, *109*, 52-58.

Provencher, M. D., Ladouceur, R., & Dugas, M. J. (2006). La comorbidité dans le trouble d'anxiété généralisée: prévalence et évolution suite à une thérapie cognitivo-comportementale. *The Canadian Journal of Psychiatry*, *51*(2), 91-99.

Pruitt, L. D. (2010). *New directions in the psychopathology of generalized anxiety disorder: An investigation of the role of emotion regulation in the development and maintenance of chronic worry and anxiety*. (Unpublished doctoral thesis). University of Nevada.

Ramsawh, H. J., Raffa, S. D., Edelen, M. O., Rende, R., & Keller, M. B. (2009). Anxiety in middle adulthood: effects of age and time on the 14-year course of panic disorder, social phobia and generalized anxiety disorder. *Psychological medicine*, *39*(4), 615-624.

Ramsawh, H. J., Weisberg, R. B., Dyck, I., Stout, R., & Keller, M. B. (2011). Age of onset, clinical characteristics, and 15-year course of anxiety disorders in a prospective, longitudinal, observational study. *Journal of affective disorders*, *132*(1-2), 260-264.

Ranney, R. M., Behar, E., & Yamasaki, A. S. (2020). Affect variability and emotional reactivity in generalized anxiety disorder. *Journal of behavior therapy and experimental psychiatry*, *68*, 101542.

Rapee, R. M. (1991). Generalized anxiety disorder: A review of clinical features and theoretical concepts. *Clinical Psychology Review*, *11*(4), 419-440.

Rebello, T. J., Keeley, J. W., Kogan, C. S., Sharan, P., Matsumoto, C., Kuligyna, M., ... & Zhong, N. (2019). Anxiety and fear-related disorders in the ICD-11: results from a global case-controlled field study. *Archives of medical research*, *50*(8), 490-501.

Reed, G. M., First, M. B., Kogan, C. S., Hyman, S. E., Gureje, O., Gaebel, W., ... & Claudino, A. (2019). Innovations and changes in the ICD-11 classification of mental, behavioural and neurodevelopmental disorders. *World Psychiatry*, *18*(1), 3-19.

Reed, G. M., Sharan, P., Rebello, T. J., Keeley, J. W., Elena Medina-Mora, M., Gureje, O., ... & Pike, K. M. (2018). The ICD-11 developmental field study of reliability of diagnoses of high-burden mental disorders: results among adult patients in mental health settings of 13 countries. *World psychiatry*, *17*(2), 174-186.

Regier, D. A., Narrow, W. E., Clarke, D. E., Kraemer, H. C., Kuramoto, S. J., Kuhl, E. A., & Kupfer, D. J. (2013). DSM-5 field trials in the United States and Canada, part II: Test-retest reliability of selected categorical diagnoses. *American Journal of Psychiatry*, *170*, 59–70.

Rhebergen, D., Aderka, I. M., van der Steenstraten, I. M., van Balkom, A. J., van Oppen, P., Stek, M. L., ... & Batelaan, N. M. (2017). Admixture analysis of age of onset in generalized anxiety disorder. *Journal of anxiety disorders*, *50*, 47-51.

Rickels, K., & Rynn, M. A. (2001). What is generalized anxiety disorder?. *The Journal of clinical psychiatry*, *62 Suppl 11*, 4–14.

Rivas-Vazquez, R. A. (2001). Antidepressants as first-line agents in the current pharmacotherapy of anxiety disorders. *Professional Psychology: Research and Practice*, *32*(1), 101-104.

Rodriguez, B. F., Bruce, S. E., Pagano, M. E., & Keller, M. B. (2005). Relationships among psychosocial functioning, diagnostic comorbidity, and the recurrence of generalized

anxiety disorder, panic disorder, and major depression. *Journal of anxiety disorders*, *19*(7), 752-766.

Rodriguez, B. F., Weisberg, R. B., Pagano, M. E., Bruce, S. E., Spencer, M. A., Culpepper, L., & Keller, M. B. (2006). Characteristics and predictors of full and partial recovery from generalized anxiety disorder in primary care patients. *The Journal of nervous and mental disease*, *194*(2), 91-97.

Roemer, L., & Orsillo, S. M. (2002). Expanding our conceptualization of and treatment for generalized anxiety disorder: Integrating mindfulness/acceptance-based approaches with existing cognitive-behavioral models. *Clinical Psychology: Science and Practice*, *9*(1), 54-68.

Roemer, L., & Orsillo, S. M. (2005). An acceptance-based behavior therapy for generalized anxiety disorder. In S.M. Orsillo, L. Roemer (Eds.), *Acceptance and mindfulness-based approaches to anxiety* (pp. 213-240). Springer.

Roemer, L., & Orsillo, S. M. (2007). An open trial of an acceptance-based behavior therapy for generalized anxiety disorder. *Behavior therapy*, *38*(1), 72-85.

Roemer, L., Molina, S., & Borkovec, T. D. (1997). An investigation of worry content among generally anxious individuals. *The Journal of nervous and mental disease*, *185*(5), 314-319.

Roemer, L., Salters, K., Raffa, S. D., & Orsillo, S. M. (2005). Fear and avoidance of internal experiences in GAD: preliminary tests of conceptual model. Cognitive Therapy and Research, 29, 71–88.

Rogers, M. P., Warshaw, M. G., Goisman, R. M., Goldenberg, I., Rodriguez-Villa, F., Mallya, G., ... & Keller, M. B. (1999). Comparing primary and secondary generalized anxiety disorder in a long-term naturalistic study of anxiety disorders. *Depression and Anxiety*, *10*(1), 1-7.

Roth, W. T., Doberenz, S., Dietel, A., Conrad, A., Mueller, A., Wollburg, E., ... & Kim, S. (2008). Sympathetic activation in broadly defined generalized anxiety disorder. *Journal of psychiatric research*, *42*(3), 205-212.

Roy, M. A., Neale, M. C., Pedersen, N. L., Mathe, A. A., & Kendler, K. S. (1995). A twin study of generalized anxiety disorder and major depression. *Psychological medicine*, *25*(5), 1037-1049.

Roy-Byrne, P. P., & Wagner, A. (2004). Primary care perspectives on generalized anxiety disorder. *Journal of Clinical Psychiatry*, *65*, 20-26.

Ruscio, A. M. (2002). Delimiting the boundaries of generalized anxiety disorder: differentiating high worriers with and without GAD. *Journal of Anxiety Disorders*, *16*(4), 377-400.

Ruscio, A. M., & Borkovec, T. D. (2004). Experience and appraisal of worry among high worriers with and without generalized anxiety disorder. *Behaviour research and therapy*, *42*(12), 1469-1482.

Ruscio, A. M., Borkovec, T. D., & Ruscio, J. (2001). A taxometric investigation of the latent structure of worry. *Journal of abnormal psychology*, *110*(3), 413-422.

Ruscio, A. M., Chiu, W. T., Roy-Byrne, P., Stang, P. E., Stein, D. J., Wittchen, H. U., & Kessler, R. C. (2007). Broadening the definition of generalized anxiety disorder: effects on prevalence and associations with other disorders in the National Comorbidity Survey Replication. *Journal of anxiety disorders*, *21*(5), 662-676.

Ruscio, A. M., Hallion, L. S., Lim, C. C., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., ... & De Almeida, J. M. C. (2017). Cross-sectional comparison of the epidemiology of DSM-5 generalized anxiety disorder across the globe. *JAMA psychiatry*, *74*(5), 465-475.

Ruscio, A. M., Lane, M., Roy-Byrne, P., Stang, P. E., Stein, D. J., Wittchen, H. U., & Kessler, R. C. (2005). Should excessive worry be required for a diagnosis of generalized anxiety disorder? Results from the US National Comorbidity Survey Replication. *Psychological Medicine*, *35*(12), 1761-1772.

Salguero, J. M., Ramos-Cejudo, J., & García-Sancho, E. (2019). Metacognitive beliefs and emotional dysregulation have a specific contribution on worry and the emotional symptoms of generalized anxiety disorder. *International Journal of Cognitive Therapy*, *12*(3), 179-190.

Salkovskis, P. M. (1999). Understanding and treating obsessive—compulsive disorder. *Behaviour Research and Therapy*, *37*, S29-S52.

Salters-Pedneault, K., Roemer, L., Tull, M. T., Rucker, L., & Mennin, D. S. (2006). Evidence of broad deficits in emotion regulation associated with chronic worry and generalized anxiety disorder. *Cognitive Therapy and Research*, *30*(4), 469-480.

Sarisoy, G., Pazvantoğlu, O., Özturan, D. D., Ay, N. D., Yilman, T., Mor, S., ... & Gümüş, K. (2014). Metacognitive beliefs in unipolar and bipolar depression: A comparative study. *Nordic journal of psychiatry*, *68*(4), 275-281.

Sassaroli, S., Bertelli, S., Decoppi, M., Crosina, M., Milos, G., & Ruggiero, G. M. (2005). Worry and eating disorders: A psychopathological association. *Eating Behaviors*, *6*(4), 301–307.

Scholten, W. D., Batelaan, N. M., van Balkom, A. J., Penninx, B. W., Smit, J. H., & van Oppen, P. (2013). Recurrence of anxiety disorders and its predictors. *Journal of affective disorders*, *147*(1-3), 180-185.

Shear, M. K. (2012). Generalized anxiety disorder in ICD-11. *World Psychiatry*, *11*(Suppl 1), 82-88.

Shevlin, M., McElroy, E., & Murphy, J. (2017). Homotypic and heterotypic psychopathological continuity: a child cohort study. *Social Psychiatry and Psychiatric Epidemiology*, *52*(9), 1135-1145.

Sibrava, N. J., & Borkovec, T. D. (2006). The Cognitive Avoidance Theory of Worry. In G. C. L. Davey & A. Wells (Eds.), *Worry and its psychological disorders: Theory, assessment and treatment* (pp. 239–256). Wiley Publishing.

Slade, T. I. M., & Watson, D. (2006). The structure of common DSM-IV and ICD-10 mental disorders in the Australian general population. *Psychological medicine*, *36*(11), 1593-1600.

Slade, T., & Andrews, G. (2001). DSM-IV and ICD-10 generalized anxiety disorder: discrepant diagnoses and associated disability. *Social Psychiatry and Psychiatric Epidemiology*, *36*(1), 45-51.

Sloan, E., Hall, K., Moulding, R., Bryce, S., Mildred, H., & Staiger, P. K. (2017). Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review. *Clinical psychology review*, *57*, 141-163.

Somers, J. M., Goldner, E. M., Waraich, P., & Hsu, L. (2006). Prevalence and incidence studies of anxiety disorders: a systematic review of the literature. *The Canadian Journal of Psychiatry*, *51*(2), 100-113.

Spitzer, R. L., Endicott, J., & Robins, E. (1978). Research diagnostic criteria: rationale and reliability. *Archives of general psychiatry*, *35*(6), 773-782.

Springer, K. S., Levy, H. C., & Tolin, D. F. (2018). Remission in CBT for adult anxiety disorders: a meta-analysis. *Clinical psychology review*, *61*, 1-8.

Stapinski, L. A., Abbott, M. J., & Rapee, R. M. (2010). Evaluating the cognitive avoidance model of generalised anxiety disorder: Impact of worry on threat appraisal, perceived control and anxious arousal. *Behaviour Research and Therapy*, *48*(10), 1032-1040.

Starcevic, V. (2006). Review: worldwide lifetime prevalence of anxiety disorders is 16.6%, with considerable heterogeneity between studies. *Evidence-based mental health*, *9*(4), 115.

Starcevic, V., Berle, D., Milicevic, D., Hannan, A., Lamplugh, C., & Eslick, G. D. (2007). Pathological worry, anxiety disorders and the impact of co-occurrence with depressive and other anxiety disorders. *Journal of Anxiety Disorders*, *21*(8), 1016-1027.

Starcevic, V., Portman, M. E., & Beck, A. T. (2012). Generalized anxiety disorder: between neglect and an epidemic. The Journal of nervous and mental disease, 200(8), 664-667.

Startup, H., Freeman, D., & Garety, P.A. (2007). Persecutory delusions and catastrophic worry in psychosis: developing the understanding of delusion distress and persistence. *Behaviour Research and Therapy*, *45*(3), 523-537.

Startup, H., Pugh, K., Dunn, G., Cordwell, J., Mander, H., Černis, E., … Freeman, D. (2016). Worry processes in patients with persecutory delusions. *British Journal of Clinical Psychology*, *55*(4), 387-400.

Stein, D. J. (2005). Generalized anxiety disorder: rethinking diagnosis and rating. *CNS Spectrums*, *10*(12), 930-934.

Stein, D. J., Scott, K. M., de Jonge, P., & Kessler, R. C. (2017). Epidemiology of anxiety disorders: from surveys to nosology and back. *Dialogues in clinical neuroscience*, *19*(2), 127–136.

Stein, D. J., Szatmari, P., Gaebel, W., Berk, M., Vieta, E., Maj, M., ... & Brewin, C. R. (2020). Mental, behavioral and neurodevelopmental disorders in the ICD-11: an international perspective on key changes and controversies. *BMC medicine*, *18*(1), 1-24.

Sternheim, L., Startup, H., Saeidi, S., Morgan, J., Hugo, P., Russell, A., & Schmidt, U. (2012). Understanding catastrophic worry in eating disorders: Process and content characteristics. *Journal of Behavior Therapy and Experimental Psychiatry*, *43*(4), 1095-1103.

Sun, X., Zhu, C., & So, S. H. W. (2017). Dysfunctional metacognition across psychopathologies: a meta-analytic review. *European Psychiatry*, *45*, 139-153.

Sunderland, M., Mewton, L., Slade, T., & Baillie, A. J. (2010). Investigating differential symptom profiles in major depressive episode with and without generalized anxiety disorder: true co-morbidity or symptom similarity?. *Psychological medicine*, *40*(7), 1113-1123.

Thayer, J. F., Friedman, B. H., & Borkovec, T. D. (1996). Autonomic characteristics of generalized anxiety disorder and worry. *Biological psychiatry*, *39*(4), 255-266.

Titov, N., Andrews, G., Johnston, L., Robinson, E., & Spence, J. (2010). Transdiagnostic Internet treatment for anxiety disorders: A randomized controlled trial. *Behaviour research and therapy*, *48*(9), 890-899.

Tull, M. T., Stipelman, B. A., Salters-Pedneault, K., & Gratz, K. L. (2009). An examination of recent non-clinical panic attacks, panic disorder, anxiety sensitivity, and emotion regulation difficulties in the prediction of generalized anxiety disorder in an analogue sample. *Journal of anxiety disorders*, *23*(2), 275-282.

Turk, C. L., Heimberg, R. G., Luterek, J. A., Mennin, D. S., & Fresco, D. M. (2005). Emotion dysregulation in generalized anxiety disorder: A comparison with social anxiety disorder. *Cognitive Therapy and Research*, *29*(1), 89-106.

Tyrer, P. (2018). Against the Stream: Generalised anxiety disorder (GAD)–a redundant diagnosis. *BJPsych bulletin*, *42*(2), 69-71.

Tyrer, P., & Baldwin, D. (2006). Generalised anxiety disorder. *The Lancet*, *368*(9553), 2156-2166.

Vaingankar, J. A., Rekhi, G., Subramaniam, M., Abdin, E., & Chong, S. A. (2013). Age of onset of life-time mental disorders and treatment contact. *Social psychiatry and psychiatric epidemiology*, *48*(5), 835-843.

Vesga-López, O., Schneier, F., Wang, S., Heimberg, R., Liu, S. M., Hasin, D. S., & Blanco, C. (2008). Gender differences in generalized anxiety disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *The Journal of clinical psychiatry*, *69*(10), 1606-1616.

Vollebergh, W. A., Iedema, J., Bijl, R. V., de Graaf, R., Smit, F., & Ormel, J. (2001). The structure and stability of common mental disorders: the NEMESIS study. *Archives of general psychiatry*, *58*(6), 597-603.

Vrana, S. R., Cuthbert, B. N., & Lang, P. J. (1986). Fear imagery and text processing. *Psychophysiology*, *23*(3), 247-253.

Watson, D. (2005). Rethinking the mood and anxiety disorders: a quantitative hierarchical model for DSM-V. *Journal of abnormal psychology*, *114*(4), 522-536.

Watson, D., Gamez, W., & Simms, L. J. (2005). Basic dimensions of temperament and their relation to anxiety and depression: A symptom-based perspective. *Journal of Research in Personality*, *39*(1), 46-66.

Watson, D., O'Hara, M. W., & Stuart, S. (2008). Hierarchical structures of affect and psychopathology and their implications for the classification of emotional disorders. *Depression and Anxiety*, *25*(4), 282-288.

Watson, D., Stanton, K., & Clark, L. A. (2017). Self-report indicators of negative valence constructs within the research domain criteria (RDoC): A critical review. *Journal of Affective Disorders*, *216*, 58-69.

Weisberg, R. B. *(*2009*).* Overview of generalized anxiety disorder: Epidemiology, presentation, and course*. Journal of Clinical Psychiatry, 70(*suppl 2*),* 4–9*.*

Wells, A. (1994). A multi-dimensional measure of worry: Development and preliminary validation of the Anxious Thoughts Inventory. *Anxiety, Stress and Coping*, *6*(4), 289-299.

Wells, A. (1995). Meta-cognition and worry: A cognitive model of generalized anxiety disorder. *Behavioural and cognitive psychotherapy*, *23*(3), 301-320.

Wells, A. (1999). A metacognitive model and therapy for generalized anxiety disorder. *Clinical Psychology & Psychotherapy: An International Journal of Theory & Practice*, *6*(2), 86-95.

Wells, A. (2004). A cognitive model of GAD. *Generalized anxiety disorder: Advances in research and practice*, 164-186.

Wells, A. (2005). The metacognitive model of GAD: Assessment of meta-worry and relationship with DSM-IV generalized anxiety disorder. *Cognitive Therapy and Research*, *29*(1), 107-121.

Wells, A. (2010). Metacognitive theory and therapy for worry and generalized anxiety disorder: Review and status. *Journal of Experimental Psychopathology*, *1*(1), 133-145.

Wells, A., & Carter, K. (1999). Preliminary tests of a cognitive model of generalized anxiety disorder. *Behaviour research and therapy*, *37*(6), 585-594.

Wells, A., & Carter, K. (2001). Further tests of a cognitive model of generalized anxiety disorder: Metacognitions and worry in GAD, panic disorder, social phobia, depression, and nonpatients. *Behavior therapy*, *32*(1), 85-102.

Wells, A., & Papageorgiou, C. (1998). Relationships between worry, obsessive–compulsive symptoms and meta-cognitive beliefs. *Behaviour research and therapy*, *36*(9), 899-913.

Wittchen, H. U. (2002). Generalized anxiety disorder: Prevalence, burden, and cost to society. *Depression and Anxiety*, 16, 162–171.

Wittchen, H. U., & Hoyer, J. (2001). Generalized anxiety disorder: nature and course. *The Journal of clinical psychiatry*, *62*(suppl 11), 15-19.

Wittchen, H. U., Kessler, R. C., Beesdo, K., Krause, P., Höfler, M., & Hoyer, J. (2002). Generalized anxiety and depression in primary care: Prevalence, recognition, and management. *The Journal of Clinical Psychiatry, 63*(Suppl 8), 24–34.

Wittchen, H. U., Kessler, R. C., Pfister, H., Höfler, M., & Lieb, R. (2000). Why do people with anxiety disorders become depressed? A prospective-longitudinal community study. *Acta Psychiatrica Scandinavica*, *102*, 14-23.

World Health Organization. (1975). *International statistical classification of diseases and related health problems* (9th ed.). World Health Organization.

World Health Organization. (2004). *International statistical classification of diseases and related health problems* (10th ed.). World Health Organization.

World Health Organization. (2018). *International statistical classification of diseases and related health problems* (11th ed.). World Health Organization.

Yonkers, K. A., Bruce, S. E., Dyck, I. R., & Keller, M. B. (2003). Chronicity, relapse, and illness—course of panic disorder, social phobia, and generalized anxiety disorder:

findings in men and women from 8 years of follow-up. *Depression and anxiety*, *17*(3), 173-179.

Yonkers, K. A., Dyck, I. R., Warshaw, M., & Keller, M. B. (2000). Factors predicting the clinical course of generalised anxiety disorder. *The British Journal of Psychiatry*, *176*(6), 544-549.

Yonkers, K. A., Warshaw, M. G., Massion, A. O., & Keller, M. B. (1996). Phenomenology and course of generalised anxiety disorder. *The British Journal of Psychiatry*, *168*(3), 308-313.

Yook, K., Kim, K., Suh, S. Y., & Lee, K. S. (2010). Intolerance of uncertainty, worry, and rumination in major depressive disorder and generalized anxiety disorder. Journal of Anxiety Disorders, 24, 623–628.

Zavos, H. M., Rijsdijk, F. V., & Eley, T. C. (2012). A longitudinal, genetically informative, study of associations between anxiety sensitivity, anxiety and depression. *Behavior Genetics*, *42*(4), 592-602.

Zbozinek, T. D., Rose, R. D., Wolitzky-Taylor, K. B., Sherbourne, C., Sullivan, G., Stein, M. B., ... & Craske, M. G. (2012). Diagnostic overlap of generalized anxiety disorder and major depressive disorder in a primary care sample. *Depression and anxiety*, *29*(12), 1065-1071.

Zhou, Y., Cao, Z., Yang, M., Xi, X., Guo, Y., Fang, M., ... & Du, Y. (2017). Comorbid generalized anxiety disorder and its association with quality of life in patients with major depressive disorder. *Scientific reports*, *7*(1), 1-8.

Zitrin, C. M., Klein, D. F., & Woerner, M. G. (1978). Behavior therapy, supportive psychotherapy, imipramine, and phobias. *Archives of General Psychiatry*, *35*(3), 307-316.

Zohar, J., & Westenberg, H. G. M. (2000). Anxiety disorders: a review of tricyclic antidepressants and selective serotonin reuptake inhibitors. *Acta Psychiatrica Scandinavica*, *101*, 39-49.

Part 2: Empirical Paper

Characterising the Symptom Profiles and Stability of Subtypes of Generalized Anxiety Disorder

Abstract

Background: Generalized Anxiety Disorder (GAD) remains a poorly understood disorder characterised by heterogeneity in presentations, high rates of comorbidity and blurred diagnostic boundaries with depressive and anxiety disorders. It remains one of the least reliably and accurately diagnosed disorders. The current study aimed to explore whether there are different subtypes of GAD characterised by different patterns of GAD and depression symptom endorsement and characterise their stability and transitions between subtypes over the initial sessions of therapy to aid understanding of what constitutes GAD.

Methods: Latent transition analysis was conducted on two large samples to classify patients into latent states based on their endorsement of GAD and depression symptoms from sessional item-level self-report data and the probabilities of transitioning within and between states was quantified. Data came from multiple outpatient clinics. The main sample included patients with a presenting problem of any depressive or anxiety disorder and the second sample included only those with GAD as their presenting problem of GAD. Multinomial logistic regression was used to identify any baseline characteristics associated with later transition to the “GAD” state in sample two.

Results: Six latent states were found in sample one and five in sample two. Both samples were composed of mostly latent states classified as four mixed anxiety and depression subgroups of increasing severity and a “GAD” state with an additional “depression” subgroup in sample one. Subgroups were most likely to remain stable, however the disorder specific subgroups were the least stable. By time 3, a large portion of those in the “GAD” states presented with mixed symptoms. States between samples were qualitatively similar and within models, states were only distinguished by overall scores on the measures as opposed to individual items.

Conclusions: GAD is a disorder characterised by high levels of both GAD and depression symptoms with most presentations of the disorder endorsing both to a similar severity with

few distinguishing features. A “GAD” profile was found to emerge in a small portion after the first session, demonstrating the potential for GAD to be masked in initial sessions but later emerge. This pattern of symptom endorsement remains similar to subgroups within the wider group of anxiety and depressive disorders. As such, this highlights the challenge for clinicians to accurately identify GAD.

Introduction

Generalized anxiety disorder (GAD) is a disorder of excessive worry, apprehension, and anxiety with associated somatic symptoms of tension and sleep disturbance. It is one of the most common mental health conditions with estimated lifetime prevalence rates between 3 and 5% (Baxter et al., 2013). The disorder is thought to be one of the most prevalent mental health disorders in primary care settings, second only to depression, with estimates of around 8% prevalence and accounting for 22% of all anxiety presentations to primary care (Ballenger, 2001; Wittchen, 2002). When first introduced as a diagnostic entity GAD was viewed as a mild disorder with sufferers simply the "worried well" but as research into the disorder increased, its chronic course, resistance to change, and associated high levels of disability and health service use have become more apparent (Ballenger et al. 2001; Weisberg et al., 2010). Studies suggest the impact on individuals' quality of life is greater than that associated with major medical conditions such as type II diabetes, hypertension, or congestive heart failure (Weisberg et al., 2010).

Despite its prevalence and impact on both individuals and society, as discussed in chapter 1, the diagnosis of GAD continues to be poorly understood. There remains a lack of clarity surrounding what constitutes GAD and the particular unique target symptoms that are able to reliably distinguish it from other disorders, resulting in issues reliably detecting the disorder. In current thinking the cardinal symptom is considered to be excessive worry, yet excessive worry features in many other disorders including depression (e.g., Kertz et al., 2012), panic disorder (e.g., Gladstone et al., 2005), health anxiety (e.g., Noyes, 1999), psychosis (e.g., Startup et al., 2007), and OCD (e.g., Olatunji et al., 2010). The diagnostic criteria have poor specificity to GAD leading to overlap and blurred boundaries with depressive disorders (Brown et al., 2001; Clark & Watson, 1991; Mennin et al., 2008; Sunderland et al., 2010; Zbozinek et al., 2012) with only muscle tension found to reliably distinguish GAD and depression (Faravelli et al., 2012). This diagnostic overlap is thought in part to influence the high rates of comorbidity with depressive and anxiety disorders in GAD

and the rarity of “pure” presentations (Kessler et al., 2002; Lamer et al., 2011; Lieb et al., 2005; Murray & Lopez, 1996; Nutt et al., 2006; Ter Meulen et al., 2021; Wittchen et al., 1994) and difficulties recognising GAD with individuals most frequently misdiagnosed with depression, dysthymia, and anxiety not otherwise specified (Brown et al., 2001).

GAD is thought to be heterogeneous disorder with different presentations characterised by different constellations of symptoms, yet GAD often co-occurs with comorbid disorders making it difficult to recognise. Comorbid disorders, such as depression, can be more prominent and camouflage the presence or symptoms of GAD (Argyropoulos et al., 2006; Portman et al., 2011), leaving the disorder undetected. The current diagnostic criteria are also thought not to capture the heterogeneity of presentations making detection particularly difficult in presentations where worry does not have a defining role (Lydiard, 2000; Portman et al., 2011, Roth, 2008). This is a particular issue in primary care as current focus on the cognitive features of worry and anxiety contrasts with the typical presentation of GAD in primary care where most patients present with somatic symptoms of anxiety such as insomnia, muscle tension, heart palpitations, and gastrointestinal problems (Roy-Byrne & Wagner, 2004; Davidson et al., 2010). One study found only 13% of those with GAD presented with anxiety as their main complaint at their first appointment (Wittchen et al., 2002). This disparity is thought to be due to individuals not viewing symptoms such as worry or anxiety to be a medical issue but instead part of their personality (Arroll & Kendrick, 2009; Culpepper & Conner, 2004). When presented with the somatic symptoms of GAD by patients who view their symptoms as a sign of physical illness, clinicians may not recognise the presentation as an anxiety disorder so not ask about anxiety. As a result, individuals with GAD are frequently referred physical health investigations prior receiving a GAD diagnosis (Arroll & Kendrick, 2009; Tylee & Walters, 2007). There are clearly issues in the recognition of GAD by clinicians but also for individuals themselves with the disorder, something that is acknowledged in national guidance which highlights the need for services to make individuals aware of the symptoms of anxiety and encourage individuals to present with them

as a medical issue (National Collaborating Centre for Mental Health [NCCMH], 2020). It may be that clinically significant GAD, that is individuals scoring above clinical thresholds on measures such as the Generalised Anxiety Disorder scale 7-items (GAD-7, Spitzer et al., 2006), may emerge after initial contact with a healthcare professional who describes what GAD is. Through this information and description of the disorder, individuals may gain a new understanding of their difficulties, resulting in a change in their perception of their 'anxiety' symptoms which they previously did not view as the issue (Arroll & Kendrick, 2009; Culpepper & Conner, 2004), but also a change in the clinician's understanding of the issues, and the potential utility of the diagnosis "GAD" in capturing these experiences.

Different factors have been shown to influence the rates of detection of GAD. Individuals are more likely to be diagnosed with GAD when it is comorbid with depression than when "pure" (Weiller et al., 1998; Wittchen & Jacobi, 2005), studies finding detection rates in 34.4% in pure compared to 43% in comorbid cases (Wittchen et al., 2002), and are also far more likely to seek treatment (e.g., Bland et al., 1997; Kessler et al., 2001; Mojtabai et al., 2002; Newman et al., 2010), but perhaps for the comorbid disorder. Likewise, more intense GAD symptom severity has also been found to increase recognition by practitioners and help-seeking (Allugander, 2006; Culpepper, 2002; Roberge et al., 2015).

Due to these issues, GAD is a challenge to consistently detect due to the lack of distinguishing features, overlap with other disorders and potential for presentations to change due to comorbidity or individual awareness of the symptoms of GAD. As such the disorder continues to be one of the least reliably diagnosed disorders (Reed et al., 2018; Regier et al., 2013) and in clinical practice the disorder is under diagnosed and under treated (Bebbington et al., 2000; National Institute for Health & Care Excellence [NICE], 2011). Estimated recognition rates in primary care range from 34.4% to 72.5% (Wittchen et al., 2002). It has been estimated that only 30% of those with the condition obtain a diagnosis (Allgulander, 2006) but in some populations this has been as low as 1.5% (Calleo et al., 2009). These difficulties detecting and reliably diagnosing the disorder for even experienced

clinicians mean many, if not most, with GAD do not receive any treatment for the disorder. Accurate detection is important as a longer duration of untreated GAD is associated with a poorer course and worse outcomes (Altamura et al., 2008) and poor recognition and misdiagnosis means many receive the incorrect treatment (Hales et al., 1997). However, there remains lack of studies investigating the presence of subtypes within the heterogeneity of GAD presentations and the stability of their constellations of symptoms.

One method that has been used to explore subgroups within populations are data-driven latent variable mixture model approaches such as latent class analysis (LCA) and latent transition analysis (LTA). These are closely related approaches which assume that underlying grouping variables, called latent variables, explain the association between the responses in observable data (Collins & Lanza, 2010). LCA is used to identify latent classes within cross-sectional data whereas LTA is the longitudinal extension allowing for exploration of transitions between classes over multiple time points modelling both the heterogenous subgroups within the sample but also the individual-level changes between subgroups over time to see the stability of classes (Nylund, 2007). The potential for change in GAD presentations means that constellations of symptoms in different subgroups may not be stable therefore longitudinal analysis allows for investigation to understand the levels and patterns of change within different GAD presentations and also allow for better understanding of groups who may later emerge with the disorder.

Such methods have been used to identify subtypes depression and latent class transitions over the course of therapy with transitions occurring early within therapy (e.g., Catarino et al., 2020; Simmonds-Buckley et al., 2021; Ulbricht et al., 2018). However, at present only one study has applied such techniques to a sample including individuals with GAD. The study by Rhebergen and colleagues (2014) conducted an LCA to questionnaire data from individuals with GAD, dysthymia disorder or both disorders and found no disorder-specific profiles separated the data as had been predicted with the classes of mixed

symptoms best fitting the data. However, no studies have explored the presence of subgroups within GAD and their stability over time using these methods.

Aim

The present study aims to address this gap in the literature by exploring whether there are different subgroups of GAD characterised by different dimensions of features measured by routine anxiety and depression questionnaires within a large patient sample using an LTA approach. An LTA approach has the potential to aid the understanding of GAD by identifying different subgroups within a sample of people defined as having probable GAD, classifying their symptom profiles characterised by different clusters of symptoms of different rated severity and any dominant symptoms and determining the stability of these statuses over the course of initial sessions of therapy. This would be the first application of LTA in a GAD population and exploration of the stability in symptom constellations in different presentations of the disorder.

It is anticipated that different profiles of GAD symptoms will be identified, and that the identification of these could be clinically useful to aid further understanding of the presentations within the disorder and therefore recognition of GAD.

The current study had the following aims:

1) To explore whether there are different subtypes of GAD characterised by different patterns of GAD and depression symptoms and any symptoms able to distinguish states.

2) To characterise the stability of the subgroup over three initial sessions of therapy where GAD presentations may emerge and transitions between statuses.

3) To compare the GAD profiles identified to profile solutions, the different states characterised by different symptoms within a model, identified in a group of patients with depressive and anxiety disorders.

Method

Data Sources

Fully anonymised sessional data were provided by eight Improving Access to Psychological Therapies (IAPT) services from four National Health Service (NHS) Trusts within the North and Central East London (NCEL) IAPT Service Improvement and Research Network (SIRN; Saunders et al., 2020). The data were naturalistic, observational cohort practice-based data collected between 2008 and 2020 as part of standardised national outcome monitoring procedures mandated within IAPT (NHS Digital, 2019). IAPT services offer evidence-based psychological interventions for common mental health disorders in a stepped-care model with patients receiving “Low Intensity” psychological interventions such as guided self-help and group interventions or “High Intensity” psychological interventions, consisting predominantly of cognitive behavioural therapy in addition to interpersonal psychotherapy and dynamic interpersonal therapy, in accordance with the NICE guidelines (NICE, 2011).

Sample Selection

The current study used two samples. The first sample included all cases with presenting problems (informal diagnosis used by IAPT services) of any depressive or anxiety disorder, except specific phobia, on the clinical records and the second included only those with a recorded presenting problem of GAD, this second sample being a subgroup from patients within sample 1. Two samples were used due to the issues in accurate diagnosis of

GAD on the system and the likelihood of GAD cases misdiagnosed as a depressive or another anxiety disorder. The second sample, with only those patients allocated a GAD presenting problem, therefore would provide a sample of “probable” GAD allowing for a comparison in models between the classes from the wider group and a “GAD” subgroup.

Due to the focus on presenting problem, only cases from 2015 onwards were selected as this followed a service initiative to improve the recording of presenting problems to improve accuracy in the system, and better match patients to specific treatment-protocols. Individual data was included in each sample if they had at least three contacts with the service and had at least half of the items completed for each measure at each of the time points.

Following this selection, sample 1 consisted of 15920 patients whereas sample 2 consisted of 6017 patients, see table 1 for a comparison of characteristics of both samples.

Table 1

Descriptive statistics for Sample 1 and 2

Characteristics	**Sample 1: "Depressive and anxiety disorders" (n = 15920)**	**Sample 2: "Probable GAD" (n = 6017)**
Age, mean (S.D.)	39.22 (14.25)	37.28 (13.80)
Female, % (n)	67.70 (10346)	72.50 (4361)
Prescribed Medication, % (n)	39.20 (5998)	31.80 (1916)
Self-reported long-term condition, % (n)	26.80 (4102)	24.40 (1471)
Employed, % (n)	71.40 (10916)	85.30 (5134)
Baseline GAD-7, mean (S.D.)	13.65 (4.86)	14.77 (4.53)
Baseline PHQ-9, mean (S.D.)	15.12 (5.92)	12.35 (5.67)
Baseline WSAS, mean (S.D.)	19.17 (9.21)	16.19 (8.46)
Received low intensity treatment, % (n)	88.20 (13487)	93.67 (5636)

Measures

All patients complete questionnaires at the beginning of each session of their therapy as part of standardised outcome monitoring within IAPT. The primary outcome measures were the GAD-7 (Spitzer et al., 2006) and Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001).

Generalized Anxiety Disorder-7 (GAD-7)

The GAD-7 is a seven-item questionnaire measuring presence and severity of symptoms of Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) generalised anxiety in the past 14 days. The GAD-7 was developed from the diagnostic criteria for GAD within the DSM-IV in addition to four items from other established anxiety measures (Spitzer et al., 2006). Individual item scores are rated from 0 to 3 to indicate the frequency an individual experiences each symptom, ranging from “Not at all” to “Nearly every day” with an overall score of 8 or higher viewed as caseness for GAD in IAPT settings (NCCMH, 2020). The GAD-7 has demonstrated high internal consistency and sensitivity to change (Dear et al., 2011) and convergent and discriminant validity (Johnson et al., 2019).

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 is a measure of depression and is a subset of the Patient Health Questionnaire (PHQ) which is a self-administered version of the Primary Care Evaluation of Mental Disorders (PRIME-MD) diagnostic screening tool for common mental disorders (Spitzer et al., 1999). The PHQ-9 measures the presence and severity of symptoms of DSM-IV major depression in the past 14 days. Again, individual items are rated from 0 to 3 to indicate the frequency an individual experiences each symptom, ranging from “Not at all” to “Nearly every day”. Overall scores of 10 or higher have been determined to meet threshold for caseness of depression (NCCMH, 2020). The PHQ-9 has been demonstrated to have high internal consistency, reliability, convergent and discriminant validity, and responsiveness to change (Titov et al., 2011).

Despite the GAD-7 being a measure of GAD, as the disorder is frequently comorbid with depression and as the disorders share many features, the PHQ-9 was also included in the analysis as it could inform possible subgroups. Inclusion of this measure also allowed for

comparison of symptoms from the profiles within the wider group of depressive and anxiety disorders.

Work and Social Adjustment Scale (WSAS)

The WSAS (Mundt et al., 2002) is a five-item questionnaire which measures the impairment of functioning in the domains of work, home management, social leisure activities, private leisure activities and close relationships. Each item is rated on a scale of 0 to 8 to indicate the level of impact an individual views their mental health on their ability to function in each domain, with higher ratings representing more severe impairment. The WSAS has been demonstrated to have high internal reliability, convergent and discriminant validity, and sensitivity to change (Mundt et al., 2002; Zahra et al., 2014).

Other Data

Other data included in the analysis to capture baseline characteristics related to patients' demographics, including age, gender, employment status, long-term condition status, medication status, and levels of deprivation.

Statistical Analyses

An LTA was selected to meet the aims of this project as it allows for the measurement of the stability of latent classes over time and can model changes in the qualitative nature of the statuses. The term "latent status" has been proposed for use in LTA to represent latent classes which have been measured longitudinally and to indicate that membership can change in contrast to "latent class" used in LCA with cross-sectional data which cluster into more rigid classes (Collins & Lanza, 2010). LTAs estimate three parameters within the model: i) the latent status membership probabilities meaning the proportion individuals belonging to each latent class at each time point, ii) item-response probabilities which are the probability of a particular item (e.g., a symptom) being present in

membership to a certain class which allows for identification of potential key items to the class, and iii) transition probabilities which are the probabilities of transitioning from one latent class to another latent class at a later time point (Collins & Lanza, 2010). In the current study, the LTA approach was selected to model the stability of different subgroups within a broader population of those with depressive and anxiety disorders (except specific phobia) and a probable GAD population, examine any patterns in subgroup transitions, capture the varying intensity of symptom profiles that constitute the different subgroups with any particular dominant features, and the prevalence of statuses.

The LTA was conducted in Mplus Version 8 (Muthén & Muthén, 2017) using the mixture package on the item-level data of the GAD-7 and PHQ-9 from the first three sessions of therapy. The selection of only data from the first three timepoints was made as change is most likely to occur within the first 3 sessions (e.g., Catarino et al., 2020; Simmonds-Buckley et al., 2020) and to keep computational demands manageable.

The analytic procedure included fitting of multiple basic LTA models with the number of statuses successively increased until the best-fitting model is identified. Selecting the best fit of model was to be informed by the fit statistics Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC), the interpretability of statuses and, in accordance with prior modelling studies, which recommend classes each contain at least 5% of the sample to be clinically meaningful and interpretable (e.g., Gueorguieva et al., 2011; Saunders et al., 2019) with smaller classes argued to be spurious (Hipp & Bauer, 2006).

The internal consistency of the measures, GAD-7 and PHQ-9, was also calculated using McDonald's coefficient (McDonald, 1999).

If a subgroup (or subgroups) with typical GAD profiles of symptoms, namely higher endorsement on GAD-7 items, are found within the model for sample 2, exploratory multinomial logistic regressions will be used to determine if there are any features in the baseline demographic variables (age, gender, ethnicity, WSAS score, medication

prescription, and employment) that predict transition to any GAD subgroups. This aims to determine if there are any client variables that are predictive to later transition to emergent GAD. The analysis will be conducted in IBM SPSS Statistics (Version 25).

Results

Reliability of Measures

As an indicator of internal consistency, McDonald's coefficient (ω; McDonald, 1999) was calculated for each measure for both of the samples. In sample 1, ω = 0.832 for the GAD-7 and ω = 0.834 for the PHQ-9 and in sample 2, ω = 0.816 for the GAD-7 and ω = 0.827 for the PHQ-9. As the values for ω for both measures in each sample were between 0.7 and 0.95, the internal consistency was determined to be acceptable (McDonald, 1999).

Modelling Depressive and Anxiety Disorders States (Sample 1)

For the "Depressive and Anxiety disorders" sample, the LTA found the optimal fit of 6 states following the 5% rule to determine classes of clinical meaningfulness with frequency dropping below 5% at all time points for models utilising more than 6 states. The goodness-of-fit statistics did not indicate an alternative solution, as the AIC, BIC and sample-adjusted BIC values continued to decrease, (see Table 2).

Table 2

Goodness-of-fit indices and percentage sample of the smallest state for the 2- to 7-state models for the depressive and anxiety disorders sample

Number of States	AIC	BIC	Sample-adjusted BIC	% sample for smallest state
2	1657286.910	1658058.041	1657737.071	36.76
3	1594037.992	1595244.315	1594742.203	15.58
4	1568708.912	1570380.967	1569685.002	10.72
5	1548541.097	1550709.424	1549806.894	7.79
6	1535458.855	1538153.994	1537032.187	7.70
7	1523923.760	1527176.250	1525822.455	4.47

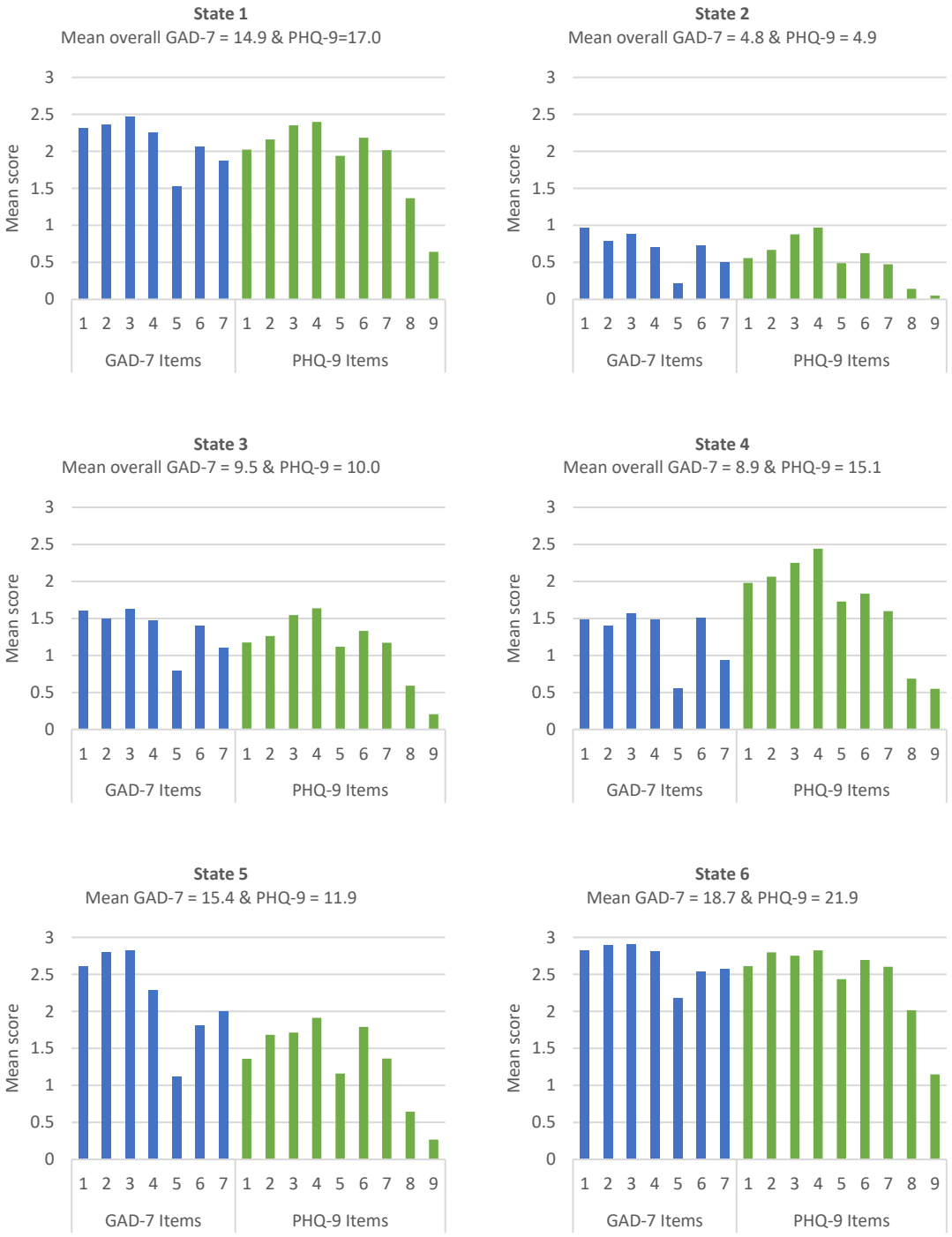
Figure 1 displays the mean total scores for both measures and mean rating intensity for each symptom-level item within these measures for each state. States 3, 1, and 6 showed similar patterns in endorsement of items across both measures with variation in the levels of intensity in ratings, which were considered to be mixed anxiety and depression with mild/moderate, moderate and severe groups. State 2 displayed low severity ratings across both measures, remaining below IAPT caseness level (GAD-7 ≥ 8 and PHQ-9 ≥ 10, NCCMH, 2020) and was considered a minimal symptoms group. State 4 was more focused towards PHQ-9 items with higher intensity ratings compared to those for GAD-7 items, appearing to be a loosely “depression” group. In contrast, State 5 had more severe intensity ratings for the GAD-7 items, with the most intense scores relating to items of worry (items 2 and 3 on GAD-7) and anxiety or feeling on edge (item 1), with some moderate intensity ratings on PHQ-9 items and was considered to be a “GAD” group. Across all states the

lowest intensity scores were the restless item on GAD-7 (item 5) and suicide and self-harm item on PHQ-9 (item 9).

With regards to individual items, there was a general pattern in the order of item severity ratings, with all subgroups rating the first four GAD-7 items the highest (relating to worry, feeling nervous and having trouble relaxing) with either the items related to irritability (item 6) or feeling afraid (item 7) the next highest and feeling restless (item 5) rated the lowest, apart from the “depression” subgroup which differed with irritability (item 6) on the rated second highest. As for the PHQ-9, the item related to feeling tired (item 4) was the highest rated item across all subgroups but with items 1 to 4 (little interest, feeling down, trouble sleeping, feeling tired), 6 (feeling bad about yourself) and 7 (trouble concentrating) were all rated to similar levels within each subgroup with the item regarding feeling better off dead (item 9) rated lowest.

Figure 1

A summary of the symptom profile and item intensity ratings for each depressive and anxiety disorders state from the optimal 6-state model.



The frequencies for the respective states in the depression and anxiety disorders sample are displayed in Table 3. State 1, the mixed moderate group, was the least frequent group at time 1 (7.69%) but the second most frequent by time 3 (21.03%). The most frequent state at time 1 was State 6 (25.26%), mixed severe group. State 2, the minimal symptoms group, and State 3, mixed mild/moderate group, were the only states to increase in frequency over the timepoints with State 3 becoming the most frequent group at time 3 (25.08%), with the two groups with lowest intensity symptoms constituting the highest proportion by time 3 again suggesting improvement on scores in early sessions. The “GAD” group, State 5, was the second most common state at time 1 (19.83%) but the second least frequent at time 3 (11.67%). The “depression” group, State 4, remained low frequency in comparison to the other groups, being the second least frequent group at time 1 (12.67%) and the least frequent group at times 2 and 3 time 3 (9.93% and 7.74% respectively).

Table 3

Membership frequencies and percentages at time 1, 2 and 3 for the 6 depression and anxiety cases

	Time 1	Time 2	Time 3
State 1	2989.08 (19.55)	2934.57 (19.19)	2736.95 (17.90)
State 2	1175.79 (7.69)	2172.20 (14.21)	3215.61 (21.03)
State 3	2293.37 (15.00)	3228.52 (21.12)	3835.40 (25.08)
State 4	1936.95 (12.67)	1518.26 (9.93)	1183.32 (7.74)
State 5	3031.98 (19.83)	2318.92 (15.17)	1785.00 (11.67)
State 6	3862.84 (25.26)	3117.53 (20.39)	2533.73 (16.57)

The probability of latent transitions within and between the different states over the three timepoints provide a picture of the stability of each state and trends in transitions between states. These transition probabilities between and within the different states for sample 1 are displayed in Table 4. Overall, states were most likely to remain in their starting state. State 2, minimal symptoms group, was the most stable of all states across both timepoints and any between-state transitions were most likely to be to State 3, mixed mild/moderate group, with 11.5% and 7.2% transitioning at times 2 and 3 respectively.

State 5, the “GAD” group, was one of the least stable with only 54.1% and 58.1% remaining in the State from time 2 and 3 respectively, although other states 1, 3, and 4 had similar levels. The most likely between-state transition for State 5 was to State 3 (21.1% and 23.4% from time 2 and 3), the mixed mild/moderate group. While the most likely between-state transition for State 3 was to State 2, the minimal symptoms, but second most likely to State 5 at time 2 (7.5%) but third most likely between-state transition at time 3 (5.4%) with transitioning within the mixed group more likely (6.2%). State 4, the “depression” group, were the second least likely at time 2 and least likely at time 3 to transition to State 5 (4.1% and 1% at time 2 and 3).

Table 4

Latent Transition Probabilities of States from Time 1 To Time 2 and Time 2 to Time 3

Time 1 Latent State Membership	Time 2 Latent State Membership					
	State 1	State 2	State 3	State 4	State 5	State 6
State 1	0.532	0.021	0.222	0.055	0.049	0.121
State 2	0.004	0.814	0.115	0.022	0.039	0.004
State 3	0.071	0.230	0.599	0.013	0.075	0.011
State 4	0.102	0.112	0.129	0.547	0.041	0.069
State 5	0.056	0.122	0.211	0.026	0.541	0.043
State 6	0.209	0.009	0.043	0.041	0.060	0.637
Time 2 Latent State Membership	Time 3 Latent State Membership					
	State 1	State 2	State 3	State 4	State 5	State 6
State 1	0.591	0.024	0.249	0.032	0.025	0.079
State 2	0.002	0.885	0.072	0.013	0.026	0.002
State 3	0.062	0.224	0.643	0.009	0.054	0.008
State 4	0.077	0.136	0.138	0.601	0.010	0.038
State 5	0.033	0.111	0.234	0.019	0.581	0.022
State 6	0.193	0.011	0.039	0.025	0.038	0.693

Intensity of Therapy

The percentage of patients receiving Low and High Intensity therapy in each state is displayed in Table 5. Overall, proportions of the two therapy intensities were similar between states. State 4, the “depression” group, received the highest percentage of Low Intensity therapy whereas State 6, the mixed severe group, received the highest percentage of High Intensity therapy.

Table 5

Percentage of Patients Within Each State Receiving Low or High Intensity Therapy

Class	Therapy **Intensity**	
	Low	High
1	91.64%	8.36%
2	90.77%	9.23%
3	92.83%	7.17%
4	93.33%	6.67%
5	91.07%	8.93%
6	88.59%	11.41%

Modelling GAD States (Sample 2)

For the probable GAD sample, the LTA produced an optimal model of 5 states following the 5% rule to determine classes of clinical meaningfulness with frequency dropping below 5% at all time points for models utilising more than 5 states. Again, the

goodness-of-fit statistics did not indicate an alternative solution, as the AIC, BIC and sample-adjusted BIC values continued to decrease (see Table 6).

Table 6

Goodness-of-fit indices and percentage sample of the smallest state for the 2- to 6-state models

Number of states	AIC	BIC	Sample-adjusted BIC	% sample for smallest state
2	602962.932	603634.260	603313.312	35.49
3	579741.873	580792.070	580792.070	13.41
4	569938.785	571394.438	570698.521	12.00
5	562752.239	564639.935	563737.467	5.97
6	558359.935	560706.261	559584.532	4.74

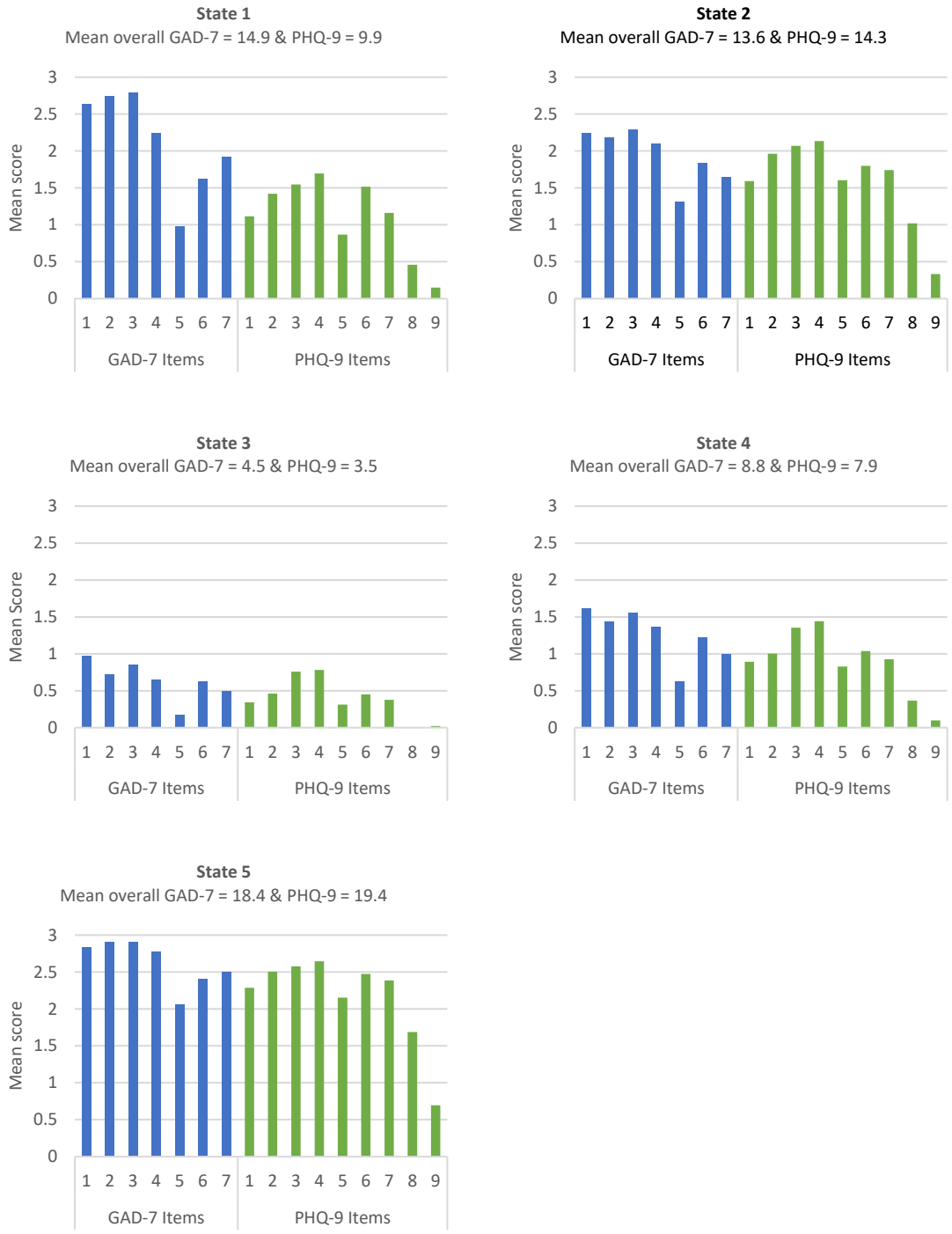
Figure 2 displays the mean overall scores for both measures and mean rating intensity for each symptom-level item within these measures for each state. State 1 shows a profile higher endorsement of GAD-7 items, particularly those items relating to worry (items 2 and 3 on the GAD-7) and anxiety or feeling on edge (item 1), with lower ratings for PHQ-9 items, therefore displaying a more distinct endorsement on GAD-7 items than the other states. As such, State 1 was considered to belong to a “GAD” group. States 2, 4 and 5 showed similar symptom profiles with similar levels of endorsement across both GAD-7 and PHQ-9 items in each but with variation in the item-level intensity between different the states, displaying a picture of mixed anxiety and depression with mild, moderate and severe presentations. State 3 displayed low severity ratings across all of the items, suggesting a low/minimal group and below caseness for IAPT on both measures. State 4 was also below

caseness for PHQ-9 but just met caseness for GAD-7. For all states the lowest endorsed items related to feelings of restlessness (item 5 on GAD-7) and suicide and self-harm (item 9 on PHQ-9). In contrast the peak item on GAD-7 varied between states whereas the peak PHQ-9 item was related to having trouble relaxing (item 4).

With regards to individual items, again there was a general pattern in the order of item severity ratings with items 1 to 4 on the GAD-7 rated the highest in all subgroups followed by items 6 or 7 and item 5 lowest. In the PHQ-9 ratings, items 3 and 4 were rated highest for all subgroups followed by either items 2 or 6 and then item 7 with items 8 and 9 rated lowest for all.

Figure 2

A summary of the symptom profile and item intensity ratings for each probable GAD state from the optimal 5-state model.



The frequencies for the respective states at each time point are displayed in Table 7. State 1 and State 5, the “GAD” and mixed severe groups respectively, were the most frequent states at time 1 but reduced in frequency over the timepoints to become the least frequent states at time 3. In contrast, State 3, the minimal symptoms group, made up lowest frequency by far (5.97%) but increased in prevalence over timepoints to become the second most common state (20.75%). By time 3, the most common state was State 4. Both States 3 and 4 were the only ones to increase in frequency over each timepoint whereas State 1, the “GAD” group, almost halved in frequency by time 3 reducing in frequency from the most common state at time 1 (27.30%) to the least frequent at time 3 (13.89%). By time 3, the most frequent was State 4 (31.03%), the mixed mild symptoms group. As State 3 and 4 suggest minimal symptoms, the increase in these classes likely represents patients getting better with a reduction in symptoms through the early sessions in therapy.

Table 7

Membership frequencies and percentages at times 1, 2 and 3 for the 5-state model of probable GAD cases

	Time 1	Time 2	Time 3
State 1	1554.13 (27.30)	1044.57 (18.35)	790.42 (13.89)
State 2	1085.37 (19.07)	1218.46 (21.41)	1100.63 (19.34)
State 3	339.53 (5.97)	759.70 (13.35)	1180.85 (20.75)
State 4	1193.53 (20.96)	1583.96 (27.83)	1766.05 (31.03)
State 5	1519.84 (26.70)	1085.31 (19.07)	854.05 (15.00)

The transition probabilities between and within states over the timepoints are displayed in Table 8. Overall, states were most likely to remain in their starting state, with

State 3 (the minimal symptoms group) being the most stable across all three timepoints with few transitions to more severe states with the highest transitions between time 1 and 2 to State 4 (12%), mixed mild symptoms group. Trends across the states were if they did transition to another state, they were most likely to transition to State 4 at both timepoints apart from State 5, the severe group, and all states were least likely to transition to State 5. In the mixed groups of increasing severity, States 4, 2 and 5, when transitioning between states there was a trend to most likely transition to the lower severity mixed group.

Focusing on the “GAD” group, State 1 was the least stable of all the states with only 50.9% and 57.1% remaining in the State from time 2 and 3 respectively. There were very few transitions at either time point from States 2 and 3 to State 1. State 4, mixed mild group, was the most likely to transition to State 1, with 7.7% and 6.3% transitioning at time 2 and 3 respectively. State 5, mixed severe group, 7% transitioned at time 2 and 6% time 3 to State 1.

Table 8

Latent transition probabilities of states from time 1 to time 2 and time 2 to time 3

Time 1 Latent State Membership	Time 2 Latent State Membership				
	State 1	State 2	State 3	State 4	State 5
State 1	0.509	0.056	0.105	0.282	0.049
State 2	0.034	0.575	0.029	0.274	0.088
State 3	0.044	0.009	0.824	0.120	0.004
State 4	0.077	0.075	0.228	0.603	0.017
State 5	0.073	0.273	0.009	0.058	0.587
Time 2 Latent State Membership	Time 3 Latent State Membership				
	State 1	State 2	State 3	State 4	State 5
State 1	0.571	0.038	0.100	0.271	0.020
State 2	0.014	0.587	0.031	0.274	0.094
State 3	0.018	0.006	0.911	0.064	0.002
State 4	0.063	0.065	0.212	0.654	0.007
State 5	0.059	0.220	0.012	0.060	0.650

Intensity of Therapy

The percentage of Low and High Intensity therapy received by patients in each state is displayed in Table 9. Overall, percentages of the two therapy types were very similar with range of less than 2% between all states for each therapy. State 4, the mixed mild group, received the highest proportion of Low Intensity therapy whereas State 5, mixed severe group, had the highest proportion of High Intensity therapy.

Table 9

Percentage of Patients Within Each State Receiving Low or High Intensity Therapy

Class	Intensity	
	Low	High
1	94.83%	5.17%
2	93.59%	6.41%
3	93.88%	6.12%
4	95.16%	4.84%
5	93.18%	6.82%

Comparisons Between the Two Models

The models of the two samples, the “Depressive and Anxiety disorders sample” (Sample 1) and the “probable GAD sample” (Sample 2), shared some similar features but also differed in particular aspects.

Both models included a “GAD” group, mixed anxiety and depression groups with similar patterns of increasing severity, and a minimal symptoms group. Both “GAD” groups appeared to have similar pattern of item-level severity rating although the PHQ-9 items were of slightly higher intensity in sample 1. The groups of mixed symptoms increasing intensity followed similar patterns in item intensity ratings across both but with more intense PHQ-9 item ratings also in sample 1. The model for sample 1 also had the additional “depression” group which did not feature in sample 2 states.

In the proportions of each state in the two samples differed in their highest proportion at time 1. For sample 1, the most common state was the severe mixed group whereas for sample 2 this was the “GAD” group. By time 3, in both models the mixed mild symptoms group represented the highest membership and while in both the minimal symptoms groups were initially the least frequent group but by time 3 were the second most frequent. In sample 1 the least common group at time 3 was the “depression” group whereas for sample 2 it was the “GAD” group.

For the group transition probabilities for both samples, groups were most likely to remain in their starting state over the timepoints. For both “GAD” groups in either sample, the most likely between-state transitions were from the mixed mild groups (with 7.5% and 7.7% transitioning at time 2, and 5.4% and 6.3% at time 3) followed by the mixed severe groups (6.0% and 7.3% at time 2 and 3.8% and 5.9% at time 3). The moderate and severe mixed groups were most likely to transition within the mixed groups transition to a less severe state and the mild mixed groups were most likely to transition to the minimal symptoms group.

Subgroups in both samples displayed a similar pattern of symptom endorsement with all subgroups, only differing on the rating severity. For the GAD-7, items 1 to 4 were rated highest across all subgroups in both samples and item 5 the lowest, apart from the depression subgroup in sample 1 in which item 6 was rated second highest. For the PHQ-9,

item 4 was rated highest in all subgroups with the next four highest rated items varying between subgroups but items 5, 8 and 9 rated lowest in order.

Finally, the proportion of High and Low Intensity Therapies differed slightly between the two models, with those States in sample 2 overall receiving a higher proportion of Low Intensity therapies than those in sample 1. Both Severe mixed groups received the highest percentage of High Intensity therapy compared to other states in their models however this percentage was larger for this State for sample 1 (6.82% versus 11.41%). In contrast, the "depression" group from sample 1 and mixed mild group from sample 2 received the highest rates of Low Intensity therapy in their respective models and rates were similar with 93.33% receiving this in "depression" group and 95.16% in the mixed mild group.

Baseline Variables Associated with Transition to State 1 At Time 2 Or 3

Exploratory post-hoc analysis was conducted to explore the association between time 1 variables for States 2 to 5 a later transition to State 1 ("GAD" group) in the probable GAD sample (sample 2). These were analysed using multinomial logistic regression models with transition to State 1 as a binary variable with the reference category as No transition. Table 10 displays the baseline variables included in the analysis, the Odds Ratios (ORs), 95% confidence intervals (CI) and p-values for each in reference to odds of transition from the baseline state to State 1.

Most variables were found not to be associated with transition to State 1. Being female in State 4 at time 1 was significantly associated with transition to State 1 and lower WSAS score was associated with transition from State 5. No other variables were found to be associated with the likelihood of transitioning to State 1 in time 2 or 3.

Table 10

Associations between characteristics at baseline with transition to State 1 at time 2 or 3 in sample 2 (probable GAD)

Time 1 predictor		State at time 1 ORs (95% CI), *p*-value			
		State 2	State 3	State 4	State 5
	Age	.99(.97-1.02) *p*=.567	1.01(.98-1.04) *p*=.525	1.00(.99-1.02) *p*=.615	1.01(.99-1.02) *p*=.325
Gender	Female	.58(.30-1.12), *p*=.106	3.73(.81-17.16), *p*=.091	1.72(1.08-2.73), ***p*<0.05**	1.20(.79-182), *p*=.407
	Male	1.0	1.0	1.0	1.0
Ethnicity	White	1.35(.58-3.11), *p*=.485	1.00(.26-3.80), *p*=.996	1.33(.73-2.40), *p*=.351	1.09(.72-1.64), *p*=.685
	BAME	1.0	1.0	1.0	1.0
	WSAS Score	1.01(.96-1.06) *p*=.780	.99(.90-1.08) *p*=.810	1.01(.98-1.04) *p*=.533	.96(.94-.98) ***p*<0.001**
Medication	Not prescribed	1.23(.61-2.49) *p*=.570	.55(.17-1.80) *p*=.326	1.15(.72-1.84) *p*=.555	1.08(.74-1.58) *p*=.674
	Prescribed	1.0	1.0	1.0	1.0
Employment status	Employed	.85(.34-2.11) *p*=.723	0.92 *p*=1.000	1.14(.53-2.43) *p*=.742	1.50(.96-2.37) *p*=.078
	Unemployed	1.0	1.0	1.0	1.0

Discussion

This study represents the first investigation using an LTA to explore the nosology of GAD using a large sample of people attending routine psychological treatment services. The study aimed to determine the presence of subgroups within the disorder and their characteristics in terms of their patterns of different anxiety and depression symptoms, temporal stability over the first three sessions and how these symptom profiles compared between a wider sample of cases from a population of those with depressive and anxiety disorders and those with probable GAD.

For sample 1, the study identified 6 anxiety and depressive states based on symptoms endorsed in self-report patient's data from GAD-7 and PHQ-9 questionnaires. Based on their qualitative features, the 6 states were classified as "depression" (12.67% of the sample at time 1), "GAD" (19.83%), minimal depression and anxiety symptoms (7.69%), mild mixed depression and anxiety (15.00%), moderate mixed depression and anxiety (19.55%), and severe mixed depression and anxiety (25.26%) states. By time 3, the "GAD" and "depression" states made up the lowest portions of the sample (11.67% and 7.74% respectively).

For the probable GAD sample, the study identified 5 GAD states. Based on their qualitative features, the 5 states were classified as "GAD" (27.30% of the sample at time 1), minimal depression and anxiety symptoms (5.97%), mild mixed depression and anxiety (20.96%), moderate mixed depression and anxiety (19.07%), and severe mixed depression and anxiety (26.70%) states. By time 3, the "GAD" state constituted only 13.89% of the sample.

The primary objective of this study was to use an LTA to identify subtypes of GAD represented by different profiles of GAD and depression symptoms. The identified subgroups for sample 2, the probable GAD sample, demonstrated that the majority of the cases labelled with and receiving treatment for GAD in this population (over 65% of the

sample) had mixed depression and anxiety presentations with each of these mixed subgroups having a roughly uniform endorsement of anxiety and depression symptoms but differing in levels of severity ratings of these items. However, the “GAD” subgroup which was found in both samples was characterised by a split within the measures with noticeably higher scores on the GAD-7 than PHQ-9, and particularly higher intensity ratings on the items related to feeling anxious and both worry items (items 1, 2, and 3 on the GAD-7). When including patients with depression and other anxiety disorders in the sample (sample 1) the same classes were identified, but with one addition of depressive-type subgroup. It therefore seems that while a proportion of individuals with probable GAD present with predominant GAD symptoms, the majority present with mixed, non-disorder-specific features with no distinguishing symptom features between subgroups of differing severity. This is in line with substantial evidence of depressive disorders comorbidity in GAD presentations (Nutt et al., 2006; Ter Meulen et al., 2021). While most in the “GAD” subgroup remained in the same state by time 3, it was the least stable of all the subgroups and by time 3 the “GAD” subgroup represented only 13% of sample 2, a reduction of over half, with the remaining proportion made up from subgroups of mixed depression and anxiety symptoms of differing severity. The high proportion of mixed symptoms in a purported sample of individuals with probable GAD perhaps demonstrate the blurred boundaries between GAD and depressive disorders and lack of clear features distinguishing the disorders which make GAD difficult to detect for clinicians (e.g., Brown et al., 2001; Zbozinek et al., 2012). Prior research has found that overlap symptoms is particularly common in subthreshold cases of anxiety and depression (Wittchen et al., 1999), which may be applicable to cases in this study.

In the probable GAD sample, for those in the “GAD” subgroup at baseline, when transitioning between groups most transitioned into the mixed mild subgroup (28.2% and 27.1% at times 2 and 3) followed by the minimal symptoms subgroup (10.5% and 10.0%), with all symptom ratings reducing to at most mild levels. Very few transitioning to the

moderate and severe mixed groups, a change which would be characterised by higher ratings of severity endorsement on the depression measures. Yet, instead a reduction in ratings of particularly GAD symptom intensity was the more common transition with almost 40% of baseline “GAD” states transitioning in this way over the timepoints. It seems despite initially appearing more anxious, and a more typical GAD-like presentation, from the second session onwards ratings on both the GAD-7 and PHQ-9 dropped to similar levels. Perhaps related to the anxiety of beginning therapy, communicating a need, or feeling less anxious after engagement with services or receipt of a diagnosis followed by the real presentation afterwards of symptoms below caseness and not true GAD cases. Such an increase in these milder classes also may be representative of patterns within IAPT with improvement and reduction in symptoms shown to occur early within therapy for particular groups (Saunders et al., 2019).

In contrast when considering those subgroups which transitioned into the “GAD” subgroup in the probable GAD sample, the most frequent transition came from the mild mixed subgroup (7.7% and 6.3% at times 2 and 3) was characterised by an increase in GAD symptom endorsement, particularly items 1 to 4, and most with only a slight increase in depression scores. Similar transition rates were found from the severe mixed subgroup (7.3% and 5.9%) with the change characterised by slight reduction in GAD symptom severity whilst GAD-7 items 1 to 4 remained high, alongside a large reduction in severity ratings of depression symptoms. Perhaps in these instances there is a re-evaluation of symptoms, either an increase in GAD ratings in the former or a reduction of depression ratings in the latter after being labelled with GAD, and a GAD presentation emerging after learning about the condition and perhaps re-evaluating their experiences which were not previously considered an issue as a disorder requiring treatment (Arroll & Kendrick, 2009; Culpepper & Conner, 2004). Such a pattern would be in line with evidence that few individuals with GAD present for support with worry, the main feature of GAD, and instead seek help for other associated symptoms such as somatic complaints and view cognitive features of the

disorder such as worry as part of themselves and not the issue (Culpepper & Conner, 2004). Interestingly, those in the moderate mild subgroup, who had a higher endorsement of depression symptoms, were the least likely to transition to the “GAD” state. Of note is the increased likelihood of females to transition to the “GAD” subgroup from the mixed mild subgroup which is in line with evidence that GAD is more prevalent in women (e.g., Kessler et al., 1994; Mclean et al., 2011).

The “GAD” and “depressive” groups in sample 1 were the least likely to transition to one another, suggesting more distinct states which contrasts some who argues for the disorders to be grouped (e.g., Vollebergh et al., 2001). However, notably in both samples the majority of the population was made up of states of mixed symptom profiles. Unlike Rhebergen and colleague’s (2014) study which only found mixed groups of anxiety and depression symptoms in an LCA of a GAD and dysthymia population, the current study found seemingly disorder-like profiles in addition to the mixed states which comprised most of the sample. This may be due to the overlap in symptoms within dysthymia and GAD (Andrews et al., 2002; Shores et al., 1992) whereas the current study included a range of diagnoses including depression. However, the mixed states identified in both samples did increase in proportion of the sample over the timepoints to comprise most of the sample at time 3 in both samples, with the samples therefore becoming a homogenous group over time akin to that found in previous research (Rhebergen et al., 2014).

Interestingly, no individual symptom or groups of symptoms were able to distinguish the different states with the only quality differentiating the subgroups in either sample was the overall total GAD-7 and PHQ-9 scores. In both samples, the mixed subgroups displayed similar trends in symptom endorsement across both measures and only differing in overall severity rating for the items whereas the “GAD” and “depression” subgroups were distinguished by higher endorsement of items on the corresponding disorder-specific measure and lower for those on the other measure. This lack of distinguishing features and with groups only differentiated by overall scores as opposed to any key features was a

similar finding to that found by Rhebergen and colleagues (2014) but crucially differing with the current study finding the emergence of more disorder specific subgroups from both samples however, like previous research, the majority of cases presented with mixed symptoms.

As for the psychological interventions, both samples received overall similar proportions of Low to High Intensity therapy but with the probable GAD sample receiving slightly higher rates of Low Intensity therapy. Comparing states within each model, proportions were similar across all in sample 2 and for all except the severe mixed group in sample 1 which received higher rates of High Intensity therapy compared to other groups in the model which would be in line with recommended treatment pathways (NICE, 2011).

Overall, it seems that the "GAD" subgroup could be distinguished from other profiles by a pattern of higher endorsement of GAD and lower endorsement of depression symptoms, rather than any specific individual features on the measures. However, most cases with probable GAD in sample 2 present with similar levels of depression and anxiety symptoms and these did not considerably differ from profiles found the wider depressive and anxiety disorders in sample 1. In line with previous research, this highlights the endorsement and norm of comorbid depression symptoms almost to similar levels of GAD symptoms in those with diagnosed GAD (Lamer et al., 2011; Lieb et al., 2005) and demonstrates the overlap between disorders in these groups with mixed symptoms presentations regardless of depression or anxiety disorder diagnosis (Rhebergen et al., 2014).

Of particular note are the cases which transition in and out of the "GAD" subgroups, with a portion reducing anxiety symptom ratings after session 1 to present with mild presentations and another portion transitioning into the disorder over sessions with a GAD picture emerging after initial contact, suggesting for some the presentation is initially masked (Argyropoulos et al., 2006; Portman et al., 2011). The similarity in states identified between the two samples, lack of dominant features in the symptom profiles with most sharing similar

patterns of features and temporal instability of states demonstrates why it is difficult to detect GAD and highlight the need to better characterise features of the disorder to aid recognition.

Strengths and Limitations

This study applied a novel statistical technique to identify changes in the constellation of symptoms within subgroups of case of probable GAD and comparison of profiles to a wider anxiety and depressive disorders group. The current approach allowed for the capture of transitions in subgroups beyond one time point, as would be the case for LCA which has been used in prior studies in this area, and so demonstrated the reduction in the frequency disorder specific presentation in the sample and the increase in mixed symptoms which otherwise would not have been captured using previous approaches. The study also had large sample of patients accessing psychological treatment in IAPT services and the dataset included sessional item-level questionnaire data.

A key limitation of the study is the reliability of the GAD presenting problem used to determine inclusion into the probable GAD sample (sample 2). A challenge was determining a method to identify those with a GAD diagnosis using the dataset. As per IAPT protocol, the allocation of the presenting problem would be completed by Psychological Wellbeing Practitioners who assess patients referred to IAPT services and allocate to the relevant stepped care intervention for their presenting problem. As a result, the diagnoses recorded as the presenting problem are not reliable and therefore the subgroup analysis represents those perhaps more likely to have a GAD presentation but of which the accuracy of the diagnostic classification cannot not be confirmed, hence the “probable GAD” label and even more so given the diagnosis that is difficult to accurately diagnose for even experienced professionals (Reed et al., 2018; Wittchen et al., 2002). This led to the decision to utilise a wider sample with range of anxiety and depressive disorders and to compare similarities between the final states to that in a probable GAD sample. This therefore limits the validity of

conclusions that can be drawn about the diagnosis of GAD from the subgroup analysis. The option to select those with a GAD presenting problem who also presented with initial GAD-7 scores above certain thresholds to deem caseness or a certain level of severity was considered however it was determined this would potentially also remove those with less severe cases of GAD which could inform presentations of the disorder and would also not remove the high likelihood that a portion in the selected group did not have GAD.

The conclusions may also be limited as the individual patient data is taken from urban IAPT services, while likely similar it the findings may not be representative of presentations outside such areas. Additionally, the sample are self-selecting individuals who sought treatment for their condition and were deemed suitable for a primary care level intervention so will not capture all presentations of GAD, for example many with the disorder are thought to view their worry as part of their personality and less likely to seek help (Culpepper & Conner, 2004) or those with more severe presentations which would not meet criteria for an IAPT intervention. The states presented in this study are therefore only representative of mild to moderate disorders which are treated in IAPT settings (NICE, 2011). However, the sample is therefore representative of patients presenting with common mental health disorders and therefore relevant to practice in IAPT settings.

While the GAD-7 and PHQ-9 are valid measures of DSM-IV GAD and depression, a limitation of using these measures to investigate the nosology of a disorder is that features are limited to those in contained in the items of the measures and so does not allow for exploration beyond these. This is crucial given the proposition by some that other symptoms such as muscle tension (Faravelli et al., 2012) or anger (Hackmann et al., 2019) could be potential candidates for alternative key features in GAD which could aid conceptualisation and detection of the disorder, and particularly given high overlap with depressive symptoms in the diagnostic criteria, and seen in this sample, could potentially provide features which better distinguish GAD from depression.

Clinical Implications

As the data was obtained from IAPT settings, the current study has particular relevance and clinical applicability such services. The current study highlights how often depression is present in cases of GAD with the different symptom profiles demonstrating that the most common presentations are ones of mixed anxiety and depression symptoms which may aid recognition by acknowledging common presentations in the disorder. Also, awareness of the nature of transitions within these GAD presentations from baseline could aid detection of the disorder, highlighting profiles likely to transition early within therapy and particularly those symptom profiles which are more likely to transition to present with emergent GAD, who may not receive the correct diagnosis at assessment and receive treatment for another disorder. The association of females with the likelihood of transitioning from a mild state to GAD group provides a demographic for clinicians to be aware of who may initially present with mixed anxiety and depressive symptoms but are more likely to emerge with a GAD presentation. Additionally, the prevalence of depression symptoms within all GAD profiles suggests that it may be key for interventions to focus on features from both disorders.

Future Directions for Research

The current study demonstrates the presence of subgroups within GAD and the stability of features and transitions within these groups. There has been little research investigating the impact of different symptom profiles in GAD the course and outcome of therapy which may provide insight around which subgroups of GAD may benefit most from therapy. The heterogeneity within the disorder may influence the course of therapy and could be a factor in the modest response rates to current GAD interventions (Hofmann et al., 2012; Springer et al., 2018), therefore research into the impact of different GAD presentations on therapy outcomes may provide a valuable insight. LTAs provide an

approach to investigate how individuals with different subtypes of GAD respond to therapy and so identifying which type or types of presentation are more responsive to treatment to better inform future CBT approaches or targeting of therapy offerings and improve outcomes. This approach could also be applied to GAD presentations in other settings, namely those with more severe presentations, and to other mental health conditions to better understand subgroups in the presentations and their responsiveness to therapy.

With the use of the routine outcome measures of GAD-7 and PHQ-9 in the current study limiting profiles to only features captured within these questionnaires, future research could also investigate the nosology of GAD using a similar approach but using additional measures of GAD that include somatic items or other features potentially relevant to the disorder, for example the Penn State Worry Questionnaire (Meyer et al., 1990) or The State-Trait Anxiety Inventory (Spielberger, 1983), which could identify other potential symptoms within subgroups of GAD, particularly any distinguishing features which the disorder currently lacks (Starcevic et al., 2012). Further research could also investigate different variables to look at the potential mechanisms for transition to GAD subgroups.

An alternative approach could involve using a qualitative approach to understand why GAD-7 scores increased in some cases, explore the potential for GAD symptoms to be re-evaluate leading to later emergence of GAD and factors involved in this transition.

Conclusions

GAD is a disorder constituted of mixed presentations of anxiety and depressive symptom with subgroups with few distinguishing features and, while most subgroups remaining stable, a large portion change in presentation over the initial sessions. Notably, a large portion of individuals with the disorder present with mixed anxiety and depressive symptoms which is a pattern shared by profiles within a broader group of anxiety and depressive disorders, highlighting the challenge for clinicians to accurately identify GAD. For

a portion GAD-7 scores were found to increase suggesting that for some the presentation of GAD emerges over the initial sessions.

References

Allgulander, C. (2006). Generalized anxiety disorder: What are we missing?. *European Neuropsychopharmacology*, *16*, S101-S108.

Altamura, A. C., Dell'Osso, B., D'Urso, N., Russo, M., Fumagalli, S. A. R. A., & Mundo, E. (2008). Duration of untreated illness as a predictor of treatment response and clinical course in generalized anxiety disorder. *CNS spectrums*, *13*(5), 415-422.

Andrews, G., Slade, T. I. M., & Issakidis, C. (2002). Deconstructing current comorbidity: data from the Australian National Survey of Mental Health and Well-being. *The British Journal of Psychiatry*, *181*(4), 306-314.

Arroll, B. & Kendrick, T. (2009) Anxiety. In *Primary Care Mental Health* (eds L. Gask, H. Lester, T. Kendrick & R. Peveler), pp. 147–149. Glasgow: Bell and Bain Ltd.

Ballenger, J. C., Davidson, J. R., Lecrubier, Y., Nutt, D. J., Borkovec, T. D., Rickels, K., ... & Wittchen, H. U. (2001). Consensus statement on generalized anxiety disorder from the International Consensus Group on Depression and Anxiety. *The Journal of clinical psychiatry*, *62*(suppl 11), 53-58.

Baxter, A. J., Scott, K. M., Vos, T., & Whiteford, H. A. (2013). Global prevalence of anxiety disorders: a systematic review and meta-regression. *Psychological medicine*, *43*(5), 897-910.

Bebbington, P. E., Brugha, T. S., Meltzer, H., Jenkins, R., Ceresa, C., Farrell, M., & Lewis, G. (2000). Neurotic disorders and the receipt of psychiatric treatment. *Psychol Med*, *30*(6), 1369-1376.

Bland, R. C., Newman, S. C., & Orn, H. (1997). Help-seeking for psychiatric disorders. *The Canadian Journal of Psychiatry*, *42*(9), 935-942.

Brown, T. A., Di Nardo, P. A., Lehman, C. L., & Campbell, L. A. (2001). Reliability of DSM-IV anxiety and mood disorders: implications for the classification of emotional disorders. *Journal of abnormal psychology*, *110*(1), 49-58.

Calleo, J., Stanley, M. A., Greisinger, A., Wehmanen, O., Johnson, M., Novy, D., ... & Kunik, M. (2009). Generalized anxiety disorder in older medical patients: diagnostic recognition, mental health management and service utilization. *Journal of clinical psychology in medical settings*, *16*(2), 178-185.

Carter, R. M., Wittchen, H. U., Pfister, H., & Kessler, R. C. (2001). One-year prevalence of subthreshold and threshold DSM-IV generalized anxiety disorder in a nationally representative sample. *Depression and anxiety*, *13*(2), 78-88.

Catarino, A., Fawcett, J. M., Ewbank, M. P., Bateup, S., Cummins, R., Tablan, V., & Blackwell, A. D. (2020). Refining our understanding of depressive states and state transitions in response to cognitive behavioural therapy using latent Markov modelling. *Psychological Medicine,* 1–10.

Clark, L. A., & Watson, D. (1991). Tripartite model of anxiety and depression: psychometric evidence and taxonomic implications. *Journal of abnormal psychology*, *100*(3), 316-336.

Collins, L. M., & Lanza, S. T. (2010). *Latent class and latent transition analysis: With applications in the social, behavioral, and health sciences* (Vol. 718). John Wiley & Sons.

Culpepper, L. (2002). Generalized anxiety disorder in primary care: emerging issues in management and treatment. *Journal of Clinical Psychiatry*, *63*, 35-42.

Culpepper, L., & Conner, K. (2004). Effective recognition and treatment of generalized anxiety disorder in primary care. *Prim. Care Companion J. Clin. Psychiatry*, *6*, 35-41.

Davidson, J. R., Feltner, D. E., & Dugar, A. (2010). Management of generalized anxiety disorder in primary care: identifying the challenges and unmet needs. *Primary care companion to the Journal of clinical psychiatry*, *12*(2), PCC.09r00772.

Dear, B. F., Titov, N., Sunderland, M., McMillan, D., Anderson, T., Lorian, C., & Robinson, E. (2011). Psychometric comparison of the generalized anxiety disorder scale-7 and the Penn State Worry Questionnaire for measuring response during treatment of generalised anxiety disorder. *Cognitive behaviour therapy*, *40*(3), 216-227.

Faravelli, C., Castellini, G., Benni, L., Brugnera, A., Landi, M., Sauro, C. L., ... & Ricca, V. (2012). Generalized anxiety disorder: is there any specific symptom?. *Comprehensive psychiatry*, *53*(8), 1056-1062.

Gladstone, G. L., Parker, G. B., Mitchell, P. B., Malhi, G. S., Wilhelm, K. A., & Austin, M. P. (2005). A Brief Measure of Worry Severity (BMWS): Personality and clinical correlates of severe worriers. *Journal of Anxiety Disorders*, *19*(8), 877-892.

Gueorguieva, R., Mallinckrodt, C., & Krystal, J. H. (2011). Trajectories of depression severity in clinical trials of duloxetine: insights into antidepressant and placebo responses. *Archives of general psychiatry*, *68*(12), 1227-1237.

Hackmann, C., Balhara, Y. P. S., Clayman, K., Nemec, P. B., Notley, C., Pike, K., ... & Shakespeare, T. (2019). Perspectives on ICD-11 to understand and improve mental health diagnosis using expertise by experience (INCLUDE Study): an international qualitative study. *The Lancet Psychiatry*, *6*(9), 778-785.

Hales R. E., Hilty, D. A. & Wise, M. G. (1997) A treatment algorithm for the management of anxiety in primary care practice. *Journal of Clinical Psychiatry*, *59* (Suppl. 3), 76–80.

Hipp, J. R., & Bauer, D. J. (2006). Local solutions in the estimation of growth mixture models. *Psychological methods*, *11*(1), 36-53.

Hofmann, S. G., Asnaani, A., Vonk, I. J., Sawyer, A. T., & Fang, A. (2012). The efficacy of cognitive behavioral therapy: A review of meta-analyses. *Cognitive therapy and research*, *36*(5), 427-440.

Johnson, S. U., Ulvenes, P. G., Øktedalen, T., & Hoffart, A. (2019). Psychometric properties of the general anxiety disorder 7-item (GAD-7) scale in a heterogeneous psychiatric sample. *Frontiers in psychology*, *10*, 1713.

Kertz, S. J., Bigda-Peyton, J. S., Rosmarin, D. H., & Björgvinsson, T. (2012). The importance of worry across diagnostic presentations: Prevalence, severity and associated symptoms in a partial hospital setting. *Journal of anxiety disorders*, *26*(1), 126-133.

Kessler, R. C., Andrade, L. H., Bijl, R. V., Offord, D. R., Demler, O. V., & Stein, D. J. (2002). The effects of co-morbidity on the onset and persistence of generalized anxiety disorder in the ICPE surveys. *Psychological Medicine*, *32*(7), 1213-1225.

Kessler, R. C., McGonagle, K. A., Zhao, S., Nelson, C. B., Hughes, M., Eshleman, S., ... & Kendler, K. S. (1994). Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. *Archives of general psychiatry*, *51*(1), 8-19.

Kessler, R. C., Keller, M. B., & Wittchen, H. U. (2001). The epidemiology of generalized anxiety disorder. *Psychiatric Clinics of North America*, *24*(1), 19-39.

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine*, *16*(9), 606-613.

Lamers, F., Comijs, H. C., Smit, J. H., Spinhoven, P., Nolen, W. A., Zitman, F. G., ... & Penninx, B. W. (2011). Comorbidity patterns of anxiety and depressive disorders in a large cohort study: the Netherlands Study of Depression and Anxiety (NESDA). *The Journal of clinical psychiatry*, *72*(3), 341-348.

Lieb, R., Becker, E., & Altamura, C. (2005). The epidemiology of generalized anxiety disorder in Europe. *European Neuropsychopharmacology*, *15*(4), 445-452.

Lydiard, R. B. (2000). An overview of generalized anxiety disorder: disease state—appropriate therapy. *Clinical therapeutics*, *22*, A3-A24.

McDonald, R. P. (1999). *Test Theory: A Unified Treatment*. L. Erlbaum Associates.

McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. *Journal of psychiatric research*, *45*(8), 1027-1035.

Mennin, D. S., Heimberg, R. G., Fresco, D. M., & Ritter, M. R. (2008). Is generalized anxiety disorder an anxiety or mood disorder? Considering multiple factors as we ponder the fate of GAD. *Depression and Anxiety*, *25*(4), 289-299.

Meyer, T. J., Miller, M. L., Metzger, R. L., & Borkovec, T. D. (1990). Development and validation of the penn state worry questionnaire. *Behaviour research and therapy*, *28*(6), 487-495.

Mojtabai, R., Olfson, M., & Mechanic, D. (2002). Perceived need and help-seeking in adults with mood, anxiety, or substance use disorders. *Archives of general psychiatry*, *59*(1), 77-84.

Mundt, J. C., Marks, I. M., Shear, M. K., & Greist, J. M. (2002). The Work and Social Adjustment Scale: a simple measure of impairment in functioning. *The British Journal of Psychiatry*, *180*(5), 461-464.

Muthén, L.K., & Muthén, B.O. (1998-2017). *Mplus User's Guide*. (8th ed.). Muthén & Muthén.

National Collaborating Centre for Mental Health (2020). *The Improving Access to Psychological Therapies Manual.* https://www.england.nhs.uk/publication/the-improving-access-to-psychological-therapies-manual/

National Institute for Health and Care Excellence. (2011). Common mental health problems: identification and pathways to care. [NICE Guideline No. 123]. https://www.nice.org.uk/guidance/cg123

National Institute for Health and Care Excellence. (2019). *Generalised anxiety disorder and panic disorder in adults: management* [NICE Guideline No. 113]. https://www.nice.org.uk/guidance/cg113

Newman, M. G., Przeworski, A., Fisher, A. J., & Borkovec, T. D. (2010). Diagnostic comorbidity in adults with generalized anxiety disorder: Impact of comorbidity on psychotherapy outcome and impact of psychotherapy on comorbid diagnoses. *Behavior Therapy*, *41*(1), 59-72.

NHS Digital. (2019). *Psychological Therapies A guide to IAPT data and publications.* Retrieved from:

https://digital.nhs.uk/binaries/content/assets/website-assets/data-and-information/data-sets/iapt/guide-to-iapt-data-and-publications.pdf

Noyes Jr, R. (1999). The relationship of hypochondriasis to anxiety disorders. *General Hospital Psychiatry*, *21*(1), 8-17.

Nutt, D., Argyropoulos, S., Hood, S., & Potokar, J. (2006). Generalized anxiety disorder: a comorbid disease. *European neuropsychopharmacology*, *16*, S109-S118.

Nylund, K. (2007). Latent transition analysis: Modeling extensions and an application to peer victimization (Unpublished doctoral dissertation). University of California, Los Angeles. Retrieved from http://www.statmodel.com/download/Nylund%20dissertation%20Updated1.pdf

Olatunji, B. O., Wolitzky-Taylor, K. B., Sawchuk, C. N., & Ciesielski, B. G. (2010). Worry and the anxiety disorders: A meta-analytic synthesis of specificity to GAD. *Applied and Preventive Psychology*, *14*(1-4), 1-24.

Portman, M. E., Starcevic, V., & Beck, A. T. (2011). Challenges in assessment and diagnosis of generalized anxiety disorder. *Psychiatric Annals*, *41*(2), 79-85.

Preisig, M., Merikangas, K. R., & Angst, J. (2001). Clinical significance and comorbidity of subthreshold depression and anxiety in the community. *Acta Psychiatrica Scandinavica*, *104*(2), 96-103.

Reed, G. M., Sharan, P., Rebello, T. J., Keeley, J. W., Elena Medina-Mora, M., Gureje, O., ... & Pike, K. M. (2018). The ICD-11 developmental field study of reliability of diagnoses of high-burden mental disorders: results among adult patients in mental health settings of 13 countries. *World psychiatry*, *17*(2), 174-186.

Regier, D. A., Narrow, W. E., Clarke, D. E., Kraemer, H. C., Kuramoto, S. J., Kuhl, E. A., & Kupfer, D. J. (2013). DSM-5 field trials in the United States and Canada, part II: Test-retest reliability of selected categorical diagnoses. *American Journal of Psychiatry*, *170*, 59–70.

Rhebergen, D., van der Steenstraten, I. M., Sunderland, M., De Graaf, R., Ten Have, M., Lamers, F., ... & Andrews, G. (2014). An examination of generalized anxiety disorder and dysthymic disorder by latent class analysis. *Psychological Medicine*, *44*(8), 1701-1712.

Roberge, P., Normand-Lauzière, F., Raymond, I., Luc, M., Tanguay-Bernard, M. M., Duhoux, A., ... & Fournier, L. (2015). Generalized anxiety disorder in primary care: mental health services use and treatment adequacy. *BMC family practice*, *16*(1), 1-11.

Roth, W. T., Doberenz, S., Dietel, A., Conrad, A., Mueller, A., Wollburg, E., ... & Kim, S. (2008). Sympathetic activation in broadly defined generalized anxiety disorder. *Journal of psychiatric research*, *42*(3), 205-212.

Roy-Byrne, P. P., & Wagner, A. (2004). Primary care perspectives on generalized anxiety disorder. *Journal of Clinical Psychiatry*, *65*, 20-26.

Saunders, R., Buckman, J. E., Cape, J., Fearon, P., Leibowitz, J., & Pilling, S. (2019). Trajectories of depression and anxiety symptom change during psychological therapy. *Journal of affective disorders*, *249*, 327-335.

Saunders, R., Cape, J., Leibowitz, J., Aguirre, E., Jena, R., Cirkovic, M., ... & Buckman, J. E. (2020). Improvement in IAPT outcomes over time: are they driven by changes in clinical practice?. *the Cognitive Behaviour Therapist*, *13*.

Shores, M. M., Glubin, T., Cowley, D. S., Dager, S. R., Roy-Byrne, P. P., & Dunner, D. L. (1992). The relationship between anxiety and depression: a clinical comparison of generalized anxiety disorder, dysthymic disorder, panic disorder, and major depressive disorder. *Comprehensive psychiatry*, *33*(4), 237-244.

Simmonds-Buckley, M., Catarino, A., & Delgadillo, J. (2021). Depression subtypes and their response to cognitive behavioral therapy: A latent transition analysis. *Depression and Anxiety*.

Spielberger, C. D. (1983). *Manual for the State-Trait Inventory STAI (Form Y)*. Palo Alto, CA: Mind Garden.

Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of internal medicine*, *166*(10), 1092-1097.

Spitzer, R. L., Kroenke, K., Williams, J. B., Patient Health Questionnaire Primary Care Study Group, & Patient Health Questionnaire Primary Care Study Group. (1999). Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. *Jama*, *282*(18), 1737-1744.

Springer, K. S., Levy, H. C., & Tolin, D. F. (2018). Remission in CBT for adult anxiety disorders: a meta-analysis. *Clinical psychology review*, *61*, 1-8.

Starcevic, V., Portman, M. E., & Beck, A. T. (2012). Generalized anxiety disorder: between neglect and an epidemic. The Journal of nervous and mental disease, 200(8), 664-667.

Startup, H., Freeman, D., & Garety, P.A. (2007). Persecutory delusions and catastrophic worry in psychosis: developing the understanding of delusion distress and persistence. *Behaviour Research and Therapy*, *45*(3), 523-537.

Sunderland, M., Mewton, L., Slade, T., & Baillie, A. J. (2010). Investigating differential symptom profiles in major depressive episode with and without generalized anxiety disorder: true co-morbidity or symptom similarity?. *Psychological medicine*, *40*(7), 1113-1123.

Ter Meulen, W. G., Draisma, S., van Hemert, A. M., Schoevers, R. A., Kupka, R. W., Beekman, A. T., & Penninx, B. W. (2021). Depressive and Anxiety Disorders in Concert–a synthesis of Findings on Comorbidity in the NESDA study. *Journal of Affective Disorders, 284,* 85-97.

Titov, N., Dear, B. F., McMillan, D., Anderson, T., Zou, J., & Sunderland, M. (2011). Psychometric comparison of the PHQ-9 and BDI-II for measuring response during treatment of depression. *Cognitive behaviour therapy*, *40*(2), 126-136.

Tylee, A. & Walters, P. (2007) Underrecognition of anxiety and mood disorders in primary care: why does the problem exist and what can be done? *Journal of Clinical Psychiatry*, *68*, 27–30.

Ulbricht, C. M., Chrysanthopoulou, S. A., Levin, L., & Lapane, K. L. (2018). The use of latent class analysis for identifying subtypes of depression: A systematic review. *Psychiatry research*, *266*, 228-246.

Vollebergh, W. A., Iedema, J., Bijl, R. V., de Graaf, R., Smit, F., & Ormel, J. (2001). The structure and stability of common mental disorders: the NEMESIS study. *Archives of general psychiatry*, *58*(6), 597-603.

Weiller, E., Bisserbe, J. C., Maier, W., & Lecrubier, Y. (1998). Prevalence and recognition of anxiety syndromes in five European primary care settings: a report from the WHO study on Psychological Problems in General Health Care. *The British Journal of Psychiatry*, *173*(S34), 18-23.

Weisberg, R. B., Beard, C., Pagano, M. E., Maki, K. M., Culpepper, L., & Keller, M. B. (2010). Impairment and functioning in a sample of primary care patients with generalized anxiety disorder: results from the primary care anxiety project. *Primary care companion to the Journal of clinical psychiatry*, *12*(5).

Wittchen, H. U. (2002). Generalized anxiety disorder: prevalence, burden, and cost to society. *Depression and anxiety*, *16*(4), 162-171.

Wittchen, H. U., Kessler, R. C., Beesdo, K., Krause, P., & Hoyer, J. (2002). Generalized anxiety and depression in primary care: prevalence, recognition, and management. *The Journal of clinical psychiatry*, *63*(suppl 8), 24-34.

Wittchen, H. U., Zhao, S., Kessler, R. C., & Eaton, W. W. (1994). DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. *Archives of general psychiatry*, *51*(5), 355-364.

Wittchen, H. U. & Jacobi. F. (2005). Size and Burden of mental disorders in Europe: a critical review and appraisal of 27 Studies. *European Neuropsychopharmacology, 15,* 357-376.

Zahra, D., Qureshi, A., Henley, W., Taylor, R., Quinn, C., Pooler, J., ... & Byng, R. (2014). The work and social adjustment scale: reliability, sensitivity and value. *International journal of psychiatry in clinical practice*, *18*(2), 131-138.

Zbozinek, T. D., Rose, R. D., Wolitzky-Taylor, K. B., Sherbourne, C., Sullivan, G., Stein, M. B., ... & Craske, M. G. (2012). Diagnostic overlap of generalized anxiety disorder and major depressive disorder in a primary care sample. *Depression and anxiety*, *29*(12), 1065-1071.

Part 3: Critical Appraisal

Introduction

This critical appraisal will discuss some of the themes and topics of reflection that occurred whilst completing the conceptual introduction and empirical research. Firstly, will begin reflections on nosological approaches to psychopathology which arose following my investigation into the literature around different elements of the nosology of Generalized Anxiety Disorder (GAD) and consider the role of psychologists in diagnostic services and challenging such systems. I will then discuss the process and reflections on the process of deciding the research methodology and how decisions were made to select the final approach and limits this potentially imposed on the final conclusions. Finally, I will reflect on the experience of completing a secondary data analysis with flawed systems and the impact this had on the research.

Challenging The Status Quo Of Current Diagnoses

Prior to beginning the research, I had never given much thought to the historical origins of any mental health disorder or questioned the validity of disorders, but particularly common disorders, as being independent entities. Perhaps assuming they had already been studied to a high standard and based on a certain level of evidence, I simply accepted them as an unquestionable element of any work within mental health services. However, over the course of completing this thesis I began more to question my own stance of default acceptance of current nosology as the only possible way of working with classification of disorders and organisation of mental health care provision.

As the standard approach, diagnostic classification systems are central to current policy, research, and treatment of mental health disorders (Hackmann et al., 2019; Harper, 2013). The level of influence varies in current planning and organisation of services with the some trusts opting for explicit disorder-specific services or even “pseudo-diagnostic” groupings of similar disorders under one service with typically the only non-diagnostic

informed provision coming from services catered to individuals grouped by certain experiences such as specialist trauma clinics or veteran services but still using diagnostic labels within their work (Allsopp & Kinderman, 2021). Therefore, diagnoses play a large role in the work of psychologists in any of these services.

I can appreciate that while diagnostic classifications are far from perfect, they serve a key purpose. Diagnoses provide a unified framework for clinicians, clients and researchers by defining the clusters of symptoms that constitute a disorder allowing them to be recognised reliably by different parties with agreement of what the entity represents. This also allows for research to be conducted into disorders and different treatments. For individuals with the disorders, having a label for their difficulties can also validate and help understand their experiences (Hackmann et al., 2018). Any new approach to classification of mental health difficulties would therefore need to at least provide similar functions or improve upon the current system.

However, having the time to research one diagnosis in-depth for the conceptual introduction provided a live example of the weaknesses of current classification systems. GAD's poor validity and reliability, symptom and diagnostic overlap with other disorders, norm of comorbidity and temporal heterogenetic continuity are seemingly just representative of the wider issues of using the current categorical system to define naturally multidimensional entities (Clark et al., 2017). The current diagnostic system appears unable to capture the heterogeneity and complexity of mental health presentations (Cuthbert & Insel, 2013), reducing presentations down to certain features whilst ignoring the close relationships and overlap between disorders. Some have argued the current system has aimed for reliability of concepts at the cost of validity (Insel, 2013).

While other alternative approaches to classifying mental health needs have been proposed, none have become established enough to challenge the two prevailing systems of *Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Classification of Diseases (ICD).* The Research Domain Criteria (RDOC, Insel, 2014) was suggested by its

authors to be a more evidence-based framework, focused on identifying underlying neurobiological causes for dimensional behaviours as opposed to the traditional approach in current systems of focusing only on observable behaviours. However, it is yet to be implemented within clinical work and remains within a conceptual framework stage. Even psychological formulations have been positioned by some as an alternative to diagnosis (Johnstone, 2018) on the basis that diagnoses ignore the social and adversity factors leading to difficulties but currently formulation remains mostly only within psychological systems. Yet psychological formulations, apart from perhaps those using a psychodynamic approach have been shown to have worse reliability than diagnoses with little agreement between psychologists (Flinn et al., 2015). More recently within psychology, the Power Threat Meaning Framework (Johnstone & Boyle, 2018) has also been proposed as an optional alternative to diagnostic approaches to classifying different patterns of presentation into groups based on the influence of power imbalances within different psychological and sociological factors but has been met with criticism for reducing all mental health as caused by psychosocial adversities and threats and remains a single document unlikely to challenge current systems.

Despite the existence of proposed alternatives each with evidence of varying levels, none have challenged the current diagnostic systems and it is unclear how an alternative system would be implemented. Any move away from the established approaches would be costly, time-consuming and require a lot of research to overhaul a system that is currently ingrained at many levels of current mental health provision. For example, any change would involve revising legal or regulatory barriers that invoke psychiatric diagnoses like the mental health act or mental capacity act or change in the way mental health difficulties are researched. Some have argued that for change to happen the view that diagnoses are needed for service planning and delivery needs to be challenged and there is evidence of some trusts already achieving this through movement away from diagnosis-informed

provision to those aimed at those who have experienced particular adversities or for certain populations such as homelessness (Kinderman & Allsopp, 2018).

Yet if, as is most likely at least for the foreseeable future, the current diagnostic system remains perhaps it is important to acknowledge the empirical and conceptual limitations of nosology and be aware of its impact. With my changing view, I have looked at the influence of diagnoses in my own clinical work and question the impact of working rigidly to diagnoses, for example reflecting on my own use of CBT for GAD in individuals with comorbid disorders or use of diagnostic labels when assessing new clients. Change whilst within diagnosis ingrained services could involve a move away from belief that mental health difficulties are discrete entities akin to those of physical health conditions to potentially something less concrete and clear, potentially informed by the other approaches such as RDOC or psychological formulation. Key to any changes would be the inclusion of service user views to consider which approaches better capture their experiences and what would be most useful to them.

Regardless, any potential challengers the current system would require a lot of investment in research and development to be accepted instead of the established categorical diagnostic system which has been in place for many decades with vast amounts of evidence. Psychologists however seem well positioned to challenge the current status quo this through their non-medical perspective within their clinical work, training in different approaches, formulation and to engage in research to inform change.

Deciding on The Approach to Researching GAD

After deciding on a focus for the project, the next challenge was deciding on the methodology and due to paucity of research into GAD there were a lot of potential approaches. For the initial research proposal, the plan was to adopt a mixed approach with an analysis of secondary data, as occurred in the final project, and if distinct profiles were

found to conduct qualitative interviews with individuals diagnosed with GAD who were representative of each or some of the profiles. The latter was thought provide rich, client perspectives of their experiences of having these different presentations of GAD to compliment the quantitative element and help understand the qualitative differences of these subgroups. However, due to issues of timescale and the level of research required for the doctoral thesis the additional qualitative element was removed at the proposal stage.

There are many benefits of a large secondary dataset, in this case with the breadth of the information collected it allowed for a range of potential approaches to exploring the nosology and the number of cases provided the power to detect small effects. Yet, service user involvement can also be important in such studies of nosology with experts-by-experience offering crucial perspective to understanding disorders and key symptoms through their first-hand experience, for example previously highlighting the absence of anger as a key element of GAD in the diagnostic criteria (Hackmann et al., 2019). Given the research aim was to improve the understanding of what constitutes the diagnosis of GAD, having both types of data may have benefitted the study for interpretation of classes aided by real life examples from service user experiences. Yet in the absence of current nosological research into the disorder and a range of valid approaches to understanding the symptoms within the disorder, either approach would have added to the current understanding and perhaps prompted informed further research.

While in the ideal situation data would meet all the required needs to answer the research question, the reality is that secondary data poses some issues for research as it created within a specific context be that clinical, research, social or other settings and so naturally will not fit perfectly with research questions as it was not designed primarily for the purpose of research (Schofield & Das-Munshi, 2018). In the current study, the raw data had many missing entries with sparse data for certain periods or for some services perhaps highlighting different cultures to data entry between services. Beyond this missing data, one of the challenges was working with the issues inherent to the dataset to design a method

that would help to explore nosology of GAD. For example, the use of GAD-7 and Patient Health Questionnaire-9 (PHQ-9) as the primary measures, being routine outcome measures in Improving Access to Psychological Therapy (IAPT) and valid measures of the disorders (Kroenke et al., 2001; Spitzer et al., 2006), limited the symptom profiles to features these questionnaires measured. Importantly for the exploratory nature of this study into the nosology of GAD, notably this meant that potential key symptoms to the disorder that were not currently in the diagnostic criteria but identified in the conceptual introduction, namely muscle tension or other somatic symptoms, were not studied and so the results only focused on current symptoms of GAD, leaving exploration of new or alternative symptoms unanswered. Here is where perhaps an additional qualitative element may have added to the study, with the possibility of symptoms identified beyond those included in pre-existing measure. However, importantly this does not mean that such data cannot be used within research nor provide valuable insight into different concepts. Here the dataset allowed for exploration of the nosology in GAD using an approach that few datasets would be able to accomplish due to the size and breadth of information made available to researchers through IAPT Service Improvement and Research Network (SIRN). Research from datasets such as this can easily apply to and influence practice within settings from which the data came, in this case the vast number of IAPT settings, to improve in the provision of evidence-based therapies to many individuals, highlighting the value of such practice-based evidence to improve care.

Another issue this dataset posed was how to select individuals with “true” GAD from the wider dataset of all who had contact with the IAPT services. Part of this was acceptance that no sample would truly capture all this group but choosing a particular approach to selection could improve the odds of this with the final selection including those with GAD as the presenting problem and only cases since 2015 following an initiative to improve diagnostic labels across IAPT. An issue with this approach was that GAD is a diagnosis notoriously difficult to identify even for medical professionals (Allgulander, 2006; Wittchen et

al., 2002) so this approach to selection likely led to the inclusion of many without GAD into the sample whilst also missing many with GAD who had been wrongly labelled. Other ways of attempting to capture of more reliable sample of those "true" GAD were considered such as only selecting cases that were a certain threshold above caseness on the GAD-7, however even this approach would still mean some cases would be missed, in this case perhaps those with milder GAD which is just as valid and important to considering the nosology of the disorder. This lack of reliability in diagnosis led to the inclusion of a second sample made of those recorded as having any anxiety and depressive disorders was included given their overlap, comorbidity, and the frequent misdiagnosis between all these disorders and allowed the opportunity to see how these groups differed. These decisions highlighted the challenge of sample selection, whether is it better to have a more certain sample but miss cases or a broader selection but likely to include those with other disorders. Given the pre-existing uncertainty around GAD and its relationship with depressive and other anxiety disorders, the decision was to opt for the latter. When interpreting the results, I experienced how the context of the data shape the research and the importance of taking this into account when drawing conclusions or otherwise risking misinterpretation. Again, perhaps the addition of qualitative interviews could have helped with this.

Challenges of Working with and Analysing Large Secondary Data

Completing thesis offered my first experience of working with a secondary data set and seeing the potential that big data can offer mental health research. Having worked in services which collect routine outcome measure data from service users and submitting them onto systems without knowing how they would be used beyond the therapy session, working with this data on a large scale has allowed me to see the potential locked away in electronic patient notes. Such data collected naturally within daily practice in a range of services could provide insight into areas unable to by traditional experimental means. There is a growing recognition of the potential that data collected within typical practice has to

influence mental health disorders and shape care provision (Gyani et al., 2011; McIntosh et al., 2016; Raghupathi & Raghupathi, 2014). As such, familiarity and working with big data seems to be something that is going to be more relevant to the role of a psychologist as research practitioners and within a wider context of needing to prove value of services in the NHS. However, despite being an area with such potential, I also experienced many challenges from working within a new approach and with such large data.

The initial challenge was learning new skills to complete the analysis and to work with large datasets. Through the support of my supervisor and also reading books and watching lectures online, I slowly began to understand the coding more but at times it felt like learning a new language and was confusing and frustrating. However, I am glad I took the opportunity to try different skills, go out of comfort zone and to do something other than a more traditional experimental approach. Psychologists' training in clinical work and research methods places them in a key position to use and interpret findings from secondary data. Yet it is also an area few have experience in with such approaches not taught on training and experience only gained if individuals opt to conduct research utilising it, which sadly seems at odds with the growing role these approaches have in future health care research and the increasingly influential role of routine outcome measure data in development of mental health services (McIntosh et al., 2016; Raghupathi & Raghupathi, 2014).

Big data also provides the opportunities contribute to the evidence base within mental health where traditional means such as randomised control trials are not feasible or suitable and also provides more ecologically valid findings that are more of use to services despite the issues with datasets of routine outcome measures and issues potentially limiting wider applications such as self-selection bias (Schofield & Das-Munshi, 2018). Analysis of routine outcome measure data provides an invaluable opportunity to research different areas related to mental health care such as effectiveness of interventions or learning about therapeutic issues. As in this study, IAPT is a prime example of services collecting big data as part of routine practice which is later in turn influenced by the research produced from the

data is has provided. With services to likely to remain diagnostically informed using flawed categorical clinical entities, big data may perhaps be one method for helping to answer questions around nosology and compliment more traditional methods. Research like the current study provides an example of how sessional, routinely collected outcome data can be used to better understand diagnostic entities providing data on a scale would be difficult to collect by any other means.

However, the challenge of working with such volumes of data in the current study, and perhaps the biggest challenge, was working with very large files and facing technical issues on the systems and software needed to work with data of this size. Due to server issues, analyses for each increasing numbers of classes took increasingly longer, taking days instead of hours, to the extent that the server was unable to process large numbers of classes within the weekly system reset time. Even sometimes when seemingly running smoothly, due to the server or software issues the analysis would result in errors wasting hours or days which was very frustrating having to depend on an unpredictable system. As a result, the analysis was limited by software and server issues with the final classes having to be decided upon via the 5% statistic as opposed to the preferred method of using model fit statistics of Akaike information criterion (AIC) or Bayesian information criterion (BIC) as these would have been indicated by models with higher numbers of classes which was not possible to run with the system limitations. Perhaps in hindsight the alternative option would have been to use a smaller subset of the data or binarize the data with items on the GAD-7 and PHQ-9 either being indicated as present or not present as opposed to using the ratings to provide levels of present for each item. Yet, in using the ratings this provided a more vivid picture of the classes, especially without the original qualitative element and potentially larger number of classes would have provided classes with similar features as was the case for a previous study which used a latent transition analysis on IAPT data to explore subgroups of depression (Catarino et al., 2020). However, there is also the possibility this may not have been the case for GAD.

During the process of running the analysis, it felt as though I was at the mercy of the software and servers with the process of data cleaning and analyses taking far longer than expected and planned. Depending on a system that was out of my control was at odds with my preference to take time and plan deadlines and led to so much frustration. This was only furthered with any mistake I made in my coding coming at the cost of wiping out hours of analysis. If ever re-visiting my foray into secondary data analysis in the future, I would face the challenge very differently having learnt from my mistakes for example allowing for more time whilst also spending more time checking any coding. This experience also showed me how factors out of a researcher's control, such as technical issues on a secure server, and can have a huge impact on study and the necessity to have backup plans if faced with issues.

Conclusions

Researching the literature and conducting a secondary data analysis focused on the nosology of GAD allowed me to see the challenges to defining and researching a clinical entity. While part of the medical approach, this experience has shown that psychologists are well positioned to support the understanding of nosology and promote alternative ways to understanding mental health disorders and distress. Whilst many psychologists may be focused on improving efficacy of treatments, this thesis has shown that it remains just as important that the conceptualisation of disorders remains within research agendas with poor conceptualisations of disorders leading to poor interventions. The conceptual introduction and empirical paper demonstrate just two of the many approaches to explore and add to understanding nosology of a disorder.

Working with secondary data proposed many challenges but also allowed me to see the wealth of opportunities such data provides and with the increasing use of outcome measures in many services, the potential locked away in patients' records that could be used

to inform understanding of disorders or interventions. While few psychologists have worked with secondary data, this experience has allowed me to see how well such approaches fit into the role of a psychologist, especially in a healthcare system increasingly influenced by big data.

References

Allgulander, C. (2006). Generalized anxiety disorder: What are we missing?. *European Neuropsychopharmacology*, *16*, S101-S108.

Allsopp, K., & Kinderman, P. (2021). The use of diagnoses in mental health service eligibility and exclusion criteria. *Journal of Mental Health*, *30*(1), 97-103.

Catarino, A., Fawcett, J. M., Ewbank, M. P., Bateup, S., Cummins, R., Tablan, V., & Blackwell, A. D. (2020). Refining our understanding of depressive states and state transitions in response to cognitive behavioural therapy using latent Markov modelling. *Psychological Medicine,* 1–10.

Clark, L. A., Cuthbert, B., Lewis-Fernández, R., Narrow, W. E., & Reed, G. M. (2017). Three approaches to understanding and classifying mental disorder: ICD-11, DSM-5, and the National Institute of Mental Health's Research Domain Criteria (RDoC). *Psychological Science in the Public Interest*, *18*(2), 72-145.

Cuthbert, B. N., & Insel, T. R. (2013). Toward the future of psychiatric diagnosis: the seven pillars of RDoC. *BMC medicine*, *11*(1), 1-8.

Flinn, L., Braham, L., & das Nair, R. (2015). How reliable are case formulations? A systematic literature review. *British Journal of Clinical Psychology*, *54*(3), 266-290.

Gyani, A., Shafran, R., Layard, R. & Clark, D.M. (2011). Enhancing Recovery Rates in IAPT Services: Lessons from Analysis of the Year One Data. Available at www.iapt.nhs.uk.

Hackmann, C., Balhara, Y. P. S., Clayman, K., Nemec, P. B., Notley, C., Pike, K., ... & Shakespeare, T. (2019). Perspectives on ICD-11 to understand and improve mental health diagnosis using expertise by experience (INCLUDE Study): an international qualitative study. *The Lancet Psychiatry*, *6*(9), 778-785.

Hackmann, C., Wilson, J., Perkins, A., & Zeilig, H. (2019). Collaborative diagnosis between clinician and patient: why to do it and what to consider. *BJPsych Advances*, *25*(4), 214-222.

Harper, D. J. (2013). On the persistence of psychiatric diagnosis: Moving beyond a zombie classification system. *Feminism & Psychology*, *23*(1), 78–85.

Insel, T. (2014). The NIMH Research Domain Criteria (RDoC) Project: Precision medicine for psychiatry. *American Journal of Psychiatry*, *171*, 395–397.

Insel, T. (2013*, April 29). Post by Former NIMH Director Thomas Insel: Transforming Diagnosis. National Institute of Mental Health. https://www.nimh.nih.gov/about/directors/thomas-insel/blog/2013/transforming-diagnosis.*

Johnstone, L. (2018). Psychological formulation as an alternative to psychiatric diagnosis. *Journal of Humanistic Psychology*, *58*(1), 30-46.

Johnstone, L. & Boyle, M. with Cromby, J., Dillon, J., Harper, D., Kinderman, P., Longden, E., Pilgrim, D. & Read, J. (2018). *The Power Threat Meaning Framework: Towards the identification of patterns in emotional distress, unusual experiences and troubled or troubling behaviour, as an alternative to functional psychiatric diagnosis.* Leicester: British Psychological Society.

Kinderman, P., & Allsopp, K. (2018). Non-diagnostic recording of mental health difficulties in ICD-11. *The Lancet Psychiatry*, *5*(12), 966.

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine*, *16*(9), 606-613.

McIntosh, A. M., Stewart, R., John, A., Smith, D. J., Davis, K., Sudlow, C., … Porteous, D. J. (2016). Data science for mental health: a UK perspective on a global challenge. *The Lancet Psychiatry*, *3*(10), 993–998.

Raghupathi, W., & Raghupathi, V. (2014). Big data analytics in healthcare: promise and potential. *Health information science and systems*, *2*(1), 1-10.

Schofield, P., & Das-Munshi, J. (2018). Big data: what it can and cannot achieve. *BJPsych Advances*, *24*(4), 237-244.

Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of internal medicine*, *166*(10), 1092-1097.

Wittchen, H. U., Kessler, R. C., Beesdo, K., Krause, P., & Hoyer, J. (2002). Generalized anxiety and depression in primary care: prevalence, recognition, and management. *The Journal of clinical psychiatry*, *63*(suppl 8), 24-34.

Appendix 1: Item-Response Probabilities For GAD-7 And PHQ-9 In Sample 1 ("Anxiety and Depressive disorders" Sample)

GAD-7 items	Item rating	State 1	State 2	State 3	State 4	State 5	State 6
1) Feeling nervous, anxious or on edge	0	0.002	0.209	0.015	0.126	0.009	0.005
	1	0.092	0.639	0.450	0.440	0.086	0.027
	2	0.493	0.122	0.454	0.260	0.194	0.108
	3	0.413	0.029	0.081	0.174	0.711	0.859
2) Not being able to stop or control worrying	0	0.000	0.329	0.021	0.150	0.002	0.001
	1	0.070	0.574	0.482	0.441	0.025	0.012
	2	0.494	0.079	0.474	0.268	0.150	0.078
	3	0.435	0.018	0.023	0.142	0.823	0.909
3) Worrying too much about different things	0	0.002	0.254	0.010	0.119	0.009	0.006
	1	0.044	0.625	0.399	0.391	0.020	0.010
	2	0.434	0.104	0.541	0.295	0.111	0.056
	3	0.521	0.017	0.050	0.195	0.861	0.928
4) Trouble relaxing	0	0.002	0.387	0.031	0.176	0.033	0.007
	1	0.098	0.542	0.510	0.377	0.162	0.021
	2	0.545	0.055	0.413	0.228	0.289	0.127
	3	0.355	0.016	0.047	0.219	0.515	0.845
5) Being so restless that it is hard to sit still	0	0.102	0.812	0.371	0.643	0.357	0.097
	1	0.372	0.169	0.482	0.224	0.324	0.131
	2	0.422	0.014	0.135	0.073	0.168	0.269
	3	0.104	0.005	0.013	0.060	0.151	0.503
6) Becoming easily annoyed or irritable	0	0.022	0.396	0.087	0.186	0.114	0.033
	1	0.205	0.495	0.499	0.356	0.299	0.083
	2	0.458	0.088	0.337	0.217	0.252	0.203
	3	0.315	0.021	0.076	0.241	0.335	0.682
7) Feeling afraid as if something awful might happen	0	0.057	0.587	0.216	0.420	0.110	0.034
	1	0.261	0.343	0.499	0.332	0.224	0.078
	2	0.432	0.054	0.248	0.143	0.228	0.169
	3	0.250	0.016	0.037	0.105	0.438	0.719
PHQ-9 Items	**Item rating**	**State 1**	**State 2**	**State 3**	**State 4**	**State 5**	**State 6**
1) Little interest or pleasure in doing things	0	0.007	0.505	0.079	0.044	0.148	0.027
	1	0.213	0.441	0.678	0.266	0.470	0.056
	2	0.529	0.045	0.229	0.353	0.255	0.196
	3	0.251	0.009	0.013	0.336	0.127	0.721
2) Feeling down, depressed, or hopeless	0	0.001	0.385	0.039	0.023	0.062	0.001
	1	0.139	0.568	0.676	0.248	0.413	0.026
	2	0.558	0.041	0.273	0.367	0.306	0.147
	3	0.302	0.006	0.013	0.361	0.220	0.826
3) Trouble falling or staying sleep, or sleeping too much	0	0.013	0.382	0.100	0.076	0.160	0.013
	1	0.121	0.424	0.402	0.154	0.287	0.037
	2	0.365	0.124	0.356	0.215	0.232	0.136
	3	0.500	0.069	0.143	0.555	0.321	0.815
4) Feeling tired or having little energy	0	0.004	0.265	0.034	0.024	0.072	0.004
	1	0.082	0.551	0.416	0.125	0.289	0.020
	2	0.430	0.131	0.429	0.238	0.293	0.121
	3	0.485	0.052	0.121	0.613	0.346	0.855
5) Poor appetite or overeating	0	0.054	0.629	0.258	0.203	0.341	0.047
	1	0.234	0.279	0.430	0.220	0.317	0.093
	2	0.432	0.065	0.249	0.221	0.184	0.237
	3	0.280	0.027	0.063	0.355	0.159	0.623

6) Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	0.015	0.467	0.104	0.129	0.130	0.020
	1	0.148	0.453	0.518	0.258	0.283	0.044
	2	0.475	0.068	0.322	0.258	0.252	0.154
	3	0.362	0.012	0.057	0.354	0.335	0.781
7) Trouble concentrating on things, such as reading the newspaper or watching television	0	0.017	0.595	0.168	0.200	0.233	0.019
	1	0.215	0.349	0.532	0.286	0.363	0.054
	2	0.503	0.043	0.260	0.228	0.215	0.229
	3	0.265	0.013	0.040	0.286	0.190	0.697
8) Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	0.167	0.873	0.520	0.588	0.578	0.127
	1	0.383	0.113	0.381	0.218	0.261	0.155
	2	0.363	0.009	0.091	0.109	0.096	0.293
	3	0.086	0.004	0.009	0.084	0.065	0.425
9) Thoughts that you would be better off dead or of hurting yourself in some way	0	0.523	0.950	0.811	0.608	0.783	0.371
	1	0.335	0.048	0.172	0.274	0.177	0.277
	2	0.119	0.002	0.016	0.079	0.029	0.185
	3	0.023	0.000	0.001	0.039	0.011	0.168

Appendix 2: Item-Response Probabilities For GAD-7 And PHQ-9 In Sample 2 ("Probable GAD" Sample)

GAD-7 items	Item rating	State 1	State 2	State 3	State 4	State 5
1) Feeling nervous, anxious or on edge	0	0.010	0.004	0.161	0.014	0.003
	1	0.076	0.136	0.728	0.443	0.024
	2	0.182	0.480	0.088	0.456	0.114
	3	0.732	0.381	0.023	0.086	0.859
2) Not being able to stop or control worrying	0	0.010	0.005	0.347	0.030	0.001
	1	0.036	0.134	0.593	0.519	0.010
	2	0.155	0.532	0.047	0.436	0.073
	3	0.799	0.329	0.013	0.015	0.916
3) Worrying too much about different things	0	0.014	0.005	0.245	0.021	0.004
	1	0.028	0.097	0.672	0.443	0.012
	2	0.112	0.505	0.067	0.493	0.056
	3	0.846	0.393	0.015	0.044	0.928
4) Trouble relaxing	0	0.034	0.008	0.409	0.057	0.006
	1	0.176	0.154	0.549	0.562	0.031
	2	0.303	0.573	0.026	0.336	0.154
	3	0.487	0.265	0.016	0.045	0.810
5) Being so restless that it is hard to sit still	0	0.411	0.161	0.847	0.490	0.100
	1	0.323	0.437	0.138	0.411	0.169
	2	0.150	0.334	0.009	0.084	0.306
	3	0.117	0.069	0.005	0.014	0.425
6) Becoming easily annoyed or irritable	0	0.142	0.037	0.446	0.133	0.036
	1	0.344	0.305	0.49	0.568	0.116
	2	0.258	0.441	0.055	0.244	0.258
	3	0.256	0.217	0.008	0.055	0.590
7) Feeling afraid as if something awful might happen	0	0.137	0.102	0.579	0.261	0.029
	1	0.216	0.320	0.365	0.513	0.100
	2	0.236	0.412	0.042	0.193	0.213
	3	0.411	0.166	0.014	0.032	0.659
PHQ-9 Items	**Item rating**	**State 1**	**State 2**	**State 3**	**State 4**	**State 5**
1) Little interest or pleasure in doing things	0	0.217	0.014	0.683	0.221	0.024
	1	0.526	0.467	0.293	0.675	0.149
	2	0.180	0.434	0.019	0.094	0.347
	3	0.077	0.086	0.004	0.010	0.481
2) Feeling down, depressed, or hopeless	0	0.100	0.008	0.553	0.127	0.008
	1	0.511	0.380	0.435	0.749	0.092
	2	0.258	0.522	0.010	0.115	0.287
	3	0.131	0.090	0.002	0.008	0.613
3) Trouble falling or staying sleep, or sleeping too much	0	0.201	0.031	0.421	0.165	0.027
	1	0.315	0.213	0.449	0.438	0.073
	2	0.221	0.412	0.079	0.275	0.196
	3	0.263	0.344	0.051	0.122	0.704
4) Feeling tired or having little energy	0	0.105	0.008	0.348	0.073	0.007
	1	0.355	0.184	0.551	0.516	0.061
	2	0.278	0.475	0.074	0.306	0.209
	3	0.262	0.333	0.027	0.105	0.722
5) Poor appetite or overeating	0	0.449	0.112	0.739	0.408	0.079
	1	0.322	0.344	0.222	0.400	0.164
	2	0.143	0.373	0.025	0.150	0.278
	3	0.086	0.171	0.014	0.042	0.478

6) Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	0.189	0.041	0.581	0.22	0.030
	1	0.334	0.306	0.392	0.556	0.098
	2	0.248	0.466	0.023	0.194	0.240
	3	0.229	0.187	0.004	0.031	0.632
7) Trouble concentrating on things, such as reading the newspaper or watching television	0	0.291	0.044	0.675	0.286	0.031
	1	0.384	0.351	0.288	0.53	0.121
	2	0.195	0.428	0.026	0.152	0.279
	3	0.129	0.178	0.012	0.031	0.569
8) Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	0.676	0.296	0.921	0.689	0.178
	1	0.223	0.433	0.075	0.261	0.233
	2	0.066	0.225	0.004	0.044	0.308
	3	0.035	0.046	0.001	0.006	0.280
9) Thoughts that you would be better off dead or of hurting yourself in some way	0	0.867	0.719	0.977	0.909	0.548
	1	0.119	0.235	0.022	0.085	0.272
	2	0.010	0.041	0.001	0.004	0.117
	3	0.004	0.006	0.000	0.002	0.063