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Investigating trajectories of change in psychological distress amongst patients with Depression and Generalised Anxiety Disorder treated with Internet Cognitive Behavioural Therapy

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ABSTRACT

Internet based cognitive behavioural therapy (CBT) is efficacious for the treatment of anxiety and depression. The current study aimed to examine the effectiveness of internet based CBT prescribed by primary care clinicians for the treatment of depression and generalised anxiety disorder. Psychological distress data from 302 patients who completed an online CBT course for depression and 361 patients who completed an online CBT course for generalised anxiety disorder were subjected to growth mixture analysis. For both disorders psychological distress decreased across each lesson in a quadratic trend. Two classes of individuals were identified with different trajectories of change: a large group of individuals who responded well to the courses and a smaller group of individuals with a lower response. Both groups were similar with respect to sociodemographic characteristics however the low responders tended to have higher levels of symptom severity and psychological distress at baseline in comparison to the responders. For the majority of patients (75-80%) the internet CBT courses for depression and generalised anxiety disorder were effective. Further research is required to identify and effectively treat the smaller proportion of patients who did not improve during internet CBT.

Key words: internet cognitive behavioural therapy; effectiveness; primary care; depression; anxiety.

INTRODUCTION

Depression and anxiety are chronic conditions that if left untreated are responsible for high levels of distress, impairment, and disability, equal to chronic physical conditions such as diabetes, cancer, and arthritis (Mathers, Vos, Stevenson, & Begg, 2000). Treatments such as Cognitive Behavioural Therapy (CBT) are highly efficacious at treating anxiety and/or depression (Butler, Chapman, Forman, & Beck, 2006). Internet-based CBT treatment programs, administered under the guidance of clinicians, have the potential to dramatically reduce many of the barriers to treatment that sufferers of these conditions face (Titov, 2007). To further validate the point, a meta-analysis of 22 randomised controlled trials has demonstrated the efficacy of internet based CBT programs to significantly reduce distress, disability, and symptom severity in comparison to waitlist controls (Andrews et al., 2010). With such evidence, it seems likely that initiatives designed to increase and improve access to internet based treatment for mental disorders will become the norm.

The CRUfAD clinic (www.crufadclinic.org), a not-for-profit initiative of St. Vincent's Hospital, Sydney, Australia, is one such approach to disseminate internet-based CBT programs to the wider community. The primary target of the CRUfAD clinic was patients of GPs, psychologists, mental health nurses, and other specialist health workers, particularly those working in rural and remote parts of Australia. The programs were essentially designed to be used as an 'intern in the practice', meaning that internet based CBT could be used as a mechanism for GPs and mental health workers to provide cost effective and time efficient programs for treating their patients who suffer from anxiety and depression. Clinicians could then dedicate more therapeutic time to their severe patients who require additional attention and treatment. To date, the CRUfAD clinic has had 3,600 patients enrol in one of their internet CBT courses, a large proportion of patients coming from rural areas of Australia. The efficacy of the courses has been established in multiple randomised controlled trials (e.g. Andrews et al., 2010; Perini, Titov, & Andrews, 2008; Perini, Titov, & Andrews, 2009; Robinson et al., 2010; Titov et al., 2009; Titov et al., 2010) but the true effectiveness of the internet treatment programs offered by the CRUfAD clinic, and more importantly the actual trajectory of change in psychological distress experienced by patients who complete treatment, has yet to be fully examined.

Consequently, the current study represents one facet of an ongoing quality assurance program for the CRUfAD clinic, which has the general aim to investigate the effectiveness of the internet based CBT courses as well as investigating the need for any significant improvements to the overall service. The current study aimed to investigate the trajectories of change in psychological distress amongst completers of two CRUfAD Clinic programs, one for depression and one for anxiety (Generalised Anxiety Disorder; GAD). A steadily decreasing trajectory of change across each of six lessons will demonstrate the effectiveness of the online depression and GAD courses across the wider community. It is also possible that certain groups of individuals within the total sample may experience little response to treatment and therefore improvements are required to better serve those sub-populations. Therefore, the secondary aims of the current study included: 1) to investigate the presence of any significant sub-classes of patients that exhibit different trajectories of change in psychological distress, and 2) to identify any significant factors, including socio-demographic and clinical characteristics, that may accurately predict class membership and facilitate with identifying individuals who may not benefit from online CBT programs.

METHODS

Participants

The study comprised of participants admitted to Internet CBT courses for a primary diagnosis of either depression or GAD. The courses were developed and maintained by St Vincent's Hospital, Sydney, Australia. Patients were prescribed the online courses by their

GP, psychologist, mental health nurse, or other mental health specialist and remained in the clinical care of their prescribing clinician for the entirety of the online course. The study examined patient data that was collected between the 12th February 2009 and the 19th May 2011.

There were 302 patients that completed the depression course between the dates, 58% female and 42% male, with an average age of 43 and a standard deviation of 14. Of those patients who were admitted to the depression course approximately 52% were classified as living in a rural area and the majority of patients (46%) were referred and managed by their GP. There were 361 patients that completed the GAD course between the dates of the current study, comprising of approximately 74% female and 26% male with an average age of 43 and a standard deviation of 14. Of those patients who were admitted to the GAD course approximately 37% were classified as living in a rural area and again the majority of patients (65%) were prescribed and managed by their GP. Patients admitted to either course were predominately residing in Australia with a small percentage of patients residing in New Zealand.

Intervention/Procedure

The interventions utilised in the current study were developed in conjunction with the Virtual clinic (www.virtualclinic.org.au), a not-for-profit research initiative of St Vincent's Hospital and the University of New South Wales. The Virtual clinic is a research portal with the primary purpose to design and conduct randomised controlled trials of internet based CBT programmes for anxiety and depression. Once proven efficacious, the programmes were disseminated to GPs and clinicians through a prescription and/or referral process known as the CRUfAD clinic (Andrews & Titov, 2009).

The content of the programmes has been described in detail previously (see Robinson et al., 2010; Titov et al., 2010). Briefly, the programmes comprise six online treatment lessons representing best practice principles of CBT as well as regular homework assignments and access to supplementary resources. Each lesson was designed using a cartoon narrative that describes several principles and techniques of CBT, including: psycho-education, behavioural activation, cognitive restructuring, graded exposure, problem solving, assertiveness skills, and relapse prevention. Patients were required to obtain a prescription from a GP or clinician registered with the CRUfAD clinic in order to be enrolled in one of the intervention courses. Clinical responsibility was maintained by the prescribing clinicians who were given regular updates via email regarding their patient's progress. Patients were required to complete each lesson prior to moving onto the next and were encouraged to complete the course within 10 weeks. Socio-demographic information on each patient was collected at enrolment. The primary outcome measure was collected prior to commencing each lesson whilst disorder specific outcome measures and levels of functional impairment were collected at the first and last lesson of each course.

Measures

The primary outcome measure of interest in the current study was the Kessler-10 psychological distress scale (K10). The K10 comprises 10 items ranked on a five point scale designed to measure and monitor trends of non-specific psychological distress in the past two weeks. The K10 contains items that were designed to assess levels of fatigue, nervousness, hopelessness, restlessness, depression, loss of energy, and worthlessness. Traditionally, the K10 ranges from 10 to 50 and measures psychological distress in the past 30 days, however the current version of the K10 utilised skip instructions that would skip a question depending on the response given to a previous question, therefore the total scores could range from 8 to 50. Furthermore, the K10 was altered so that it would measure psychological distress in the past 14 days (two weeks) rather than in the past 30 days. The K10 possesses strong psychometric properties, including a one factor structure, strong reliability and validity, sensitivity to change, and can be used as a valid predictor of the common DSM-IV mental disorders (Andrews & Slade, 2001; Kessler et al., 2002; Furukawa et al., 2003; Perini, Slade, & Andrews, 2006; Slade, Grove & Burgess, 2011; Sunderland et al., 2011).

The disorder specific outcome measure used for the depression course was the PHQ-9 (Kroenke, Spitzer, & Williams, 2001) whereas the disorder specific outcome measure for GAD was the GAD-7 (Spitzer, Kroenke, Williams, & Lowe, 2006). Both outcome measures are brief self-report dimensional scales that measure the presence and severity of DSM-IV major depression and anxiety in the past 14 days. The PHQ-9 contains nine items rated on a four point scale whilst the GAD-7 contains seven items rated on a four point scale. Scores for the PHQ-9 can range from 0 through to 27 whilst scores for the GAD-7 can range from 0 to 21 with higher scores reflecting higher levels of psychopathology. The PHQ-9 and GAD-7 have sound psychometric properties and have been used extensively to measure treatment outcomes during internet CBT interventions targeting depression and anxiety (Titov et al., 2011; Dear et al., 2011).

Levels of functional impairment in the past 30 days were measured using the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0). The WHODAS 2.0 contains 12 items designed to measure disability and activity limitation in a variety of domains, which include: 1) understanding and communicating, 2) self-care, 3) mobility, 4) interpersonal relationships, 5) work and household roles, and 6) community and civic roles. It has been demonstrated that each of these domains loads significantly onto one underlying latent factor of global disability (Andrews et al., 2009). The internal consistency and test-retest reliability of the WHODAS 2.0 is high as well as the concurrent validity with other measures of disability. Finally, the WHODAS 2.0 performs equally well, if not better than, the SF-12 in regards to responsiveness to change across diverse chronic conditions, including disability attributed to mental disorders (Ustun, Kostanjsek, Chatterji, & Rehm, 2010).

Statistical Analysis

The statistical analyses proceeded in three stages to address the three separate aims of the study. Each course was analysed separately. The first stage investigated the trend of change in psychological distress by specifying a conventional single class latent growth model with a mean intercept (i.e. starting value of psychological distress) and a linear growth coefficient (i.e. the slope of the growth curve over each lesson), followed by specifying a model with the inclusion of a quadratic growth coefficient. The inclusion of the quadratic growth factor defines the shape of any curvilinear change that may occur in psychological distress over each lesson. The models were compared using the Bayesian Information Criterion (BIC) with smaller values indicating better overall model fit. Likewise, significant curvilinear growth was determined by examining the significance and magnitude of the linear and quadratic coefficients included in the model. The trend of change identified in the first stage of the analysis was utilised in the remaining stages.

The second stage involved fitting a series of unconditional growth mixture models (GMM) using a robust maximum likelihood method of estimation to examine any heterogeneity in the latent growth curves (Muthén & Muthén, 2010). GMM extends conventional single-class latent growth curve models by relaxing the assumption that all individuals can be described using a single latent growth curve. Instead, GMM allows for the inclusion of a categorical latent variable (i.e. two or more latent classes) within the growth model so that individuals from different classes can vary around different mean growth curves, thus accounting for significant heterogeneity within the observed latent growth curves (Jung & Wickrama, 2008; Kreuter & Muthen, 2008; Muthen et al., 2002). Likewise, GMM also extends less flexible latent class growth models (LCGM) proposed by Nagin and Land (1993), by relaxing the assumption that the growth variances and co-variances for each class are assumed to be zero.

A series of four GMMs were fit to the data, each model consisting of two, three, four, and five classes, respectively. The mean intercepts and slopes were estimated between classes, likewise the intercept and slope variances were estimated for each latent class, however the variances were fixed to equality since models with freely estimated variances exhibited problems with convergence. Model fit was based on a combination of BIC, entropy, and the Lo-Mendall-Rubin (LMR) adjusted likelihood ratio test (Jung & Wickrama, 2008). As mentioned above, when comparing nested and non-nested models using BIC, the model with the lowest value is deemed to provide the better fit. Entropy can range from 0 to 1.0 with values closer to 1.0 indicating that the model provides a desirable level of classification accuracy between observed and predicted class membership. Finally, the LMR significance test compares the model under examination (K) with a model with one less class (K-1). Non-significant values indicate that the number of classes contained in the model under investigation does not demonstrate better fit than a model with one less class.

Other determinants of good model fit included: successful model convergence, no less than 1% of the total population in a particular class, high posterior probabilities (>=0.90), and a theoretically meaningful result. The models were estimated using random starting values to ensure that the model with the maximum likelihood value was replicated so that any issues with likelihood estimation (such as local maxima) were avoided (Jung & Wickrama, 2008). The single class growth models and the growth mixture models were estimated using Mplus version 6.0 (Muthén & Muthén, 2010)

The final stage of the analysis was to examine the classes identified in the previous stage by determining any significant predictors of class membership based on socio-demographic and clinical characteristics. Independent samples t-tests were used to compare continuous dependent variables between each class whilst χ^2 analyses were used to compare categorical dependent variables between each class. The classes were compared on a range of variables including: age, sex, prescribing clinician's profession (general practitioner, medical specialist, mental health nurse, psychologists, other mental health/health worker), rurality (yes, no), pre-course WHODAS-2.0 mean scores, post-course WHODAS-2.0 mean scores, pre-course PHQ-9 mean scores, post-course PHQ-9 mean scores, pre-course GAD-7 mean scores, and post-course GAD-7 mean scores (the use of PHQ-9 and GAD-7 depends on the course under examination), and whether each individual experienced clinically significant change in the K10 from lesson 1 to lesson 6 or not (calculated using the Jacobson & Truax (1991) reliable change index). Finally, the amount of time (measured in minutes) spent on each lesson and in total was compared between the classes using nonparametric independent samples Mann-Whitney U tests. All class comparisons were conducted using SPSS version 18.

RESULTS

Growth Modelling

The results of the growth modelling across lessons of both the depression and anxiety course are provided in Table 1 and Table 2, respectively. As demonstrated in the tables, for both courses the single class latent growth models with a quadratic growth function provided the best model fit as evidenced by BIC. The mean quadratic growth factors were highly significant in both of the course models ($p<0.001$). Likewise other indices of model fit, such as the Comparative fit index (>=0.95), the Tucker-Lewis fit index (>=0.95), and the root mean square error of approximation (<0.1) provided further evidence that the quadratic growth model provided good fit for the observed data. The significant quadratic growth function indicates that overall the decrease in psychological distress was curvilinear with the greatest decrease occurring between the first few lessons followed by a slight reduction in the decrease of psychological distress as each course progressed. Quadratic growth curves were utilised in the remaining growth mixture models.

As outlined in Table 1 and Table 2, the fit indices provide evidence that a two class growth mixture model provides the best fit for data representing change in psychological distress. For depression, the lowest BIC value was estimated for the two class model, likewise the LMR value was significant indicating that two classes fit the data better than one class alone. The entropy value was acceptable, albeit smaller than the models with three or four classes. The total proportion of patients in each class was greater than 1%, with approximately 76% of patients classified in class one with the remaining 24% classified in class two. For GAD the result varied slightly, with the lowest BIC value estimated for the model with four classes. However, the LMR value was not significant for both the four class and three class models, indicating that the addition of a third or fourth class provides no significant improvement in model fit over the two class model. The entropy value for the two class model was acceptable and the proportion of patients in each class was similar to the depression model with 80% of patients classified in class one with the remaining 20% classified in class two.

The estimates for the mean intercept and slopes of the best fitting model for the depression and GAD courses are presented in Table 3 whilst the estimated growth curves of each class for depression and GAD are presented in Figure 1 and Figure 2, respectively. It is interesting to note that for both courses the trajectories of change and the identified classes were very similar, with the only difference between the courses being that GAD patients on average tended to be slightly less distressed and also exhibited slightly less overall improvement across the lessons. The two classes in both courses can be described as 'Responders' and 'Low Responders' based on the trajectory of change. The largest class in both courses was the Responders (depression=75%, GAD=80%), who exhibited improvement across all six lessons with slightly less improvement between the final two lessons. The average mean score at lesson one for the Responder class in both courses was consistent with a score indexing the ‘high’ to ‘very high’ (>=22) distress range whilst the final mean score was consistent with a score indexing the ‘low’ to ‘moderate’ (<=21) distress range (Australian Bureau of Statistics, 2001). The smaller class of Low Responders (depression=25%, GAD=20%) experienced a minor improvement in psychological distress across the first two lessons before their trajectory of change remained flat after lesson three. In fact, patients from both courses begun to experience a minor increase in their overall psychological distress between lesson five and six. On average, Low Responders experienced higher psychological distress across all lessons in comparison to the Responders with the greatest discrepancy between K10 scores occurring at the final lesson. Average psychological distress scores for the Low responders was consistent with a score indexing the ‘very high’ (>=30) distress range and remained within that range across all six lessons (Australian Bureau of Statistics, 2001).

Predictors of change

The two classes were compared on a variety of socio-demographic and clinic characteristics to further examine predictors of class membership. For the depression course there was no significant differences between the classes when comparing age (t=0.57, p=0.57), gender (χ^2=2.52, p=0.11), or rurality (χ^2=0.05, p=0.83). In regards to the median amount of time spent on each lesson, the Responders median ranged from 9 to 13 minutes across each of the six depression lessons. Likewise, the Low Responders median ranged from 9 to 13 minutes across each lesson. The total median time spent on all depression lessons for Responders was 58 minutes compared to 60 minutes for the Low Responders. Mann-Whitney U tests indicated no significant differences between the classes on the amount of time spent on each lesson and in total (all p-values >0.08). Low Responders tended to have a significantly larger proportion of medical specialists (13% vs. 6%), mental health nurses (13 vs. 7%), and psychologists (29% vs. 22%) as the prescribing clinician’s profession in comparison to Responders ($\chi^2 = 10.27$, $p = 0.03$). Additionally, Low Responders demonstrated a significantly higher mean pre- and post-WHODAS 2.0 score (25 vs. 16, $t=-7.87$, $p<0.01$; 22 vs. 9, $t=-13.76$, $p<0.01$) as well as a significantly higher mean pre- and post-PHQ-9 scores (19 vs. 13, $t=-8.18$, $p<0.01$; 16 vs. 6, $t=-17.15$, $p<0.01$) in comparison to Responders. Likewise, the Low Responder class had a significantly lower proportion of individuals who experienced clinically significant change in comparison to the Responder class (28% vs. 83%, $\chi^2=79.25$, $p<0.01$). Each individual was then categorised into one of four categories based on their baseline PHQ-9 score (0-9=mild, 10-14=moderate, 15-19=severe, 20-27=very severe). The Responder class had significantly fewer individuals fall within the severe and very severe category in comparison to the Low Responders ($\chi^2=45.53$, $p<0.01$). These results further confirm the finding that depression Low Responders tended to be on average more severe, distressed, and impaired in comparison to depression Responders.

For the GAD course the results were similar to depression with no significant differences occurring between the classes when comparing age ($t=-0.41$, $p=0.68$), gender ($\chi^2=1.09$, $p = 0.30$), or rurality ($\chi^2=0.08$, $p = 0.77$). In regards to the median amount of time spent on each lesson, the Responders median time ranged from 16 to 24 minutes across the six GAD lessons while the Low Responders median time ranged from 15 to 22 minutes. The total median time spent on all GAD lessons for Responders was 127 minutes compared to 109 minutes for the Low Responders. Mann-Whitney U tests indicated no significant differences between the classes on the amount of time spent on each lesson and in total (all p-values >0.06). In contrast to the depression course, the classes in GAD did not differ in clinician's profession ($\chi^2 = 1.13$, $p = 0.89$). However, pre- and post-WHODAS 2.0 mean scores were again significantly higher in the Low Responders when compared to the Responders (21 vs. 12, $t=-8.31$, $p<0.01$; 21 vs. 7, $t=-16.24$, $p<0.01$) as well as pre- and post-GAD-7 mean scores (15 vs. 10, $t=-6.48$, $p<0.01$; 12 vs. 5, $t=-15.02$, $p<0.01$). Similar to the depression results, the Low Responder class had a significantly lower proportion of individuals who experienced clinically significant change in comparison to the Responder class (17% vs. 75%, χ^2=80.27, p<0.01). Each individual was then categorised into one of four categories based on their baseline GAD-7 score (0-4=mild, 5-9=moderate, 10-14=severe, 15-21=very severe). The Responder class had significantly fewer individuals fall within the very severe category in comparison to the Low Responders (χ^2=32.12, p<0.01). These results once again confirm the finding that GAD Low Responders tended to be on average more severe, distressed, and impaired in comparison to GAD Responders.

Despite the finding that Low Responders exhibited on average a higher level of severity, distress, and impairment at the beginning of each course, it is difficult to conclude from the current results whether this can be considered the *defining* feature that accurately predicts low response to internet CBT courses for anxiety and depression. Further examination of the outcome measures between the two classes reveals that a large proportion of Responders receive as high, if not higher, score on the K10, WHODAS 2.0, and PHQ-9 or GAD-7, yet they demonstrate significantly better improvement in comparison to the Low Responders. Indeed, of those patients in the depression course who scored within the very severe range on the PHQ-9 (>=20), approximately 57% were classified as Responders. Likewise, of those patients in the GAD course who scored within the very severe range on the GAD-7 (>=15), approximately 64% were classified as Responders. Relying on initial severity status alone to predict the likely outcome for internet based CBT will result in poor classification accuracy.

DISCUSSION

The current study represented one facet of an ongoing quality assurance study to improve the performance and effectiveness of a series of internet-based CBT treatment courses prescribed by GPs and mental health clinicians. By investigating the heterogeneity between individual groups in terms of their change across the six lessons, the current study is able to indicate that some individuals require further assistance and/or support in order to benefit from the online treatment courses for depression and GAD. As demonstrated by the growth mixture analyses in the current study, the trajectory of change in psychological distress decreased in a quadratic function over six lessons of two internet-based CBT programs for DSM-IV depression and GAD, meaning that changes in psychological distress were more rapid over the first few lessons compared to the latter. Furthermore, two distinct classes, Responders and Low Responders, were identified in the population with different mean growth trajectories. The first class was defined by a relatively consistent decrease in psychological distress across each lesson whilst the second class was defined by a minor decrease in psychological distress between the first two lessons, followed by a period of no change, followed by a slight increase towards the final lessons. Subsequent analyses comparing the two classes indicated that on average the Low Responders exhibited higher levels of severity, distress, and impairment in comparison to the Responders, a result that is consistent with evidence indicating that CBT is less efficacious for patients with severe disorders (Haby, Donnelly, Correy, & Vos, 2006).

The vast majority (75%-80%) of patients who underwent online CBT for depression and anxiety did experienced clinically significant change across the six lessons. For depression the mean K10 score for Responders decreased from approximately 28 to 17 whilst for GAD the mean K10 score decreased from approximately 25 to 16. When comparing the current results to studies utilising more rigorous randomised controlled designs, the change in psychological distress for the Responders found the current study was similar to the change experienced by the RCT intervention groups. Titov et al. (2009) demonstrated a decrease in the mean K10 scores of 26 at pre-treatment to 20 at post-treatment for participants with GAD, whilst Perini, Titov and Andrews (2009) demonstrated a decrease in mean K10 scores of 28 at pre-treatment to 24 at post-treatment for participants with depression. The change in K10 scores for Responders demonstrated in the current study was also similar to the K10 change demonstrated in studies that compared clinician and trained technician administration of the online CBT programs for depression and anxiety (Robinson et al., 2010; Titov et al., 2010). The similarity between the previous and current findings indicates that the online CBT programs for depression and anxiety are effective for the majority of the population when disseminated through GPs and clinicians using a prescription pathway.

The primary implication garnered from the current results is that internet based CBT for anxiety and depression, prescribed by GPs and mental health specialist, is not as effective for a smaller proportion of people within the community (approximately 20-25%). This finding provides further evidence that internet CBT for anxiety and depression may be better suited as an initial step within a stepped care model for treatment (Andrews & Titov, 2010). A stepped care model for treating anxiety and depression may work by providing low intensity, cost effective treatments, such as internet based CBT, to every individual within the community that has been identified as having minor through to severe levels of anxiety and depression. The next step would be to identify the more severe individuals within the first step who did not respond well to the low intensity treatments and provide them with further high intensity treatments, such as face-to-face therapy or medication. However, for a stepped care model to work effectively it relies on the assumption that those individuals who do not perform well can be accurately targeted and provided with efficacious treatment in the subsequent steps. Thus, the identification of a subclass of Low Responders demonstrated in the current study may be valuable starting point when determining who may benefit from and what type of additional treatment is required in the model.

It is interesting to note that the growth mixture models conducted on both courses identified very similar classes with similar proportions and characteristics, therefore what defines the classes may reflect some of the commonalities between the two disorders or a factor related to the effectiveness of the CBT treatment protocol, which was common to both courses. Consequently, it would be highly valuable for future research to focus on identifying additional predictors that accurately define class membership. For example, patients belonging to the Low Responder class in both courses may be identified through a combination of shared clinical, biological, and personality factors, such as higher levels of behavioural inhibition or neuroticism, which has demonstrated a strong relationship with severity and poorer treatment outcomes for both anxiety and depression (Goldberg, Krueger, Andrews, & Hobbs, 2009).

The current study is not without limitations and the results should be considered with these kept in mind. First, the study does not contain a control sample in order to ensure that any change in psychological distress is the result of the therapeutic intervention rather than any external factors such as spontaneous remission, natural change over time, etc. That being said, the internet CBT programs utilised in the current study have previously proven efficacious in comparison to waitlist controls when administered by trained clinicians and non-clinical technicians (Perini, Titov, & Andrews, 2009; Robinson et al.,2010; Titov et al., 2009; Titov et al., 2010). Furthermore, assuming that the Low Responder class identified in the current study demonstrated a similar trajectory to waitlist controls, then it can be concluded that the Responder class appeared to exhibit significant changes in psychological distress that could be attributed to the current intervention. Second, due to the secondary analysis of real-world patient data, the study could not analyse any additional information that could be used to accurately predict class membership. Most notably, factors that address socio-economic status and social class that may form significant barriers to benefitting from online CBT courses were not assessed. Further research with more robust experimental designs is required to address some of the questions regarding the defining features of the subclasses raised in the current study. Third, it was not possible in the current study to examine the influence of varying times spent between each lesson. As a result, the change observed in the current study can be attributable to the change across the six lessons holding the time between each lesson as a constant. Further research is required to examine the influence of varying times taken by individuals between the six lessons.

The current quality assurance study of the CRUfAD clinic has demonstrated several key findings and directions for future research. For the majority of patients (75%-80%) who completed the internet CBT courses for either GAD or depression, their level of psychological distress decreased a significant rate across each of the six lessons. Furthermore, the number of lessons offered by the CRUfAD clinic appears to be sufficient as improvements in psychological distress only decrease slightly towards the final two lessons of each course. There is a smaller proportion of patients (20%-25%) who do not respond to the internet CBT treatment courses as well as the majority of patients who respond. These patients are on average more severe, distressed, and impaired at the beginning of the course. The next step is to better identify these patients and examine additional treatment protocols that could alleviate their clinical symptoms in a stepped care model.

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TABLES

Table 1: Model fit statistics for single class growth models and unconditional growth mixture models across lessons in patients who complete an online treatment course for depression.

Model	Classes	Likelihood	BIC	Entropy	Lo-Mendall-Rubin		Proportion of cases in each class				
					2LL	p	1	2	3	4	5
Linear single class growth model	1	-5477.24	11017.30	na	na	na					
Quadratic single class growth model	1	-5433.21	10952.08	na	na	na					
Quadratic GMM Model 1	**2**	**-5411.46**	**10931.42**	**0.785**	**41.675**	**0.0065**	**0.76**	**0.24**	**na**	**na**	**na**
Quadratic GMM Model 2	3	-5404.91	10941.15	0.855	12.558	0.4743	0.74	0.24	0.01	na	na
Quadratic GMM Model 3	4	-5394.88	10943.94	0.807	20.043	0.2917	0.68	0.23	0.05	0.04	na
Quadratic GMM Model 4	5	-5385.08	10947.19	0.785	18.777	0.1466	0.37	0.27	0.25	0.05	0.05

Note: Bold indicates best fitting model. GMM = Growth mixture model, BIC = Bayesian Information Criterion, na = not applicable.

Table 2: Model fit statistics for single class growth models and unconditional growth mixture models across lessons in patients who complete an online treatment course for generalised anxiety disorder

Model	Classes	Likelihood	BIC	Entropy	Lo-Mendall-Rubin		Proportion of cases in each class				
					2LL	p	1	2	3	4	5
Linear single class growth model	1	-6344.70	12754.18	na	na	na					
Quadratic single class growth model	1	-6291.35	12671.04	na	na	na					
Quadratic GMM Model 1	**2**	**-6251.85**	**12615.58**	**0.855**	**75.796**	**0.0105**	**0.20**	**0.80**	**na**	**na**	**na**
Quadratic GMM Model 2	3	-6239.43	12614.30	0.840	23.823	0.3664	0.07	0.18	0.75	na	na
Quadratic GMM Model 3	4	-6214.95	12588.89	0.885	38.292	0.4042	0.01	0.07	0.75	0.17	na
Quadratic GMM Model 4	5	-6204.89	12592.33	0.900	19.301	0.0607	0.17	0.75	0.01	0.06	0.01

Note: Bold indicates best fitting model. GMM = Growth mixture model, BIC = Bayesian Information Criterion, na = not applicable.

Table 3: Parameter estimates for mean intercept and slopes for the best fitting growth mixture models in depression and GAD

	Depression		**GAD**	
	Class 1: Responders	Class 2: Low responders	Class 1: Responders	Class 2: Low Responders
Intercept (SE)	28.36 (0.514)	35.55 (0.754)	25.24 (0.475)	32.04 (0.781)
Linear slope (SE)	-2.98 (0.257)	-2.51 (0.508)	-2.75 (0.244)	-1.15 (0.815)
Quadratic slope (SE)	0.11 (0.044)	0.37 (0.093)	0.18 (0.047)	0.18 (0.171)

FIGURES

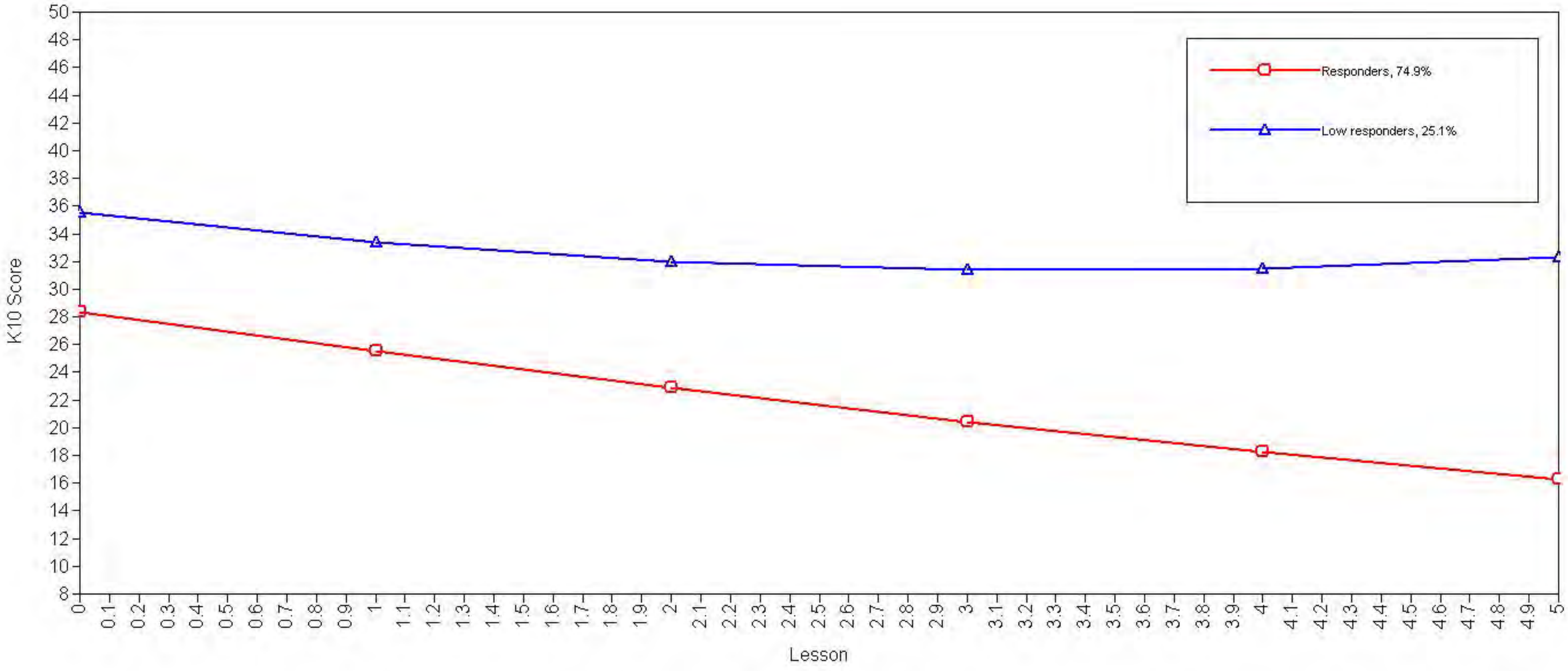

Figure 1: Estimated mean psychological distress change trajectories for each class amongst patients who completed an online treatment program for depression.

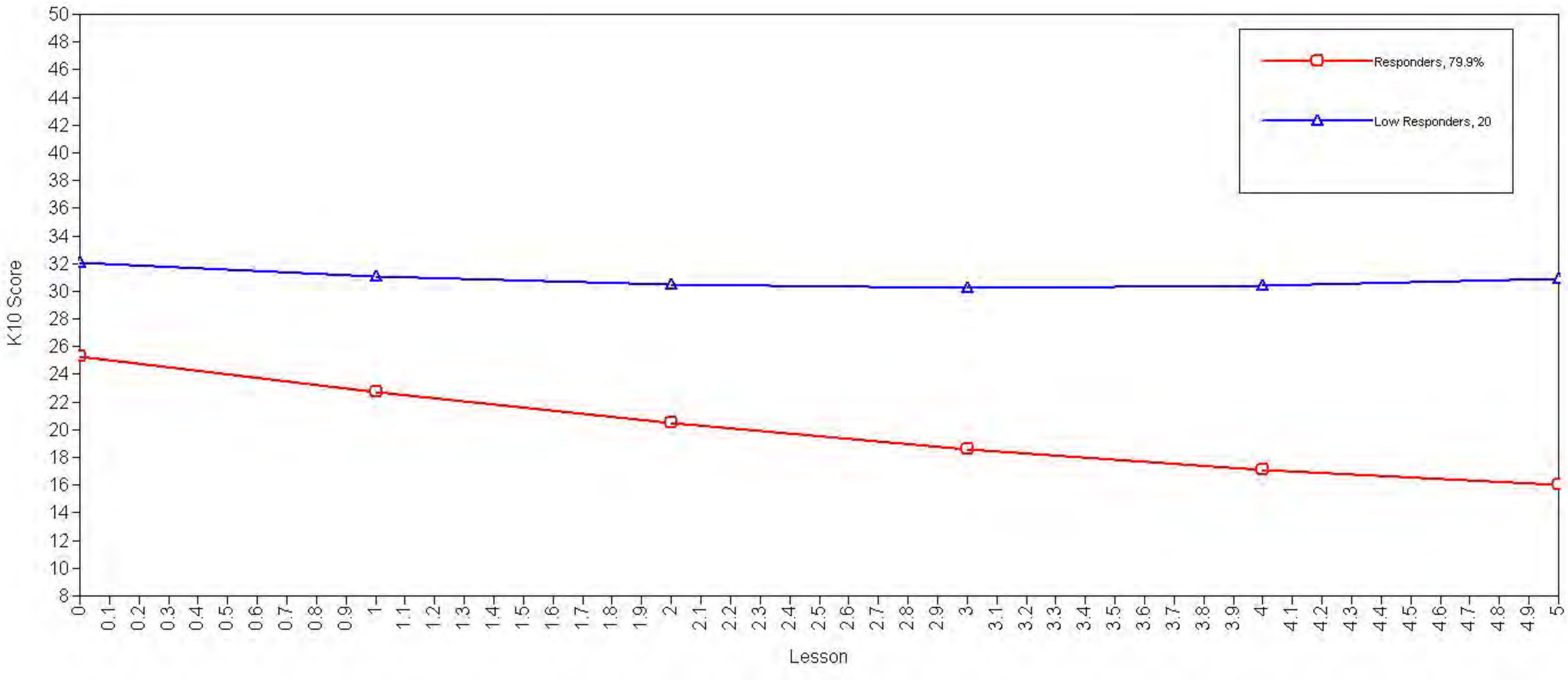

Figure 2: Estimated mean psychological distress change trajectories for each class amongst patients who completed an online treatment program for GAD.