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**A feasibility trial of an internet-delivered psychological intervention to manage mental health and functional outcomes in neurological disorders.**

Milena Gandy<sup>1</sup> (DClinPsy, PhD), Eyal Karin<sup>1</sup> (MAppStat), Sarah McDonald<sup>1</sup> (DClinPsy, PhD), Susanne Meares (MClinPsy, PhD)<sup>2</sup>, Amelia Scott<sup>1</sup> (MClinPsy, PhD), Nickolai Titov<sup>1</sup> (MClinPsy, PhD), Blake F Dear<sup>1</sup> (MClinPsy, PhD).

<sup>1</sup> *eCentreClinic, Department of Psychology, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, Australia.*

<sup>2</sup> *Department of Psychology, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, Australia.*

Corresponding Author: Milena Gandy, Department of Psychology, Macquarie University, New South Wales, Australia. Tel: 612 9850 4152. Email: [milena.gandy@mq.edu.au](mailto:milena.gandy@mq.edu.au).

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***Short running Header:*** Online Wellbeing Neuro Course

**Objective:** Mental health and cognitive difficulties are highly prevalent across neurological disorders and significantly contribute to poorer patient outcomes. Unfortunately, access to effective psychological services for these comorbidities are limited. To determine whether a novel transdiagnostic internet-delivered psychological intervention, the *Wellbeing Neuro Course*, was feasible, acceptable and efficacious a single-group feasibility open trial was employed **Methods:** The *Wellbeing Neuro Course*, targets mental health and cognitive difficulties, across a variety of neurological disorders. It is comprised of six online lessons, based on Cognitive Behavioural Therapy and Compensatory Cognitive Rehabilitation, delivered over 10 weeks and provided with weekly support from a mental health professional via email and telephone. 105 adults with diagnoses of either epilepsy, multiple sclerosis, Parkinson's disease and/or acquired brain injury, underwent the intervention. **Results:** The intervention was found to be highly acceptable with high intervention completion and levels of satisfaction (>95%). There was evidence of clinically significant improvements in primary outcomes (within-group Cohen's *d*; average reductions) of depression ( $d = 0.93$ ; avg. reduction  $\geq 36\%$ ), anxiety ( $ds = 0.66$ , avg. reduction  $\geq 36\%$ ), and disability ( $ds \geq 0.49$ ; avg. reduction  $\geq 23\%$ ) at post-intervention, maintained at 3-month follow-up. For secondary outcomes there were significant improvements in fatigue severity and perceived cognitive difficulties of attention, planning and prospective memory. Findings were achieved with minimal clinician time, highlighting its public health potential. **Conclusion:** This open trial provides preliminary evidence the *Wellbeing Neuro Course* is acceptable and reduces symptoms of depression, anxiety and disability in neurological disorders. Future controlled trials of the intervention are now needed.

Trial registration: ACTRN12617000581369.

*Keywords:* Cognitive Behavior Therapy, Online, Cognitive Rehabilitation, Disability, Mental Health, Neurological Disorders.

Mental health difficulties are highly prevalent across neurological disorders, with meta-analytic data indicating rates of anxiety and depressive disorders are as high as approximately 20 to 30% in people with epilepsy [1], multiple sclerosis (MS) [2], Parkinson's disease [3, 4] and acquired brain injury [5]. Across neurological disorders poor mental health is associated with poor quality of life, greater disability, poor treatment response, poor prognosis and disease progression [6-8]. In addition, some studies indicate that up to 30 to 50% of people with neurological disorders will experience significant cognitive difficulties [9-12], including problems with attention, memory and executive function. These cognitive difficulties are also highly disabling [13, 14] can exacerbate mental health difficulties and complicate their treatment [15]. There is some evidence psychological interventions based on cognitive behaviour therapy (CBT) can improve mental health outcomes (e.g., depression, anxiety) [16, 17], and interventions based on compensatory cognitive rehabilitation can improve cognitive outcomes (e.g., memory complaints) [18], in patients with both acquired and chronic neurological disorders. Despite this, there are numerous barriers preventing access to effective psychological care for the majority of these patients, including a lack of specialists and services, high costs and travel restrictions [19].

One innovative approach for increasing access to psychological interventions is delivery via the internet [20]. There is now substantial evidence for the effectiveness and acceptability of these interventions for common mental health [21] and physical health conditions [22]. There have also been several trials in certain neurological disorders, which highlight the potential of this approach. For instance, internet-delivered CBT based interventions have resulted in improvements in depression in epilepsy [23, 24], multiple sclerosis [25] and Parkinson's disease [26].

The present study examines the feasibility of an innovative transdiagnostic internet-delivered psychological intervention, the *Wellbeing Neuro Course*. The course teaches adults with a variety of neurological disorders psychological skills to manage both their mental health and functional abilities. A single-group open-trial was employed to gain important feasibility, acceptability and efficacy data. It was hypothesized participants would report; (1) the intervention as acceptable, (2) significant improvements on primary outcomes of depression, anxiety and disability at post-intervention and 3-month follow-up; and (3) significant improvements on secondary functional outcomes of cognitive difficulties and fatigue.

## Method

The trial was conducted via the online specialist research unit the eCentreClinic, Macquarie University, which offers free psychological interventions for common mental health and chronic health conditions via participation in clinical trials. Participants read details of the trial and made an application via the eCentreClinic website ([www.ecentreclinic.org](http://www.ecentreclinic.org)). This website can be located via online searches and is promoted by various health professionals and websites within Australia. Previous participants, who had consented to be emailed about the trial following their participation in an online national mental health survey [19] were sent a link to the website and details of the trial.

All participants self-referred and met the following inclusion criteria: (1) Australian resident, (2)  $\geq 18$  years of age, and (3) received formal diagnosis of one of the targeted neurological disorders (epilepsy, multiple sclerosis (MS), Parkinson's disease (PD), or acquired brain injury (ABI)), with clinical management by a GP or neurologist, (4) experiencing cognitive difficulties that impact day-to-day activities and quality of life; (5) wanting to learn information and skills to limit the impact of neurological disorder on their emotional and cognitive wellbeing. Exclusion criteria were: (1) an inability to access or use a computer with the internet, (2) depression symptoms in the very severe range (indicated by a total score  $> 22$  or a score  $> 2$  on item 9 of the Patient Health Questionnaire 9-item [27]), (3) acutely suicidal or recent history of attempted suicide or self-harm (i.e., last 12 months), (4) serious cognitive impairment indicative of dementia ( $< 21$  on the Telephone Interview of Cognitive Status; TICS-M) [28].

Assessments were conducted via online questionnaires and a structured telephone interview with a clinical psychologist (MG). Participants were required to provide details of their GP or neurologist who was sent a letter, notifying them of their patient's participation, and inviting contact should they have any questions or concerns. No restrictions were placed on additional treatments participants could receive during the trial.

One hundred and seventy-eight people applied for the trial between July 2017 and September 2018. Of these, 108 participants (61%) met all inclusion criteria and were allocated to receive the intervention. One participant was excluded for failing to complete pre-intervention questionnaires and two people were excluded for not commencing the intervention. Three people ( $< 3\%$ ) withdrew from the intervention, one due to hospitalisation

and two due to competing time demands. Details of participant flow are included in Figure 1, and medical and demographic characteristics are shown in Table 1 and 2, respectively.

### **Trial Registration / Ethics**

This study was approved by the Human Research Ethics Committee of Macquarie University, and registered on the Australian and New Zealand Clinical Trials Registry ACTRN12617000581369. All participants provided informed consent to participate.

### **Measures**

Primary outcome measures were completed at initial assessment, pre-intervention (i.e., immediately prior to starting the course), post-intervention (i.e., after the 10-week course finished) and 3-month follow-up. The secondary outcome measures were completed pre-intervention, post-intervention and 3-month follow-up.

#### **Primary outcome measures.**

*Depression symptoms* were assessed using the *Patient Health Questionnaire 9-Item (PHQ-9)*, which is a reliable and valid measure of the number and severity of depression symptoms [27]. Higher scores indicate greater depression severity scores ( $\leq 4$  = none, 5-9 = mild, 10-14 = moderate, 15-19 = moderately severe and  $\geq 20$  severe). Cronbach's alpha was  $\alpha = .75$ .

*Anxiety symptoms* were assessed using the widely used and psychometrically sound *Generalized Anxiety Disorder Scale 7-Item (GAD-7)* [29]. Higher scores indicate greater severity of anxiety ( $\leq 4$  = minimal, 5-9 = mild, 10-14 = moderate,  $\geq 15$  severe) [30]. In the current sample Cronbach's was  $\alpha = .88$ .

*Disability* was assessed using the *World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0)* which assesses disability associated with living with a chronic health condition. Higher scores indicate greater levels of disability [31] with a score  $\geq 10$  considered clinically significant disability [32]. The WHODAS 2.0 has good psychometric properties, [33] including acceptable reliability and validity in neurological disorders [34]. Within the current sample Cronbach's  $\alpha$  was = .88

#### **Secondary outcomes.**

*Cognitive Difficulties* were assessed using the *Perceived Difficulties Questionnaires (PDQ)* [35] 20-item measure. The PDQ assesses perceived cognitive difficulties in the four

domains (i) attention/concentration, (ii) retrospective memory, (iii) prospective memory, and (iv) planning/organisation. Higher scores indicate greater perceived cognitive impairment. The PDQ has reasonable reliability and validity, is increasingly used with people with neurological disorders, and cognitive impairment does not reduce the reliability or validity of the scores [36, 37]. In the current study Cronbach's alpha for the 4 subscales was  $>.79$ .

**Fatigue** was assessed using the *Fatigue Severity Scale (FSS)*. The FSS contains 9 items that measure the severity of fatigue and its impact on the day-to-day activities and lifestyles of patients with chronic health conditions [38]. Higher scores indicate greater fatigue. Cronbach's alpha was .94 in the current sample.

### **Weekly Measures**

To monitor participant progress and safety, the short form anxiety (GAD-2[39] and depression (PHQ-2 [40] measures, as well as Item 9 from the PHQ-9 [27], were administered weekly. A risk assessment was conducted by a registered clinical psychologist (MG) if participants reported elevations.

### **Intervention Acceptability and Satisfaction**

Consistent with previous trials [24, 41] treatment satisfaction and acceptability was assessed at post-intervention via 3 questions: (1) 'Overall, how satisfied were you with the Course?' (2) 'Would you recommend this Course to others?' (3) 'Was it worth your time doing this Course?' Participants responded on a 5-point Likert scale, which ranged from 'Very Satisfied' to 'Very Dissatisfied' and in a simple 'Yes' or 'No' format to the other questions. Participants could also respond to several free-response questions in order to guide future course revisions.

### **The Intervention**

The *Wellbeing Neuro Course* is a novel internet-delivered psychological intervention based on previous interventions for adults with chronic pain [41] and chronic physical health conditions [24, 42], but is tailored specifically for neurological disorders. The *Wellbeing Neuro Course* is unique in that it integrates principles of cognitive behaviour therapy (CBT) and compensatory cognitive rehabilitation therapy (CRT) to simultaneously address both mental health and cognitive difficulties. It was designed following a transdiagnostic model, to target several psychological domains, and to allow broad applicability across different neurological patient groups.

The course is designed to provide information and teach practical skills for managing the impact of neurological disorders on one's emotional wellbeing and daily functioning. An overview of the *Wellbeing Neuro Course* structure, content and skills is provided in Table 3. It consists of 6 core lessons and 6 summaries, which provide worksheets to help participants learn and practice several core skills. The course includes guidance and examples on how to adopt the core skills into their everyday lives, including three comprehensive case stories of adults with neurological disorders. Additional resources are provided to introduce topics and skills that are relevant for many participants, including materials on managing sleep and cognitive problems.

To facilitate engagement and retention in people with symptoms such as fatigue and inattention, the *Wellbeing Neuro Course* is brief, comprises minimal text, and is easy to read. Participants are encouraged to complete the course with a support person, such as a carer, partner or friend, if they are available. Each lesson is in the form of a slide show, and comprises of approximately 60 slides and each slide contains approximately 50 to 100 words. Participants navigate forward and backward through the lesson slides at their own pace and revise the materials as many times as desired. Course materials are released systematically over 10 weeks. Participants are unable to access new materials provided in later weeks without first having read previous materials.

The *Wellbeing Neuro Course* was delivered in conjunction with weekly contact, via telephone or email, from a registered clinical psychologist (MG) who has had >5 years' clinical experience working with people with neurological disorders. Attempts were made to contact each participant weekly for about 10 to 15 minutes, with additional time allocated if clinically indicated.

### **Analytic Plan**

Analyses were performed in SPSS version 25 (SPSS, Inc., Chicago, IL). Generalised estimation equation (GEE) modelling examined changes over time from baseline to 3-month follow-up [43]. Initial assessment data were employed as baseline from the primary outcomes and pre-intervention data for the secondary outcomes. GEE models specified a gamma with log link response scale to address skewness within the dependent variables [44] and an unstructured working correlation to account for different rates of change from pre-intervention to post-intervention (i.e., bulk of intervention effect), and post-intervention to follow-up (i.e., maintenance). Pairwise comparisons examined the statistical significance of changes in the



outcomes between time points. Clinical significance was assessed in two ways. First, the estimated marginal means from the GEE analyses were used to calculate the average percentage change across time for each of the outcome variables with 95% confidence intervals. Second, Cohen's *d* effect sizes and 95% confidence intervals were calculated for the within-groups effects based on the estimated marginal means.

To address missing values (only 7.6% post-intervention and 13.3% follow-up) a multiple imputations procedure was applied. This process first considered evidence of systematic dropout probability and non-ignorable mechanisms of missing data. [45] From the range of available patient and intervention variables, lesson completion was a single large predictor of missing data portability at post-intervention (Wald's = 21.863,  $p < 0.001$ , Nagelkerke *R* Square = 67.7%) and thus missing value imputations accounted (stratified) for this.

Post hoc longitudinal GEE power analyses demonstrated that the sample of 100 was adequately powered to test changes as low as 12% in depression (PHQ-9), 18% in anxiety (GAD-7), and 11% in disability (WHODAS 2.0). Thus, the study was sufficiently powered.

Finally, exploratory sensitivity analyses were conducted to examine the role of potential moderators of the treatment effects. These analyses are involved re-running GEE analyses for the primary outcomes while assessing the association of variables with the primary outcomes (main effect) and change over time (time\*covariate). The covariates analysed included (1) key demographic/medical variables (i.e., age, gender, education, duration of the disorder); (2) whether the participants was also underdoing any concurrent psychotherapy or cognitive rehabilitation/support with a health professional and; (3) levels of treatment adherence.

## **Results**

### **Adherence and intervention completion**

Participant flow and adherence to the intervention is shown in Figure 1. For the overall sample, 70% (73/105) completed all six lessons by post- intervention, which increased to 80% (84/105) at 3-month follow-up. Based on neurological sub-groups (epilepsy, MS, PD, ABI) post-intervention completion rates were 78% (14/18); 62% (18/29); 82% (27/33); 56% (18/32), respectively, which increased to 78% (14/18), 83% (24/29), 88% (29/33), 66% (21/32) at 3-month follow-up.

Post-intervention and follow-up measures were completed by 92% (97/105) and 87% (91/105) of participants, respectively.

### **Intervention Acceptability**

Ninety-eight percent (95/97) of participants providing feedback reported the course was worth their time and they would recommend it to others. Ninety-six percent (93/97) were either *Very Satisfied* (61%; 59/97) or *Satisfied* (35%; 34/97) with the course, with another 4% (4/97) reporting being *Neutral*. No participants reported being *Dissatisfied* with the course.

### **Clinician Contact Time**

The mean total clinician contact time per participant was 80.62 min (SD = 57.74) over the entire course duration, which comprised of time answering and making calls (M = 60.81; SD = 57.74; range = 3 to 317) and time sending or reading secure emails (M = 19.81, SD = 14.83, range = 0 to 86).

### **Primary Clinical Outcomes for the Overall Sample**

The overall means, standard deviations, percentage reductions and Cohen's *d* effect sizes for the primary outcomes are shown in Table 4. The GEE analyses revealed an overall time effect for depression (PHQ-9; Wald's  $\chi^2 = 126.9$ ,  $p < .001$ ); anxiety (GAD-7; Wald's  $\chi^2 = 38.7$ ,  $p < .001$ ) and disability (WHODAS; Wald's  $\chi^2 = 61.6$ ,  $p < .001$ ). Pairwise comparisons revealed that all measure scores were lower at post-intervention ( $p < .001$ ) and 3-month follow-up than baseline ( $p < .001$ ).

### **Primary Clinical Outcomes for Neurological Disorder Sub-groups**

Table 4 also displays the clinical outcome trends based on the four neurological sub-groups. The GEE analyses for depression (PHQ-9) revealed participants with epilepsy (Wald's  $\chi^2 = 28.1$ ,  $p < .001$ ), MS (Wald's  $\chi^2 = 40.8$ ,  $p < .001$ ), PD (Wald's  $\chi^2 = 39.9$ ,  $p < .001$ ) and ABI (PHQ-9; Wald's  $\chi^2 = 44.2$ ,  $p < .001$ ) all had overall time effects. Pairwise comparisons showed lower depression for all neurological sub-groups at post-intervention ( $p < .05$ ) and at 3-month follow-up for the MS, PD and ABI sub-groups ( $p < .001$ ), but not the epilepsy group ( $p = 0.87$ ). For anxiety (GAD-7) the GEE analyses revealed participants with MS (Wald's  $\chi^2 = 40.8$ ,  $p < .001$ ) and PD (Wald's  $\chi^2 = 19.7$ ,  $p < .001$ ) had overall time effects, with pairwise comparisons showing lower anxiety scores at both post-intervention and 3-month follow-up compared to baseline ( $p < .001$ ). There were no overall time effects in

anxiety for the epilepsy (Wald's  $\chi^2 = 5.8$ ,  $p = 0.21$ ) and ABI sub-groups (Wald's  $\chi^2 = 8.3$ ,  $p = 0.81$ ). For disability (WHODAS 2.0), the GEE analyses revealed participants with epilepsy (Wald's  $\chi^2 = 15.5$ ,  $p < .01$ ), MS (Wald's  $\chi^2 = 32.5$ ,  $p < .001$ ), PD (Wald's  $\chi^2 = 10.7$ ,  $p < .05$ ) and ABI (Wald's  $\chi^2 = 36.5$ ,  $p < .001$ ), all had overall time effects. Pairwise comparisons showed lower disability at post-intervention than baseline for all groups ( $p < .001$ ). At 3 months follow-up, these reductions remained for epilepsy, MS and ABI ( $p < .001$ ), but not PD ( $p = 0.053$ ).

### **Secondary Clinical Outcomes of Overall Sample**

The overall means, standard deviations, percentage reductions and Cohen's  $d$  effect sizes for the secondary outcomes are shown in Table 5. The GEE analyses for perceived cognitive difficulties (PDQ) revealed an overall time effect for difficulties in attention/concentration (Wald's  $\chi^2 = 20.3$ ,  $p < .01$ ), planning/organisation (Wald's  $\chi^2 = 10.9$ ,  $p = .01$ ) and prospective memory (Wald's  $\chi^2 = 8.3$ ,  $p = .04$ ). Pairwise comparisons revealed that these subscale scores were lower at post-intervention ( $p < .05$ ) but at 3-month follow-up only reductions in attention/concentration and planning/organisation remained ( $p < .05$ ), not prospective memory ( $p = 0.06$ ). There were no overall time effects for retrospective memory difficulties (Wald's  $\chi^2 = 6.1$ ,  $p = .10$ ). The GEE analyses for fatigue (FSS) revealed overall time effects (Wald's  $\chi^2 = 10.5$ ,  $p < .05$ ), with pairwise comparisons showing scores were lower at both post-intervention and 3-month follow-up than baseline ( $p > .05$ ).

### **Sensitivity Analyses**

Sensitivity analyses did not identify substantive moderators of treatment effects (see Supplementary Table 1). Only treatment adherence was associated with the primary outcomes. However, analyses are unpowered given the low number of non-completers.

### **Discussion**

The present study explored the feasibility, acceptability and preliminary efficacy of a new internet-delivered psychological intervention for adults with neurological disorders. It was hypothesized that the intervention would be acceptable and result in significant improvements in primary outcomes of symptoms of depression, anxiety and disability. These hypotheses were largely supported. The intervention was completed by most participants who reported high levels of satisfaction. For the overall sample significant improvements in the

primary outcomes were observed at post-intervention, which were maintained at 3-month follow-up. Results were achieved with minimal time per participant.

The medium to large improvements in the primary outcomes of depression, anxiety and disability are consistent with other internet-delivered interventions for the general population [21] and patients with chronic physical health conditions [22]. This is encouraging given people with neurological disorders often report significant difficulties in these areas, which can be further complicated by the neurological disease and treatment regimens [6, 19]. The magnitude of clinical improvements in depression and anxiety symptoms observed in this trial compare favourably to reviews of psychological interventions, based on CBT principles, for patients with both chronic [16] and acquired neurological disorders [17]. However, it should be noted that there are currently few benchmarks of outcomes of psychological interventions relevant across patients with different neurological disorders. Further, it is noteworthy that small but significant improvements in secondary outcomes of fatigue severity and perceived cognitive difficulties in attention, planning, and prospective memory were also observed. However, the observed reductions in fatigue are smaller than a recent randomised controlled trial of an online self-guided fatigue intervention in MS, which found moderate improvements in the Chadler Fatigue Scale [46]. The levels of treatment adherence compare well to iCBT interventions for depression in the general population [47] and neurological populations [23, 48]. Importantly, as one would expect and consistent with other work in this area [49], increased treatment adherence appears to be associated with larger treatment effects.

The current findings highlight the potential of so-called transdiagnostic interventions, which target multiple psychological domains and patients with different neurological disorders. Traditionally, psychological interventions in this area are designed for one specific neurological disorder and one specific psychological domain. For example, efforts have focused on CBT based interventions specific to epilepsy and depression [50] or multiple sclerosis and fatigue [51]. There have been some efforts to combine interventions focused on problem solving therapy for depression and memory and attention adaptation training, but these have been specific to epilepsy [52]. The broad acceptability and preliminary efficacy of the current transdiagnostic intervention suggest a single intervention can be suitable for patients with a variety of neurological disorders and comorbidities and target multiple psychological domains. Nevertheless, there was some evidence to suggest that patients with different neurological disorders may present with and respond differently to internet-

delivered interventions. For instance, in the current sample patients with multiple sclerosis had significant improvements across all three primary outcomes, which were maintained at follow-up. In comparison, patients with Parkinson's' disease obtained large improvements in depression and anxiety but improvements in disability were smaller and no longer significant at 3-month follow-up. In contrast, patients with epilepsy and ABI reported improvements in disability, which maintained or further increased at follow-up, but did not experience significant improvements in anxiety symptoms, and improvements in depression for the epilepsy sub-group were no longer significant at follow-up. There was also some evidence of differential engagement with the intervention, with, completion rates lower in patients with an ABI (66% at follow-up) compared to the other disorders ( $\geq 78\%$ ). However, the small sample sizes in each neurological sub-groups mean caution is required in interpreting these findings.

A significant strength of the intervention was the tailoring of the content and delivery to patients with neurological disorders and symptoms. Specifically, broad psychological skills were taught in the context of navigating the challenges of a neurological disorder, which included case examples and stories of people with a neurological disorder integrated throughout the intervention. Participants were also given considerable time to complete lessons and were able to work through the online materials at their own pace, with support people, and could revise materials numerous times over several months. This specialised tailoring of the intervention may explain the high levels of acceptability and engagement in this intervention, compared to some previous trials in this area [26, 48, 53]. However, it is currently unknown who responds best to internet-delivered psychological interventions and [54]. For instance, it is unclear whether these interventions are more helpful to people in an earlier stage of their diagnoses and assist with adjustment to one's diagnoses or prevention of mental health difficulties, or both. It is also unclear what components of the intervention are most effective and whether, for instance, the current intervention may benefit from more resources addressing other common issues people experience (e.g., with interpersonal relationships, self-worth regulation).

The findings of this trial should be considered in the context of several limitations. First, the absence of a control group means it is not possible to determine the effects of natural remission and caution is needed in interpreting the findings before more rigorous controlled trials are conducted. Second, the small number of participants within each of the neurological sub-groups ( $n = 18 - 33$ ), limited our ability to draw firm conclusions about the

specificity of outcomes by diagnostic group and the observations reported are trends only. Research with larger sample sizes are needed in order to explore this further. Third, the present study relied on self-report measures of symptoms of mental health and functional difficulties. Future research may benefit from more objective measures of these domains, such as the use of formal diagnostic assessments of mental health disorders and cognitive function. However, reliable and valid assessments of cognitive difficulties which can be administered remotely and have minimal practice effects, are still being developed [55]. Furthermore, the use of self-report measures of psychological difficulties is accepted practice in these types of clinical trials [22]. Fourth, the study utilised a relatively short follow-up period of 3-months. Future trials with longer follow-ups are necessary to assess whether improvements are maintained longer. Lastly, the sample was predominately female (71%), many were university educated (44%) and the majority had previously accessed some form of mental health support (79%). This may suggest that the sample is biased towards more motivated, intellectually capable or psychological minded people. However, sensitivity analyses did not find these demographic factors moderated the outcomes. Nevertheless, further work is needed to explore whether these interventions are suitable for more diverse samples of patients with these disorders and those who access neurology services.

The current study highlights the public health potential of internet-delivered psychological interventions for adults with neurological disorders. Internet-delivered interventions have significant potential because they can be scalable, relatively cost-effective and accessible intervention options [20, 21], and may represent another referral option for neurologists and clinics who treat a large number of patients with psychological comorbidities [6]. Internet-delivered interventions are increasingly used in routine mental health services in Australia and other countries and have now extended to delivering pain management interventions [56].

### **Conclusion**

The current study found that an internet-delivered psychological intervention resulted in clinically meaningful improvements in anxiety, depression and disability, and that participants found the intervention to be engaging and satisfying. These results were achieved with only a modest amount of clinician time per patient, indicating the public health potential of this model of care. Further research with larger sample sizes and appropriate control conditions is warranted.

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***Competing Interest Statement***

All authors have completed the Unified Competing Interest form at [http://www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare that Dr. Gandy received support from grants from iCare Lifetime Care and Support Authority and a Macquarie University Research Fellowship for the submitted work; Prof Titov and A/Prof Dear report to an organisation, that receives funding from the Australian Department of Health to deliver a national digital mental health service like that being evaluated in the submitted paper. Dr Gandy, Prof Titov and A/Prof Dear are the authors of the Wellbeing Neuro Course but derive no personal or financial benefit from it. The other authors have no competing interests to report.

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Figure 1. Participant Flow from Assessment to 3-month Follow-up

Notes: FU = follow-up, PHQ-9 = Patient Health Questionnaire 9-item, TICS = Telephone Interview of Cognitive Status

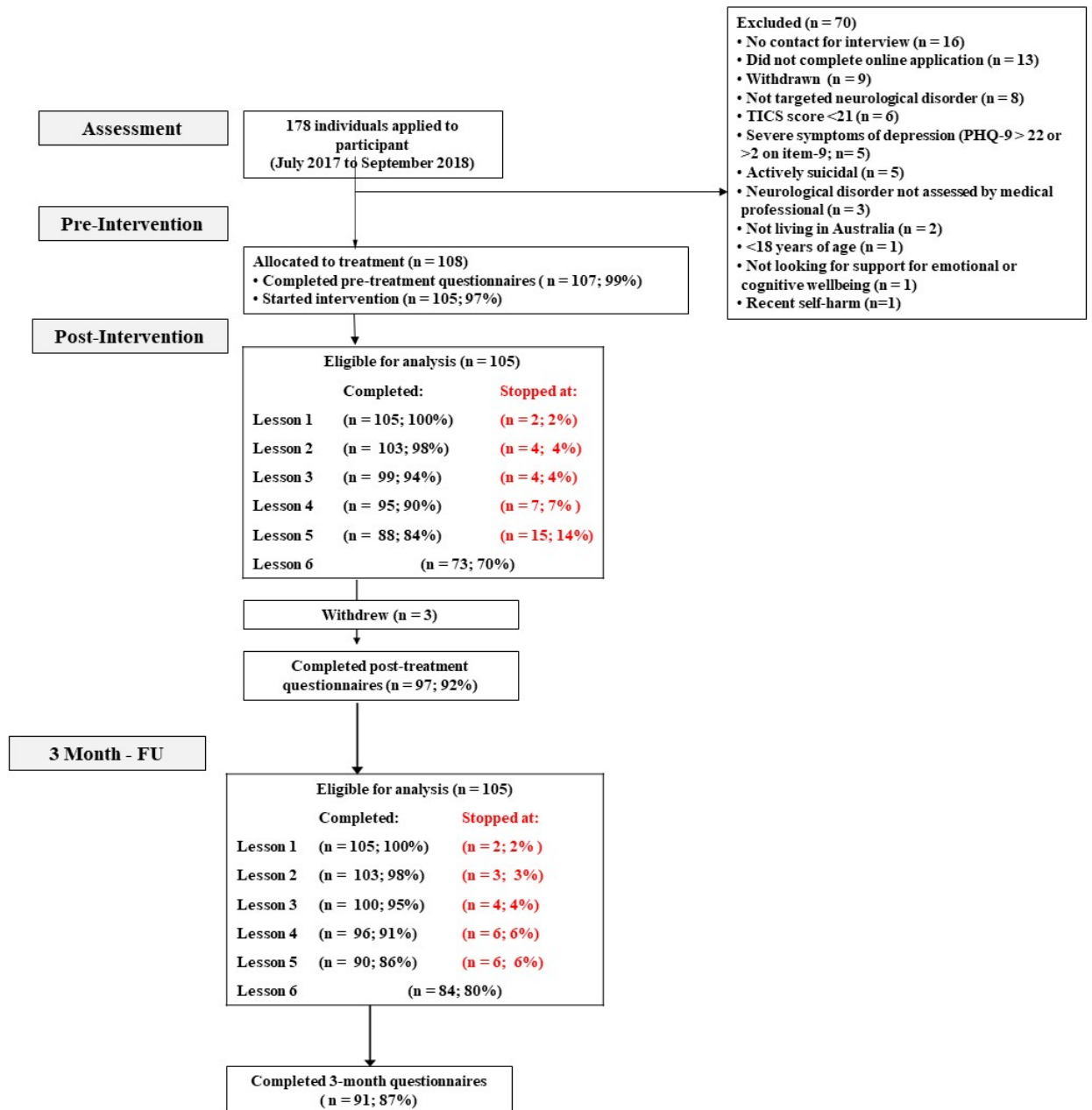


Table 1

*Medical Characteristics of Sample n = 105*

	<b>n</b>	<b>%</b>
<b>Neurological Disorder</b>		
Epilepsy <sup>a</sup>	18	17.1
Multiple Sclerosis (MS)	29	27.6
Parkinson's Disease (PD)	33	31.4
Acquired Brain Injury (ABI) <sup>b</sup>	32	30.5
Stroke	17	16.2
Traumatic Brain Injury	15	14.3
Other	2	1.9
<b>Duration Neuro Diagnoses (Years)</b>		
Mean (SD)	7.49 (7.06)	
Range	0.5 to 33	
<b>Current Neurology Medication (Yes)</b>	86	81.9
<b>Current Mental Health Medications</b>	45	42.9
Antidepressant	44	41.9
Anxiolytic	7	7
<b>Comorbid Chronic Health Condition <sup>c</sup></b>	50	47.6
<b>Previous Mental Health Intervention</b>	83	79
<b>Current Psychotherapy for Mental Health</b>	24	22.9
<b>Previous Cognitive Assessment/Rehabilitation</b>	31	29.5
<b>Current Cognitive Rehabilitation Support</b>	9	8.6

*Note.* Standard deviations are shown in parentheses.

<sup>a</sup> Includes 15 participants who reported epilepsy as primary neurological disorder and 3 where epilepsy was considered a secondary neurological disorder (2 with primary ABI, 1 with primary PD).

<sup>b</sup> Includes 28 participants who reported a primary neurological disorder of an ABI and 4 participants where the ABI was considered a secondary neurological (2 with primary MS and 2 with primary PD).

<sup>c</sup> Chronic Health Conditions included cardiovascular disease, cancer, diabetes, musculoskeletal condition, respiratory disease.

Table 2

*Demographic Characteristics of Sample n = 105*

	<b>n</b>	<b>%</b>
<b>Sex</b>		
Female	74	71
<b>Age</b>		
Mean (SD)	51.68 (12.07)	
Range	24 to 76	
<b>Marital Status</b>		
Single	16	15.2
Married/de facto/in a relationship	66	62.9
Separated/widowed/divorced	18	17.1
Other	5	4.8
<b>Education</b>		
High school or less	23	21.9
Certificate/diploma/other	36	34.3
University	46	43.8
<b>Employment/Vocational Status <sup>d</sup></b>		
Full-time/ Part-time	37	35
Student	6	6
Unemployed/ Seeking employment	15	14
Registered sick or disabled	26	25
Retired	25	24
<b>Has a Regular Carer</b>	40	38.1

*Note.* Standard deviations are shown in parentheses.

<sup>a</sup> Categories of employment were not mutually exclusive; participants could indicate more than one to best describe their situation.

Table 3.

*Timetable and Content of the Wellbeing Neuro Course*

<b>Lesson</b>	<b>Time Before Next Lesson</b>	<b>Lesson Content</b>	<b>Primary Skill Taught</b>	<b>Additional Resources</b>
<b>1</b>	1 week	Introduction to self-management. Education about how neurological disorders can impact emotional and cognitive wellbeing. Introduction of a CBT model and explanation of the functional relationship between thought, physical, behavioural and neurological symptoms. Case examples and tips to assist identifying their own symptoms and how their symptoms interact.	- Symptom identification - Symptom formulation	-Managing Sleep
<b>2</b>	2 weeks	Introduction to structured problem solving as a means of managing the impact of neurological symptoms. Instructions and examples for using structured problem solving in everyday life. Introduction to compensatory cognitive rehabilitation skills for managing common cognitive problems e.g., forgetting.	- Structured Problem Solving	-Managing Cognitive Problems
<b>3</b>	2 weeks	Introduction to the basic principles of cognitive therapy and importance of managing thoughts to manage one's wellbeing and impact of neurological disorder. Instructions and case examples for monitoring and challenging thoughts.	- Thought monitoring - Thought challenging	
<b>4</b>	2 weeks	Introduction to the physical symptoms of depression (i.e., hypo-arousal) and anxiety/anger (i.e. hyper-arousal) and relationship with wellbeing and managing neurological symptoms. Instructions about managing physical symptoms via scheduling pleasant, physical and cognitive activities. Instructions for using de-arousal strategies such as controlled breathing.	- Activity scheduling - Controlled relaxation	-Assertive Communication
<b>5</b>	2 weeks	Introduction to the behavioural symptoms of anxiety, depression and neurological disorders. Explanation of the overdoing-underdoing cycle of activity levels and issues around the fear and the avoidance of social, physical and cognitive activities. Instructions for activity pacing and gradually tackling avoidance.	- Activity pacing	-Managing Avoidance
<b>6</b>	1 week	Information about the occurrence of setbacks in thought, physical, behavioural and neurological symptoms. Information about the signs of setbacks and instructions for creating setback plans. Information about the importance of continued structured problem solving and revisions/practice of skills into the future.	- Structured Problem Solving - Relapse prevention	

**Table 4.**

Primary Outcomes: Means, Standard Deviations, Percentage Change and Effect Sizes for Overall Sample and Neurological Disorder Sub-Groups

	n	Estimated Marginal Means					Percentage Change from Baseline <sup>a</sup>		Cohen's <i>d</i> Effect Sizes from Baseline	
		Assessment	Pre-Intervention	Mid-Intervention	Post-Intervention	3-Month Follow-up	Post-Intervention	3-Month Follow-up	Post-Intervention	3-Month Follow-up
<b>Depression (PHQ-9)</b>										
<b>Overall Sample</b>	<b>105</b>	<b>10.74 (4.51)</b>	<b>9.92 (4.51)</b>	<b>7.47 (4.51)</b>	<b>6.87 (3.79)</b>	<b>7.21 (4.71)</b>	<b>36% (29%, 43%)</b>	<b>33% (25%, 41%)</b>	<b>0.93 (0.64, 1.21)</b>	<b>0.77 (0.49, 1.05)</b>
Epilepsy	18	10.89 (3.52)	11.95 (4.24)	8.73 (2.93)	8.45 (3.44)	9.01 (4.71)	22% (7%, 32%)	17% (-3%, 37%)	0.67 (0, 1.34)	0.43 (-0.23, 1.09)
MS	29	9.00 (4.74)	8.86 (5.28)	5.76 (3.55)	5.07 (3.18)	5.00 (4.25)	44% (31%, 57%)	44% (27%, 62%)	0.94 (0.4, 1.49)	0.86 (0.32, 1.4)
PD	33	10.70 (4.02)	9.09 (3.62)	7.14 (4.54)	7.02 (3.33)	7.03 (3.45)	34% (24%, 45%)	34% (23%, 45%)	0.96 (0.45, 1.47)	0.95 (0.44, 1.46)
ABI	32	12.50 (4.53)	10.44 (4.02)	8.56 (5.15)	7.45 (3.90)	8.40 (5.20)	40% (30%, 51%)	33% (18%, 47%)	1.16 (0.63, 1.69)	0.82 (0.31, 1.33)
<b>Anxiety (GAD-7)</b>										
<b>Overall Sample</b>	<b>105</b>	<b>7.88 (4.71)</b>	<b>6.76 (4.41)</b>	<b>5.82 (4.61)</b>	<b>5.02 (3.89)</b>	<b>5.06 (4.41)</b>	<b>36% (27%, 46%)</b>	<b>36% (25%, 47%)</b>	<b>0.66 (0.38, 0.94)</b>	<b>0.61 (0.34, 0.89)</b>
Epilepsy	18	9.28 (4.48)	8.83 (4.20)	7.50 (4.37)	7.33 (4.29)	7.66 (4.45)	21% (0%, 42%)	17% (-5%, 40%)	0.40 (-0.26, 1.06)	0.33 (-0.33, .99)
MS	29	7.83 (4.95)	6.73 (5.49)	4.30 (3.72)	3.73 (3.50)	3.34 (3.82)	52% (36%, 69%)	57% (40%, 75%)	0.93 (0.38, 1.47)	0.99 (0.44, 1.53)
PD	33	7.12 (3.73)	5.49 (3.33)	5.21 (3.91)	4.51 (3.10)	4.26 (2.64)	37% (22%, 51%)	40% (28%, 53%)	0.74 (0.24, 1.24)	0.87 (0.36, 1.37)
ABI	32	8.03 (4.75)	6.78 (3.68)	6.58 (5.37)	5.10 (3.79)	5.82 (5.09)	36% (20%, 53%)	28% (6%, 50%)	0.66 (0.16, 1.69)	0.44 (-0.06, 0.93)
<b>Disability (WHODAS-2.0)</b>										



<b>Overall Sample</b>	<b>105</b>	<b>18.62 (8.3)</b>	<b>17.48 (8.61)</b>	<b>15.57 (7.89)</b>	<b>14.58 (8.10)</b>	<b>14.27 (8.61)</b>	<b>22% (13%, 30%)</b>	<b>23% (15%, 32%)</b>	<b>0.49 (0.21, 0.76)</b>	<b>0.51 (0.24, 0.79)</b>
Epilepsy	18	18.95 (9.29)	17.06 (8.44)	15.47 (7.30)	14.17 (8.57)	14.36 (7.68)	25% (4%, 46%)	24% (5%, 43%)	0.51 (-0.16 , 1.17)	0.51 (-0.15, 1.17)
MS	29	16.69 (7.92)	16.00 (8.29)	14.16 (7.92)	11.31 (7.11)	11.34 (7.75)	32% (17%, 48%)	32% (15%, 49%)	0.69 (0.16, 1.22)	0.66 (0.13, 1.19)
PD	33	17.88 (7.53)	16.33 (8.16)	15.15 (8.16)	15.49 (7.98)	15.75 (9.88)	13 % (-2%, 29%)	12% (-7%, 31%)	0.30 (0.19, 0.79)	0.24 (0.25, 0.72)
ABI	32	21.47 (8.77)	20.97 (8.71)	17.23 (7.47)	17.21 (7.18)	15.22 (7.35)	20% (8%, 31%)	29% (17%, 41%)	0.52 (0.23, 1.22)	0.75 (0.24, 1.26)

*Notes:* MS = Multiple Sclerosis, PD = Parkinson's Disease, ABI = Acquired Brain Injury, PHQ-9 = Patient Health Questionnaire 9-item, GAD-7 =Generalised Anxiety Disorder 7-item questionnaire, WHODAS 2.0 = World Health Organisation Disability Scale.

Standard deviations are shown in parentheses for the means and 95% confidence intervals are shown in parentheses for effect size and percentage change statistics.

a The percentage change from baseline statistics are estimates of relative change derived from the GEE models conducted separately for each outcome.

**Table 5.**

Secondary Outcomes: Means, Standard Deviations, Percentage Change and Effect Sizes for the Overall Sample.

Overall sample (n = 105)	Estimated Marginal Means				Percentage Change from Baseline		Cohen's <i>d</i> Effect Sizes from Baseline	
	Pre- Intervention	Mid- Intervention	Post- Intervention	3-Month Follow-up	Post- Intervention	3-Month Follow-up	Post- Intervention	3-Month Follow- up
<b>Attention (PDQ)</b>	2.24 (0.82)	2.19 (0.72)	2.07 (0.72)	1.95 (0.82)	7% (1%, 14%)	13% (6%, 20%)	0.21 (-0.06 to 0.49)	0.35 (0.08 to 0.62)
<b>Planning (PDQ)</b>	2.02 (0.82)	1.98 (0.82)	1.88 (0.72)	1.79 (0.82)	7% (0%, 14%)	12% (4%, 20%)	0.17 (-0.1 to 0.44)	0.28 (0 to 0.55)
<b>Prospective Memory (PDQ)</b>	1.63 (0.82)	1.59 (0.72)	1.47 (0.72)	1.50 (0.72)	10% (2%, 18%)	8% (1%, 17%)	0.21 (-0.06 to 0.49)	0.17 (-0.1 to 0.44)
<b>Retrospective Memory (PDQ)</b>	2.00 (0.82)	1.98 (0.82)	1.88(0.82)	1.83 (0.92)	6% (-2%, 4%)	8% (0%, 17%)	0.14 (-0.13 to 0.41)	0.19 (-0.08 to 0.46)
<b>Fatigue (FSS)</b>	47.12 (12.09)	46.62 (12.81)	44.50 (12.71)	44.62 (12.60)	6% (0%, 11%)	5% (0%, 10%)	0.21 (-0.06 to 0.48)	0.20 (-0.07 to 0.47)

Notes: MS = Multiple Sclerosis, PD = Parkinson's Disease, ABI = Acquired Brain Injury, PDQ = Perceived Deficits Questionnaires, FSS = Fatigue Severity Scale.

Standard deviations are shown in parentheses for the means and 95% confidence intervals are shown in parentheses for effect size and percentage change statistics.

<sup>a</sup> The percentage change from baseline statistics are estimates of relative change derived from the GEE models conducted separately for each outcome.