



**A longitudinal observational study of patient-centered nutritional, psychological and combined therapies for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).**

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2012-001079
Article Type:	Research
Date Submitted by the Author:	27-Feb-2012
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<b>Primary Subject Heading</b>:	Patient-centred medicine
Secondary Subject Heading:	Complementary medicine, Nutrition and metabolism
Keywords:	COMPLEMENTARY MEDICINE, SOCIAL MEDICINE, REHABILITATION MEDICINE

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## **Abstract**

Background: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a condition characterised by severe and persistent fatigue, neurological disturbances, autonomic and endocrine dysfunctions and sleep difficulties that have a pronounced and significant impact on individuals' lives. Current NICE guidelines within the United Kingdom suggest that this condition should be treated with cognitive behavioural therapy and/or graded exercise therapy where appropriate. There is currently a lack of evidence-base concerning other, more integrative interventions that may be beneficial to those with ME/CFS.

Objectives: This study aimed to evaluate whether three patient-centered treatment modalities of psychology, nutrition and combined treatment, reduced symptomatology of ME/CFS over a 3-month time period and whether there were significant differences in these changes between groups.

Design and setting: This is a longitudinal observational study conducted at one private secondary health care facility in London, UK.

Participants: One-hundred and thirty-eight individuals (110 females, 79.7%; 42 participants in psychology, 44 in nutrition and 52 in combined) participated at baseline and 72 participants completed the battery of measures at follow-up (52.17% response rate; 14, 27, 31 participants in each group, respectively).

Outcome measures: Self-report measures of ME/CFS symptoms, functional ability, multidimensional fatigue, perceived control and maladaptive stress.

Results: Baseline comparisons showed those in the combined group had higher levels of fatigue. At follow-up, all groups saw improvements in fatigue, functional physical symptomatology and maladaptive stress; those within the psychology group also experienced a shift in perceived control over time. The psychology group demonstrated a significantly greater change in fatigue and perceived control than the combined group; however, the opposite relationship was observed for headaches.

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3 Conclusions: Patient-centered techniques for the treatment of ME/CFS appear promising in  
4 reducing symptomatology, fatigue and inappropriate responses to stressors and increasing  
5 function and perceived control. The need for further studies of integrative treatment with  
6 robust designs appears warranted.  
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## 10 11 **Summary**

### 12 **Article focus**

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15 • This observational study investigated three (psychological, nutritional and combined)  
16 tailored patient-centered interventions for ME/CFS over time.  
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21 • Differences between the reported changes over time between groups were also  
22 assessed.  
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### 25 **Key messages**

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27 • Patient-centered approaches for the management of ME/CFS reduce symptomatology  
28 over time.  
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32 • Functional ability, physical and social, increase with tailored interventions.  
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35 • Psychological intervention can help individuals to regain a sense of control over their  
36 condition.  
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### 38 **Strengths and limitations of this study**

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40 • The findings here are an initial step to fill the gap in the extant literature regarding the  
41 utility of tailored, multidisciplinary and patient-centered treatments for ME/CFS.  
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45 • There is bias in this study as the participants were self-selected in the sense that they  
46 chose to attend the clinic and which treatment option they preferred (with advice).  
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## **Introduction**

Chronic Fatigue Syndrome or myalgic encephalomyelitis (ME/CFS) is a condition characterized by prolonged and debilitating fatigue, although the exact cause of this disorder is still under debate. Due to the lack of a definitive biological marker, diagnosis is made on the basis of the exclusion of other explanatory conditions. The most widely used case definition by the Centers for Disease Control <sup>1</sup> states that there must be at least six months severe fatigue of new and definite onset, not the result of ongoing exertion, not alleviated by rest and resulting in reduced levels of physical activity. The CDC definition also sets out a series of minor complaints that must accompany the fatigue (cognitive impairment, sore throat, tender cervical or axillary lymph nodes, muscle pain, multi-joint pain, headaches of a new type, pattern or severity at onset, unrefreshing sleep and post-exertion malaise), with individuals needing to have the occurrence of four or more symptoms to be diagnosed with ME/CFS. Estimates of the prevalence of ME/CFS have been made as low as 3 and as high as 2,800 per 100,000 <sup>2</sup>.

The most widely researched strategies for alleviating the symptoms of ME/CFS are Cognitive Behavior Therapy (CBT) and Graded Exercise Therapy (GET). Two reviews of studies on CBT <sup>3 4</sup> found that it significantly improved physical functioning in adult out-patients as compared with medical management counseling, guided support, education and support or relaxation. However, the longitudinal evidence for CBT is inconsistent and there is a lack of evidence with regard to CBT in combination with other treatments <sup>4</sup>. Regarding GET, a systematic review illustrated that this form of therapy was potentially beneficial for people with ME/CFS, especially when combined with a patient education programme <sup>5</sup>. However, drop-out rates were high in the GET groups suggesting that individuals with ME/CFS are adverse to this type of therapy.

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5 Although CBT and GET studies have shown some promising outcomes, there is no known  
6 cure for ME/CFS. Therefore National Institute for Health and Clinical Excellence (NICE) <sup>6</sup>  
7 recommends a number of symptom management strategies and interventions aimed at  
8 helping individuals to cope with their condition and reduce physical deconditioning brought  
9 about by the illness. Pharmacological interventions are, at times, suggested for patients with  
10 poor sleep or pain, for instance, low-dose antidepressants, as these have been shown to be  
11 effective <sup>7-13</sup>. However, patient expectations must be realistic as the drugs may help elevate  
12 mood and psychological outlook but not reduce fatigue and other symptomatology associated  
13 with ME/CFS<sup>14</sup>. Numerous drugs such as thyroxin, hydrocortisone and antiviral agents are  
14 not advised by NICE due to contradictory findings <sup>15;16</sup>.

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30 In terms of function and quality of life management, NICE offers general advice concerning  
31 sleep management, appropriate rest periods, and pacing. Sleep hygiene instruction, together  
32 with pharmacological treatment tailored to the individual patient can be beneficial in  
33 combating fatigue <sup>17</sup>. Dietary management may also reduce symptomatology for those with  
34 concurrent irritable bowel syndrome (IBS). Management approaches recommended for IBS,  
35 such as diet restriction, are thus also recommended for those with ME/CFS <sup>18</sup>. Dietary  
36 supplementation has been investigated in relation to ME/CFS. Fatty acids <sup>19</sup>, folic acid <sup>20</sup>,  
37 vitamin C <sup>21</sup>, co-enzyme Q10 <sup>22</sup>, magnesium <sup>23</sup>, multivitamins <sup>24</sup> and minerals <sup>25</sup> have all been  
38 shown to reduce symptomatology in ME/CFS patients. However other studies have shown  
39 conflicting findings with regard to nutritional supplementation, therefore it is perhaps wise to  
40 treat with supplements on a case-by-case basis <sup>26;27</sup>.

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3 Due to the lack of clear and definitive treatment strategies, individuals often seek out  
4 Complementary and Alternative Medicines (CAM). Although NICE does not propose the use  
5 of CAM they do acknowledge that many people with ME/CFS use such therapies and find  
6 them beneficial for symptom management. This view is due to the lack of published evidence  
7 for the effectiveness of these treatments. Examples of CAM treatments used by individuals  
8 with ME/CFS include religious healing, massage therapy, relaxation, meditation,  
9 homeopathy, acupuncture, naturopathy and herbal therapies<sup>28;29</sup>; patient satisfaction of such  
10 approaches CAM has been high, over 80% in some instances<sup>28</sup>. A recent systematic review  
11 of such interventions identified 70 controlled clinical trials (randomized and non-randomized)  
12 and found that 86% of these studies illustrated at least one positive effect, with 74% showing  
13 a decrease of illness-related symptomatology<sup>30</sup>. Meditative or mindfulness approaches  
14 warranted further investigation based on these results as did supplement programs of  
15 magnesium, l-carnitine, and S-adenosylmethionine. A subsequent review based solely on  
16 randomized controlled trials (RCTs) of CAM techniques identified 26 such studies and  
17 observed that qigong, massage and tuina (approaches based within Chinese Traditional  
18 Medicine and based upon relaxation and connection with the body) illustrated positive effects  
19 as did supplementation studies utilizing nicotinamide adenine dinucleotide (NADH) and  
20 magnesium<sup>31</sup>. However, within both reviews it was noted that the methodological quality of  
21 reporting was poor and the sample sizes in these studies were small; hence ability to draw  
22 strong conclusions on the efficacy of CAM methods is limited. Porter et al. (2010) did note  
23 that patient-centered, individualized treatment protocols which include a range of tailored  
24 strategies are a promising area for further investigation for this complex, multi-system illness.  
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## Objectives

There is still much debate and uncertainty regarding the most effective treatment for ME/CFS. Recent reviews of CAM techniques highlight the need for further exploration of patient-centered and individually tailored interventions for the alleviation of the condition's often debilitating and intrusive symptomatology. This study therefore aims to evaluate the effectiveness of three types of patient-centered approaches to the management of ME/CFS over time (baseline and follow-up) offered at a private health-care center in the UK.

## Methods

### Study design and setting

This is a longitudinal observational study which aimed to evaluate three treatment options offered to individuals with ME/CFS. The research was conducted at one private secondary health care facility. All prospective patients of the clinic are first asked to complete a comprehensive symptom profile and medical history, including questions relating to triggering factors, psychology sub-types and structural/biological sub-types (this is distinct from the research data collected). Subsequent to this, every individual receives a 15-minute screening with one of the practitioners who recommends the best course of action for his/her needs; this will be the psychology-related interventions, nutritional advice and support or a combination of the two.

All individuals requesting treatment at the private care setting were offered the opportunity to participate in the study. Those that expressed an interest were emailed a spreadsheet that contained the questionnaires and asked to complete it at their convenience. Informed consent was obtained prior to the completion of the questionnaires and the study was approved by the University of East London Ethics Committee. Participants were told that they could withdraw

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3 from the study at any time and that withdrawal would not affect their care at the clinic.  
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5 Participants were able to ask questions at any point in the study and no deception was used as  
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7 the participants were informed of the nature of the research program before they agreed to  
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9 participate.  
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### 11 12 13 14 *Psychology*

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16 The clinic offers a 3-month intervention which consists of a combination of Neuro-linguistic  
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18 Programming (NLP), Emotional Freedom Techniques (EFT), life coaching and  
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20 hypnotherapy/self-hypnosis constructed in a manner specific to the needs to those with  
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22 ME/CFS. The primary aim of this approach is to reduce the anxiety that is associated with  
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24 having a debilitating and unpredictable condition, improve emotional well-being and help  
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26 individuals slowly manage and increase their activity within their own limits (i.e. pacing).  
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28 The program is offered as a series of group sessions and the peer support is seen as an  
29  
30 important component of the intervention, which is solidified via the use of moderated online  
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32 support forums, narratives of previous client's experiences and online materials that can be  
33  
34 accessed as often as necessary. In addition, or an alternative to this course, individuals  
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36 receive a series of one-to-one sessions and for the most severely affected ME/CFS patients,  
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38 telephone sessions are arranged and support materials can be accessed in their own homes.  
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### 45 46 *Nutrition*

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48 Tailored nutritional therapy is achieved via one-to-one consultations with individuals. To  
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50 begin, a very detailed history is taken based upon the information given in the  
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52 aforementioned symptom profile. Qualified nutritional therapists (who have been given  
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54 specialist training regarding ME/CFS from the clinic) then suggest tests consistent with  
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56 symptomatology, for instance the Adrenal Stress Index Test, comprehensive stool  
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3 analysis/gastro-intestinal function, vitamin & mineral status, etc. Results from these tests are  
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5 then used to compose an evidence-driven diet and supplement program. As most cases of  
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7 ME/CFS are complex involving multiple body systems, this process is often iterative and  
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9 follow-up consultations are necessary to check progress and make alterations to the protocol.  
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### 12 13 14 *Combined*

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16 Within the combined program, a multidisciplinary approach is taken with practitioners  
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18 discussing the patients in case meetings to ensure that the psychological and nutritional  
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20 aspects complement each other in order to achieve the best outcome.  
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### 23 24 25 **Measures**

#### 26 27 *Medical Outcomes Survey Short-Form 36 (SF-36)*

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29 This 36-item measure is the short form of the original Medical Outcomes Survey <sup>32</sup> to  
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31 measure functional impairment and contains eight sub-sections: 1) physical activity  
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33 limitations due to health problems; 2) social activity limitations due to physical or emotional  
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35 problems; 3) usual role activity limitations due to physical health problems; 4) bodily pain; 5)  
36  
37 general mental health; 6) role activity limitations in usual due to emotional problems; 7)  
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39 vitality (energy and fatigue); and 8) general health perceptions <sup>32</sup>. The items are scored so that  
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41 higher scores indicate greater functional ability. In terms of the psychometric properties of  
42  
43 this measure, reliability estimates for all sub-scales are good, exceeding a Cronbach's alpha  
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45 coefficient value of 0.70 <sup>33</sup>. In terms of validity, the SF-36 correlates amply,  $r \geq 0.40$ , with the  
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47 frequency and severity of numerous symptoms and general health conditions <sup>34;35</sup>.  
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### *Multidimensional Health Locus of Control Scale (MHLCS)*

Multidimensional Health Locus of Control <sup>36-38</sup> measures perceived control via three distinct sub-scales: 'internal', 'chance' and 'powerful others' which has two dimensions, that of 'doctors' and 'other people'. The instrument contains 18 items in total (six items each for the internal and chance scales and three items for both the powerful others scales) and is scored on a 6-point Likert scale from 'strongly agree' to 'strongly disagree'. Internal reliability of the instrument is good with Cronbach's alpha coefficients ranging from 0.67 for 'powerful others' to 0.77 for 'internal'. The measure correlates positively and significantly with associated scales from Levenson's <sup>39</sup> locus of control measure from which the MHLOC was based upon, which demonstrates good convergent validity <sup>36</sup>.

### *Multidimensional Fatigue Inventory (MFI)*

This 20-item measure contains five fatigue dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity <sup>40</sup>. Items such as 'I tire easily' are rated on a 5-point scale (1 = yes, that is true; 5 = no, that is not true) with lower scores reflecting higher levels of fatigue. The MFI has good internal consistency with average Cronbach's alpha coefficient equaling 0.84 across the sub-scales. Convergent validity based on a sample of radiotherapy patients found correlations between the sub-scales and a visual analogue fatigue scale to be 0.77 for general fatigue, 0.70 for physical fatigue, 0.61 for reduced activity, 0.56 for reduced motivation ( $p < 0.001$ ) to 0.23 for mental fatigue ( $p < 0.01$ )

<sup>40</sup>.

### *CDC CFS Symptom Inventory*

CDC CFS Symptom Inventory <sup>41</sup> was used to measure specific ME/CFS symptoms and confirm diagnosis. This instrument is based upon the CDC case definition <sup>1</sup> and includes a

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3 fatigue item and the eight distinct symptoms are also including in the CDC guidelines and an  
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5 additional ten associated symptoms. The format of this self-report measure is a six-point scale  
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7 of perceived frequency (0 = absent, 5 = all the time) and severity (0 = none, 5 = very severe).  
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9 The psychometric properties of this instrument are good: Cronbach's alpha coefficient = 0.88;  
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11  $r = .74$  convergent validity with the Chalder Fatigue Scale <sup>42</sup>;  $r = -.68$  and  $-.87$  convergent  
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13 validity with the SF-36 'vitality' and 'bodily pain' sub-scales, respectively.  
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### 16 17 18 *Maladaptive Stress Index*

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20 This 32-item measure contains three sub-scales (cognitive/mood, sleep and ME/CFS  
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22 symptoms) and was designed specifically for this population <sup>43</sup>. Items such as 'I constantly  
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24 reply or pre-empt situations and conversations' and scored on a 5-point scale where 1 = never  
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26 true and 5 = always true; higher scores illustrate a greater degree of disturbance.  
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### 30 31 32 **Statistical methods**

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34 The data was initially screened for missing data. Three cases contained substantial amounts  
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36 of missing data; therefore these were excluded from the analysis. Once this was done, all the  
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38 variables had less than 5% missing data, hence mean substitution was carried out in line with  
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40 guidance <sup>44</sup>. The baseline data was subsequently of the quality for parametric tests, except for  
41  
42 the variables CDC CFS swollen lymph nodes and glands, memory problems, abdominal pain  
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44 and depression. However, the follow-up data suffered from high levels of skew and kurtosis  
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46 which was not substantially alleviated by data transformation. This violated a key criterion  
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48 for parametric testing, that of normality of distribution, so non-parametric tests were selected.  
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50 In addition, as the sample sizes in each individual treatment group was small, the more  
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52 conservative non-parametric tests were the preferred choice as even though tests such as  
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54 analysis of variance are generally robust against non-normality, this does not hold true with  
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3 small sample sizes. For baseline data, one-way analysis of variance tests and Kruskal-Wallis  
4 tests were used to investigate difference between groups, Wilcoxon sign-rank tests were  
5 employed to look for differences over time (baseline and 3-month follow-up) and Kruskal-  
6 Wallis tests were performed to investigate group differences in measures of change as  
7 evaluated by mean change scores, with Bonferroni-corrected Mann-Whitney tests calculated  
8 to identify post-hoc differences between groups if the Kruskal-Wallis tests were significant.  
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## 19 **Results**

### 20 **Participants**

21 One-hundred and thirty-eight individuals completed the questionnaire battery at time-one  
22 (excluding the four deleted cases); 42 participants in the psychology group, 44 in the nutrition  
23 group and 52 in the combined group. There was no significant association between gender  
24 and group ( $\chi^2(2) = 0.179, p > .05$ ), all groups consisting of approximately one-fifth males  
25 (Table 1). There was not a significant difference in age ( $F(2,135) = 0.000, p > .05$ ); in fact  
26 group means for age were near identical at 42.881, 42.864 and 42.843 for psychology,  
27 nutrition and combined group, respectively. There was also a non-significant result for illness  
28 duration ( $F(2, 135) = 0.252, p > .05$ ). Therefore, in terms of demographics, the groups were  
29 comparable. With regard to the outcome measures, there were significant differences between  
30 the groups in terms of the MFI sub-scale 'general fatigue' ( $F(2, 135) = 3.219, p < .05$ ), MFI  
31 'physical fatigue' ( $F(2, 135) = 3.343, p < .05$ ) and the CDC CFS symptom 'swollen lymph  
32 nodes and glands' ( $H(2) = 7.161, p < .05$ ). To investigate the source of these differences,  
33 post-hoc tests were conducted (unrelated t-tests for the fatigue variables and Mann-Whitney  
34 tests for swollen lymph glands as the former did not meet criteria for parametric tests, all with  
35 Bonferroni correction for multiple comparisons). A significant difference was observed  
36 between the psychology and combined groups with regards to general fatigue ( $t(92) = -2.449$ ,  
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3  $p < .05$ ) and physical fatigue ( $t(92) = -2.658, p < .05$ ) and also between the nutrition and  
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5 psychology group in terms of the degree of lymph node and gland swelling ( $U = 635.00, p <$   
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7  $.05$ ). Within the fatigue measures, the combined group reported significantly higher levels of  
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9 both general and physical fatigued than the psychology group whereas those undertaking  
10  
11 nutritional support stated a higher occurrence swollen lymph nodes and glands.  
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### 14 15 16 *Retention analysis*

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18 Seventy-two of the original 138 participants completed the battery of measures at the 3-  
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20 month follow-up (52.17%). To investigate whether the individuals who did not complete the  
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22 time-two measures were significantly different from those at baseline on demographic and  
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24 outcome measures, a series of t-tests and Mann-Whitney tests were performed. Those that  
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26 dropped-out of the research (although still receiving treatment at the clinic) differed  
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28 significantly in terms of age ( $t(136) = -2.227, p < .05$ ) and illness duration ( $t(136) = -2.549, p$   
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30  $< .05$ ). Those who remained in the study were of significantly older age (mean age of those  
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32 that remained in the study = 45.056, SD = 11.535; mean age of drop-outs = 40.400, SD  
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34 =12.932) and longer illness duration than those who dropped-out (mean age of those that  
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36 remained in the study = 10.836, SD = 7.383; mean illness duration of drop-outs =7.571, SD =  
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38 7.472). Individuals who did not remain in the study did not differ significantly in terms of  
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40 gender ( $\chi^2 (2) = 1.222, p > .05$ ) or any of the outcome measures.  
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### 47 **Longitudinal data**

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49 In the sample as a whole, there were significant differences from baseline to follow-up within  
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51 the internal and doctors sub-scale of the MHLCS and all the CDC CFS Symptom Inventory  
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53 items bar swollen lymph nodes and glands, fever and abdominal pain. There were also  
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55 significant differences in all areas of the SF-36, all the fatigue sub-scales of the MFI with the  
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3 five sub-scales illustrating significant reductions in fatigue and, finally, reductions were also  
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5 observed in the Maladaptive Stress Response.  
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10 Within the psychology group significant differences were also found in the SF-36 sub-scales  
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12 'physical functioning', 'role limitations due to physical problem', 'social functioning',  
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14 'general mental health', 'vitality, energy or fatigue' and 'general health perceptions'.  
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16 Regarding perceived control, significant differences were found in internal locus of control  
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18 and the perception that chance played an influential part in the individuals' lives. Again, all  
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20 the MFI fatigue scales saw significant decreases over a 3-month period. Regarding ME/CFS  
21  
22 specific symptoms, ratings of muscle aches or muscle pains, chills, memory problems,  
23  
24 difficulty concentrating and sensitivity to light differed significantly from baseline to follow-  
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26 up in the expected direction. There was also a significant reduction in the Maladaptive Stress  
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28 Response over time.  
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34 The nutrition group saw significant improvements in role limitations due to physical  
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36 problems, social functioning, vitality, energy or fatigue and general health perceptions. No  
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38 significant differences were found from baseline to follow-up in perceived control in the  
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40 nutrition group. Once again, all the MFI fatigue scales decreased over a 3-month period and  
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42 numerous symptom-related indices also showed improvements; sore throat, swollen lymph  
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44 glands, fatigue after exertion, muscle aches or muscle pains, pain in joints, chills, headaches,  
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46 abdominal pain and sensitivity to light. The way in which the individuals in this group  
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48 responded to stress also decreased over the 3-month time period.  
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54 In terms of general health as evaluated by the SF-36 measure, the group who received both  
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56 psychological and nutritional intervention reported reductions in role limitations due to  
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3 physical difficulties, social functioning, role limitations due to emotional difficulties and  
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5 general health perceptions. No significant differences were found from baseline to follow-up  
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7 in perceived control as measured by the MHLCS in the combined treatment group. Only one  
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9 measure of fatigue, that of physical fatigue, saw significant improvements over time.  
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11 Diarrhea, fatigue after exertion, chills, headaches and sinus and nasal symptoms all illustrated  
12  
13 significant reductions over the 3-month interval, as did the Maladaptive Stress Response.  
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15 (See Table 2 for descriptive and inferential statistics associated with these findings and Table  
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17 3 for percentage of change over time.)  
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### 20 21 22 23 **Comparisons across groups**

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25 As shown in Table 3, three of the outcome measures differed significantly in terms of change  
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27 from baseline to follow up, namely the MHLCS 'chance' sub-scale ( $H(2) = 7.674, p < .05$ ),  
28  
29 the MFI 'general fatigue' sub-scale ( $H(2) = 6.790, p < .05$ ) and the CDC CFS symptom  
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31 'headaches' ( $H(2) = 6.625, p < .05$ ). In terms of perceived control and general fatigue, the  
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33 psychology group differed significantly as compared to the combined group ( $U = 110.500, p$   
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35  $< .05$ ) and ( $U = 118.000, p < .05$ ), respectively, with the psychology group seeing a greater  
36  
37 change over time as compared to the combined group on both measures. Regarding  
38  
39 headaches, the combined group ( $U = 118.000, p < .05$ ) improved significantly more than the  
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41 psychology group. No other comparisons reached statistical significance with a Bonferroni  
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43 correction for multiple comparisons.  
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### 49 **Discussion**

#### 50 **Key results**

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52 There was significant change over time of numerous measures in all groups investigated. The  
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54 psychology group contained the most significant findings, including those concerned with  
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3 daily functioning, fatigue, locus of control, the cognitive CDC CFS specific symptoms and  
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5 the Maladaptive Stress Response. As expected, changes in perceived control were not  
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7 observed in the nutrition group as this is not an area that is targeted in this program.  
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10 However, the more immune-type symptoms such as sore throat, swollen lymph nodes or  
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12 glands and pain in joints did see significant reductions over time as would be envisaged in  
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14 treatment protocols based upon nutritional expertise. The group that exhibited the least  
15  
16 significant findings was the combined group and, as noted below, this may be due to the  
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18 greater general severity in this group and the need for a more lengthy intervention.  
19  
20 Nevertheless, considering the small sample sizes in the groups at follow-up, these results are  
21  
22 very promising and warrant further attention. In terms of these preliminary findings, the  
23  
24 psychology group performed better with regard to lowering the belief that chance influences  
25  
26 the course of the condition. This is an important observation as the unpredictable nature of  
27  
28 ME/CFS can be one of the most difficult components for individuals to cope with <sup>45</sup> and  
29  
30 helping patients gain an improved sense of control over the illness is of great potential  
31  
32 benefit. The psychology group also demonstrated a significantly greater change score in  
33  
34 general fatigue as compared with the combined group which may infer that in the short term,  
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36 guiding individuals through the complex nature of the disorder, helping them to understand it  
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38 and accept that the condition itself gives rise to stresses and psychological distress may be a  
39  
40 good starting point for intervention (i.e. a stepped program could be developed).  
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### 47 **Interpretation**

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49 As noted previously <sup>30</sup> patient-centered, individualized treatment protocols which include a  
50  
51 range of tailored strategies is a favorable direction for dealing with a complex and multi-  
52  
53 system disorder such as ME/CFS. The present study has demonstrated that such interventions  
54  
55 are useful in lowering symptomatology, improving functioning and helping individuals gain a  
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3 greater sense of control over their health status. Considering that the options available on the  
4 National Health Service, mainly CBT and GET, are often perceived as coping strategies at  
5 best, and physically damaging at worst <sup>46</sup>, tailored treatments such as described here may be  
6 more palatable, and hence effective.  
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### 11 12 13 14 **Limitations and Generalisability**

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16 This study did not have a control group so the results should be treated with caution. Also,  
17 the participants were not randomly assigned to groups as this was a naturalistic, observational  
18 study. Each individual was guided to appropriate treatment within an initial screening with  
19 clinic staff, therefore the group was dependent on the nature of the individual's symptoms  
20 and their personal choice as the programs on offer were privately funded. However, as can be  
21 seen in the baseline comparisons, the groups did not differ in terms of gender, age, illness  
22 duration or the majority of outcome measures. Notably, the groups did differ in general and  
23 physical fatigue with participants in the combined groups reporting greater fatigue than those  
24 in the psychology group which suggests that this group's general symptomatology was more  
25 severe. The combined group illustrated less improvement over time compared to the  
26 psychology and nutrition groups and it is feasible to infer that individuals with a greater  
27 number and degree of complaints are referred to the combined group within the clinic. Also,  
28 it should be noted that the interventions in the combined program are phased in as it was  
29 found that asking individuals to engage in numerous therapeutic activities resulted in high  
30 drop-out rates. Therefore, changes in outcome measures may not be noted at an interval of  
31 three months for that group. Further studies underway presently will investigate follow-ups at  
32 6- and 12-months to identify whether the findings here are maintained over time and also  
33 whether those with greater severity benefit with a longer intervention. As the participants  
34 were self-selected onto these programs, the findings lack generalizability; future work should  
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3 sample from the overall ME/CFS population and be randomly-assigned to groups in order to  
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5 make valid assumptions regarding the illness-group as a whole.  
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### 9 10 **Funding**

11 No external funding was obtained for this research; the work was accomplished in-house at  
12  
13 the clinic in question.  
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### 20 21 **Data Sharing**

22 Dataset available from the corresponding author at m.a.arroll@sa.uel.ac.uk. Consent was not  
23  
24 obtained for data sharing but the presented data are anonymised and risk of identification is  
25  
26 low.  
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### 32 33 **Contributorship**

34  
35  
36 Alex Howard made a substantial contributions to conception and design and acquisition of  
37  
38 data, whilst Megan Arroll made a substantial contribution to the analysis and interpretation of  
39  
40 data. Both authors made a substantial  
41  
42 contribution to the drafting of the article and revisions for the critically of important  
43  
44 intellectual content. Final approval of the version to be published was also granted by both  
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46 authors.  
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### 52 53 **Competing Interests**

54 None  
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3 List of abbreviations  
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5 ME: myalgic encephalomyelitis  
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7 CFS: Chronic Fatigue Syndrome  
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9 NICE: National Institute for Health and Clinical Excellence  
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11 CBT: Cognitive Behavioral Therapy  
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13 GET: Graded Exercise Therapy  
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15 CAM: Complementary and Alternative Medicine  
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17 NLP: Neuro-linguistic Programming  
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19 EFT: Emotional Freedom Technique  
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21 SF-36: Medical Outcomes Survey Short-Form 36  
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23 MHLCS: Multidimensional Health Locus of Control Scale  
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25 MFI: Multidimensional Fatigue Inventory  
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**Table 1. Baseline comparisons of sample demographics and outcome variables**

		Mean	SD	95% CI for Mean		Test statistic	p-value
				Lower	Upper		
Gender	Psychology	9 (21.4%) <sup>d</sup>				.179 <sup>c</sup>	.915
	Nutrition	8 (18.2%) <sup>d</sup>					
	Combined	11 (21.2%) <sup>d</sup>					
	Total	28 (20.3%) <sup>d</sup>					
Age	Psychology	42.881	13.986	38.523	47.239	.000 <sup>a</sup>	1.000
	Nutrition	42.864	12.504	39.062	46.665		
	Combined	42.843	11.125	39.714	45.972		
	Total	42.861	12.406	40.765	44.957		
Illness duration	Psychology	8.874	8.252	6.302	11.445	.252 <sup>a</sup>	.778
	Nutrition	10.023	7.375	7.781	12.265		
	Combined	9.625	7.291	7.595	11.655		
	Total	9.523	7.580	8.247	10.800		
SF-36 Physical Functioning	Psychology	49.339	22.698	42.266	56.413	.319 <sup>a</sup>	.727
	Nutrition	47.855	26.226	39.882	55.829		
	Combined	45.299	25.479	38.206	52.393		
	Total	47.344	24.792	43.171	51.517		
SF-36 Role limitations physical	Psychology	7.143	15.894	2.190	12.096	.281 <sup>a</sup>	.755
	Nutrition	7.574	17.500	2.254	12.895		
	Combined	9.774	21.051	3.914	15.635		
	Total	8.272	18.387	5.177	11.367		
SF-36	Psychology	61.548	25.614	53.566	69.530	1.002 <sup>a</sup>	.370

Bodily pain	Nutrition	55.625	30.242	46.431	64.819		
	Combined	53.606	27.019	46.084	61.128		
	Total	56.667	27.683	52.007	61.327		
SF-36	Psychology	37.202	21.824	30.402	44.003	.536 <sup>a</sup>	.586
Social functioning	Nutrition	32.671	25.888	24.800	40.541		
	Combined	32.452	24.786	25.552	39.352		
	Total	33.967	24.212	29.892	38.043		
SF-36	Psychology	60.286	19.584	54.183	66.389	.124 <sup>a</sup>	.884
General mental health	Nutrition	59.727	19.355	53.843	65.612		
	Combined	58.308	20.948	52.476	64.140		
	Total	59.362	19.911	56.011	62.714		
SF-36	Psychology	55.554	46.368	41.104	70.004	.390 <sup>a</sup>	.678
Role limitations emotional	Nutrition	48.482	47.390	34.074	62.890		
	Combined	47.780	43.924	35.551	60.008		
	Total	50.370	45.590	42.695	58.044		
SF-36	Psychology	20.714	16.1386	15.685	25.743	.129 <sup>a</sup>	.879
Vitality Energy or Fatigue	Nutrition	20.114	14.570	15.685	24.542		
	Combined	19.039	17.658	14.123	23.955		
	Total	19.891	16.159	17.171	22.611		
SF-36	Psychology	37.024	17.945	31.432	42.616	2.769 <sup>a</sup>	.066
General health perceptions	Nutrition	28.636	15.528	23.915	33.357		
	Combined	30.962	17.575	26.069	35.854		
	Total	32.065	17.286	29.156	34.975		
MHLCS Internal	Psychology	.677	.159	.627	.726	1.216 <sup>a</sup>	.300
	Nutrition	.622	.177	.568	.675		



	Combined	.662	.174	.613	.710		
	Total	.653	.171	.625	.682		
MHLCS Chance	Psychology	.368	.156	.320	.417	.395 <sup>a</sup>	.674
	Nutrition	.340	.133	.299	.380		
	Combined	.354	.155	.311	.397		
	Total	.354	.148	.329	.379		
MHLCS Powerful Others	Psychology	.404	.134	.362	.446	.119 <sup>a</sup>	.888
	Nutrition	.417	.141	.374	.460		
	Combined	.407	.101	.379	.436		
	Total	.409	.124	.388	.430		
MHLCS Doctors	Psychology	.169	.082	.143	.194	.575 <sup>a</sup>	.564
	Nutrition	.171	.089	.144	.197		
	Combined	.191	.147	.150	.232		
	Total	.178	.112	.159	.196		
MHLCS Other People	Psychology	.235	.075	.212	.259	1.051 <sup>a</sup>	.352
	Nutrition	.264	.129	.225	.304		
	Combined	.245	.074	.224	.265		
	Total	.248	.095	.232	.264		
MFI General Fatigue	Psychology	15.952	2.845	15.066	16.839	3.219 <sup>a</sup>	.043*
	Nutrition	16.977	2.601	16.186	17.768		
	Combined	17.327	2.587	16.607	18.047		
	Total	16.797	2.716	16.340	17.254		
MFI Physical Fatigue	Psychology	15.929	3.331	14.891	16.966	3.343 <sup>a</sup>	.038*
	Nutrition	16.727	3.358	15.707	17.748		
	Combined	17.615	2.823	16.830	18.401		

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	Total	16.819	3.211	16.278	17.359		
MFI	Psychology	13.857	4.112	12.576	15.138	1.030 <sup>a</sup>	.360
Reduced Activity	Nutrition	14.136	4.027	12.912	15.361		
	Combined	14.962	3.662	13.942	15.981		
	Total	14.362	3.921	13.702	15.022		
MFI	Psychology	10.357	4.287	9.021	11.693	1.324 <sup>a</sup>	.270
Reduced Motivation	Nutrition	10.500	3.474	9.444	11.556		
	Combined	11.462	3.153	10.584	12.339		
	Total	10.819	3.639	10.206	11.431		
MFI	Psychology	13.524	4.363	12.164	14.883	.064 <sup>a</sup>	.938
Mental Fatigue	Nutrition	13.682	4.328	12.366	14.998		
	Combined	13.846	4.345	12.637	15.056		
	Total	13.696	4.315	12.969	14.422		
CDC CFS	Psychology	2.571	3.109	1.603	3.540	1.414 <sup>a</sup>	.247
Sore Throat	Nutrition	3.977	3.776	2.829	5.125		
	Combined	3.202	4.494	1.951	4.454		
	Total	3.257	3.898	2.601	3.914		
CDC CFS Swollen Lymph nodes Glands	Psychology	1.976	3.382	.922	3.030	7.161 <sup>b</sup>	.028*
	Nutrition	5.561	6.491	3.587	7.534		
	Combined	3.462	4.881	2.103	4.820		
	Total	3.679	5.250	2.795	4.563		
CDC CFS Diarrhoea	Psychology	2.071	3.249	1.059	3.084	.850 <sup>a</sup>	.430
	Nutrition	2.841	4.832	1.372	4.310		
	Combined	3.135	3.773	2.084	4.185		
	Total	2.717	3.998	2.044	3.390		

CDC CFS Fatigue after exertion	Psychology	13.286	6.271	11.331	15.240	.219 <sup>a</sup>	.803
	Nutrition	13.722	6.450	11.761	15.682		
	Combined	14.154	6.270	12.408	15.899		
	Total	13.752	6.292	12.693	14.811		
CDC CFS Muscle Aches or Muscle Pains	Psychology	8.286	6.747	6.183	10.388	.166 <sup>a</sup>	.847
	Nutrition	9.091	6.383	7.151	11.031		
	Combined	8.519	6.932	6.589	10.449		
	Total	8.630	6.664	7.509	9.752		
CDC CFS Pain In Joints	Psychology	3.476	5.334	1.814	5.138	1.373 <sup>a</sup>	.257
	Nutrition	4.696	5.560	3.006	6.386		
	Combined	5.474	6.386	3.696	7.251		
	Total	4.618	5.837	3.635	5.600		
CDC CFS Fever	Psychology	1.238	2.516	.454	2.022	.027 <sup>a</sup>	.973
	Nutrition	1.394	2.562	.615	2.173		
	Combined	1.333	3.909	.245	2.421		
	Total	1.324	3.106	.801	1.846		
CDC CFS Chills	Psychology	3.357	4.637	1.912	4.802	.206 <sup>a</sup>	.814
	Nutrition	3.750	3.924	2.557	4.943		
	Combined	3.192	4.343	1.983	4.402		
	Total	3.420	4.283	2.699	4.141		
CDC CFS Unrefreshing Sleep	Psychology	12.905	6.792	10.788	15.021	.150 <sup>a</sup>	.861
	Nutrition	12.250	7.088	10.095	14.405		
	Combined	12.154	7.147	10.164	14.144		
	Total	12.413	6.978	11.238	13.588		
CDC CFS Sleeping	Psychology	9.286	7.658	6.899	11.672	.085 <sup>a</sup>	.918

Problems	Nutrition	8.614	7.317	6.389	10.838		
	Combined	8.904	7.684	6.766	11.042		
	Total	8.928	7.509	7.664	10.192		
CDC CFS Headaches	Psychology	5.262	5.548	3.533	6.991	1.611 <sup>a</sup>	.203
	Nutrition	7.646	7.040	5.506	9.786		
	Combined	6.346	5.857	4.715	7.977		
	Total	6.431	6.200	5.3871	7.474		
CDC CFS Memory Problems	Psychology	6.333	4.996	4.777	7.890	3.403 <sup>b</sup>	.182
	Nutrition	9.409	7.183	7.225	11.593		
	Combined	8.173	7.610	6.055	10.292		
	Total	8.007	6.835	6.857	9.158		
CDC CFS Difficulty Concentrating	Psychology	8.500	6.094	6.601	10.399	.391 <sup>a</sup>	.677
	Nutrition	9.822	7.641	7.499	12.145		
	Combined	9.135	6.942	7.202	11.067		
	Total	9.161	6.903	7.999	10.323		
CDC CFS Nausea	Psychology	3.476	4.845	1.966	4.986	1.162 <sup>a</sup>	.316
	Nutrition	4.769	5.135	3.208	6.330		
	Combined	3.327	4.902	1.962	4.692		
	Total	3.832	4.966	2.996	4.668		
CDC CFS Abdominal Pain	Psychology	2.548	3.270	1.529	3.567	5.971 <sup>b</sup>	.051
	Nutrition	5.064	5.165	3.493	6.634		
	Combined	3.750	4.635	2.460	5.041		
	Total	3.803	4.535	3.040	4.566		
CDC CFS Sinus Nasal Symptoms	Psychology	3.524	4.702	2.059	4.989	1.192 <sup>a</sup>	.307
	Nutrition	5.469	6.476	3.500	7.438		

	Combined	4.789	6.304	3.034	6.544		
	Total	4.620	5.932	3.622	5.619		
CDC CFS Shortness Of Breath	Psychology	3.000	4.191	1.694	4.306	.095 <sup>a</sup>	.909
	Nutrition	3.285	4.090	2.026	4.543		
	Combined	3.392	4.788	2.046	4.739		
	Total	3.237	4.365	2.497	3.977		
CDC CFS Sensitivity To Light	Psychology	3.429	5.347	1.762	5.095	.794 <sup>a</sup>	.454
	Nutrition	5.031	6.097	3.177	6.884		
	Combined	4.481	6.360	2.710	6.251		
	Total	4.336	5.975	3.330	5.342		
CDC CFS Depression	Psychology	3.952	3.938	2.725	5.180	.160 <sup>b</sup>	.923
	Nutrition	4.477	5.450	2.821	6.134		
	Combined	5.077	5.950	3.420	6.734		
	Total	4.544	5.231	3.663	5.424		
CDC CFS Maladaptive Stress Index Scale Score	Psychology	94.381	16.836	89.134	99.628	.465 <sup>a</sup>	.629
	Nutrition	96.386	21.946	89.714	103.059		
	Combined	98.269	19.165	92.934	103.605		
	Total	96.486	19.373	93.225	99.747		

<sup>a</sup> *F*-statistic for one-way analysis of variance, d.f. = 2,134

<sup>b</sup> *H*-statistic for Kruskal-Wallis test, d.f. = 2

<sup>c</sup>  $\chi^2$ -statistic for comparison of nominal level data, d.f. = 2

<sup>d</sup> number of males

\* test is significant at the  $p < .05$  level

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Table 2. Outcome variable comparisons across time

		Baseline				3-month follow-up				Comparisons	
		Mean	SD	95% CI for Mean		Mean	SD	95% CI for Mean		z-statistic	p-value
				Lower	Upper			Lower	Upper		
SF-36	Psychology	49.339	22.698	42.266	56.413	59.267	30.346	41.745	76.788	-2.707	.007**
Physical Functioning	Nutrition	47.855	26.226	39.882	55.829	46.706	30.744	34.544	58.868	-1.136	.256
	Combined	45.299	25.479	38.206	52.393	49.288	26.403	39.604	58.973	-1.850	.064
	Total	47.344	24.791	43.171	51.517	50.260	28.818	43.488	57.032	-3.120	.002**
SF-36	Psychology	7.143	15.894	2.190	12.096	46.429	39.048	23.883	68.974	-2.379	.017*
Role limitations physical	Nutrition	7.574	17.500	2.254	12.895	19.444	20.016	11.526	27.363	-2.907	.004**
	Combined	9.774	21.051	3.914	15.635	22.742	25.161	13.513	31.971	-2.225	.026*
	Total	8.272	18.387	5.177	11.367	26.111	28.225	19.479	32.744	-4.354	.001***
SF-36	Psychology	61.548	25.614	53.566	69.530	63.929	29.786	46.731	81.127	-1.196	.232
Bodily pain	Nutrition	55.625	30.242	46.434	64.819	58.889	32.943	45.857	71.921	-1.800	.072
	Combined	53.606	27.019	46.084	61.128	58.629	27.301	48.615	68.643	-1.048	.294
	Total	56.667	27.683	52.007	61.327	59.757	29.649	52.790	66.724	-2.240	.025*
SF-36	Psychology	37.202	21.824	30.402	44.003	59.821	33.318	40.584	79.058	-2.689	.007**
Social functioning	Nutrition	32.671	25.888	24.800	40.541	43.519	33.679	30.196	56.841	-2.476	.013*
	Combined	32.452	24.786	25.551	39.352	41.936	28.604	31.443	52.428	-2.426	.015*
	Total	33.967	24.212	29.892	38.043	46.007	31.805	38.533	53.481	-4.504	.001***
SF-36	Psychology	60.286	19.584	54.183	66.389	74.571	13.276	66.906	82.237	-2.497	.013*
General mental health	Nutrition	59.727	19.355	53.843	65.612	64.741	20.548	56.612	72.869	-1.696	.090
	Combined	58.308	20.948	52.476	64.140	64.129	16.637	58.027	70.232	-.524	.600

	Total	59.362	19.911	56.011	62.714	66.389	17.897	62.183	70.594	-2.665	.008**
SF-36	Psychology	55.554	46.368	41.105	70.004	76.191	33.150	57.051	95.331	-.842	.400
Role	Nutrition	48.482	47.390	34.074	62.890	55.594	38.130	40.510	70.678	-1.788	.074
limitations	Combined	47.780	43.924	35.551	60.008	67.742	32.756	55.727	79.757	-2.313	.021*
emotional	Total	50.370	45.590	42.695	58.044	64.829	35.335	56.526	73.133	-3.159	.002**
SF-36	Psychology	20.714	16.139	15.685	25.743	41.071	20.586	29.186	52.957	-3.066	.002**
Vitality Energy	Nutrition	20.114	14.5670	15.685	24.542	31.111	23.588	21.780	40.442	-2.734	.006**
or Fatigue	Combined	19.039	17.658	14.123	23.955	27.097	19.527	19.934	34.259	-1.558	.119
	Total	19.891	16.159	17.171	22.611	31.319	21.657	26.230	36.409	-4.205	.001***
SF-36	Psychology	37.024	17.945	31.432	42.616	45.714	21.109	33.526	57.903	-2.561	.010*
General health	Nutrition	28.636	15.528	23.915	33.357	36.482	18.903	29.004	43.959	-2.157	.031*
perceptions	Combined	30.962	17.575	26.069	35.854	42.097	21.632	34.162	50.032	-2.423	.015*
	Total	32.065	17.286	29.156	34.975	40.694	20.561	35.863	45.526	-3.996	.001***
MHLCS	Psychology	.677	.159	.627	.726	.821	.251	.676	.966	-2.983	.003**
Internal	Nutrition	.622	.177	.568	.675	1.193	2.969	.019	2.368	-.687	.492
	Combined	.662	.174	.613	.710	.779	.318	.662	.896	-1.755	.079
	Total	.653	.171	.624	.682	.942	1.822	.514	1.371	-2.962	.003**
MHLCS	Psychology	.368	.156	.320	.417	.351	.152	.263	.439	-2.594	.009**
Chance	Nutrition	.340	.133	.299	.380	.911	3.020	-.284	2.105	-.143	.886
	Combined	.354	.155	.311	.397	.314	.133	.265	.363	-.672	.501
	Total	.354	.148	.329	.379	.545	1.853	.109	.980	-1.552	.121
MHLCS	Psychology	.404	.134	.362	.446	.441	.315	.259	.624	.000	1.000
Powerful	Nutrition	.418	.141	.374	.460	.804	2.244	-.084	1.691	-1.843	.065
Others	Combined	.407	.101	.379	.436	.434	.279	.331	.536	-.577	.564
	Total	.409	.124	.388	.430	.574	1.3880	.248	.900	-1.601	.109

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MHLCS	Psychology	.169	.082	.143	.194	.131	.093	.077	.185	-1.122	.262
Doctors	Nutrition	.171	.089	.144	.197	.657	2.668	-.398	1.713	-1.686	.092
	Combined	.191	.147	.150	.232	.153	.070	.128	.179	-1.384	.166
	Total	.178	.112	.159	.196	.338	1.635	-.0462	.722	-2.381	.017*
MHLCS	Psychology	.235	.075	.212	.259	.268	.189	.159	.377	-.118	.906
Other People	Nutrition	.264	.129	.225	.304	.739	2.652	-.311	1.788	-1.697	.090
	Combined	.245	.074	.224	.265	.252	.118	.209	.295	-.213	.831
	Total	.248	.095	.232	.264	.438	1.626	.055	.820	-1.186	.236
MFI	Psychology	15.952	2.845	15.066	16.839	13.786	4.441	11.222	16.350	-2.657	.008**
General	Nutrition	16.977	2.601	16.186	17.768	14.704	4.898	12.766	16.641	-2.548	.011*
Fatigue	Combined	17.327	2.588	16.607	18.047	16.645	2.811	15.614	17.676	-.854	.393
	Total	16.797	2.716	16.340	17.254	15.361	4.136	14.389	16.333	-3.692	.001***
MFI	Psychology	15.929	3.331	14.891	16.966	13.071	4.632	10.397	15.746	-2.810	.005**
Physical	Nutrition	16.727	3.358	15.707	17.748	14.222	4.987	12.249	16.195	-2.791	.005**
Fatigue	Combined	17.615	2.823	16.830	18.401	16.484	3.395	15.239	17.729	-2.364	.018*
	Total	16.819	3.211	16.278	17.359	14.972	4.453	13.926	16.019	-4.591	.001***
MFI	Psychology	13.857	4.112	12.576	15.138	10.643	5.153	7.668	13.618	-2.142	.032*
Reduced	Nutrition	14.136	4.027	12.912	15.361	12.259	5.012	10.277	14.242	-2.164	.030*
Activity	Combined	14.962	3.662	13.942	15.981	14.936	3.777	13.550	16.321	-.070	.944
	Total	14.362	3.921	13.702	15.022	13.097	4.798	11.970	14.225	-2.421	.015*
MFI	Psychology	10.357	4.287	9.021	11.693	7.286	4.214	4.853	9.719	-2.131	.033*
Reduced	Nutrition	10.500	3.474	9.444	11.556	8.963	3.736	7.485	10.441	-1.985	.047*
Motivation	Combined	11.462	3.153	10.584	12.339	10.774	3.095	9.639	11.910	-1.082	.279
	Total	10.819	3.639	10.206	11.431	9.417	3.767	8.532	10.302	-2.986	.003**
MFI	Psychology	13.524	4.363	12.164	14.883	10.500	4.468	7.920	13.080	-2.950	.003*



Mental Fatigue	Nutrition	13.682	4.328	12.366	14.998	11.926	5.334	9.816	14.036	-2.082	.037*
	Combined	13.846	4.345	12.637	15.056	12.613	3.827	11.209	14.017	-1.586	.113
	Total	13.696	4.315	12.969	14.422	11.944	4.568	10.871	13.018	-3.661	.001***
CDC CFS	Psychology	2.571	3.109	1.603	3.540	1.429	2.278	.114	2.744	-1.365	.172
Sore Throat	Nutrition	3.977	3.776	2.829	5.125	1.741	2.087	.915	2.566	-2.211	.027*
	Combined	3.202	4.494	1.951	4.454	1.904	2.821	.870	2.939	-.804	.422
	Total	3.257	3.898	2.601	3.914	1.750	2.437	1.178	2.323	-2.387	.017*
CDC CFS	Psychology	1.976	3.382	.922	3.030	1.786	3.378	-.165	3.736	-.341	.733
Swollen	Nutrition	5.561	6.491	3.587	7.534	5.000	6.760	2.326	7.674	-2.212	.027*
Lymph nodes	Combined	3.462	4.881	2.103	4.820	2.690	4.477	1.0458	4.332	-.725	.468
Glands	Total	3.679	5.250	2.795	4.563	3.380	5.385	2.115	4.646	-1.684	.092
CDC CFS	Psychology	2.071	3.249	1.059	3.084	1.643	2.818	.016	3.270	-.730	.465
Diarrhoea	Nutrition	2.841	4.832	1.372	4.310	1.444	3.274	.149	2.740	-1.649	.099
	Combined	3.135	3.773	2.084	4.185	1.631	2.483	.720	2.542	-1.996	.046*
	Total	2.717	3.998	2.044	3.390	1.563	2.827	.899	2.228	-2.481	.013*
CDC CFS	Psychology	13.286	6.271	11.331	15.240	11.071	6.673	7.218	14.925	-1.550	.121
Fatigue after	Nutrition	13.722	6.450	11.761	15.682	11.815	7.217	8.960	14.670	-2.209	.027*
exertion	Combined	14.154	6.270	12.408	15.899	11.436	6.275	9.134	13.738	-2.392	.017*
	Total	13.752	6.292	12.693	14.811	11.507	6.629	9.949	13.065	-3.574	.001***
CDC CFS	Psychology	8.286	6.747	6.183	10.388	7.429	6.892	3.450	11.408	-2.145	.032*
Muscle Aches	Nutrition	9.091	6.383	7.151	11.031	7.222	6.278	4.739	9.706	-2.901	.004**
or Muscle	Combined	8.519	6.932	6.589	10.449	6.188	5.528	4.160	8.215	-1.908	.056
Pains	Total	8.630	6.664	7.509	9.752	6.817	6.029	5.400	8.234	-3.995	.001***
CDC CFS	Psychology	3.476	5.334	1.814	5.138	2.786	4.458	.212	5.360	-1.778	.075
Pain In Joints	Nutrition	4.696	5.560	3.006	6.386	3.926	5.099	1.909	5.943	-2.022	.043*

	Combined	5.474	6.386	3.696	7.251	3.010	4.140	1.492	4.528	-1.840	.066
	Total	4.618	5.837	3.635	5.600	3.310	4.543	2.242	4.377	-3.141	.002**
CDC CFS	Psychology	1.238	2.516	.454	2.022	1.643	4.181	-.771	4.057	-.135	.892
Fever	Nutrition	1.394	2.562	.615	2.173	.630	2.041	-.178	1.437	-1.487	.137
	Combined	1.333	3.909	.245	2.421	.378	.709	.118	.638	-1.517	.129
	Total	1.324	3.106	.801	1.846	.718	2.272	.185	1.252	-1.876	.061
CDC CFS	Psychology	3.357	4.637	1.912	4.802	2.571	4.398	.032	5.111	-1.970	.049*
Chills	Nutrition	3.750	3.924	2.557	4.943	2.222	4.098	.601	3.843	-3.401	.001***
	Combined	3.192	4.343	1.983	4.402	1.908	2.797	.882	2.934	-2.049	.040*
	Total	3.420	4.283	2.699	4.141	2.155	3.614	1.306	3.004	-4.206	.001***
CDC CFS	Psychology	12.905	6.792	10.788	15.021	10.643	6.698	6.776	14.510	-.802	.422
Unrefreshing	Nutrition	12.250	7.088	10.095	14.405	9.444	7.738	6.384	12.505	-1.421	.155
Sleep	Combined	12.154	7.147	10.164	14.143	10.161	7.959	7.242	13.080	-1.513	.130
	Total	12.413	6.978	11.238	13.588	9.986	7.557	8.210	11.762	-2.295	.022*
CDC CFS	Psychology	9.286	7.658	6.899	11.672	5.286	4.921	2.444	8.127	-1.738	.082
Sleeping	Nutrition	8.614	7.317	6.389	10.838	9.482	9.200	5.842	13.121	-.190	.849
Problems	Combined	8.904	7.681	6.766	11.042	6.529	6.749	4.053	9.004	-1.794	.073
	Total	8.928	7.509	7.664	10.192	7.394	7.585	5.612	9.177	-1.983	.047*
CDC CFS	Psychology	5.262	5.548	3.533	6.991	4.357	3.411	2.388	6.326	-1.200	.230
Headaches	Nutrition	7.646	7.040	5.506	9.786	5.185	6.294	2.695	7.675	-2.084	.037*
	Combined	6.346	5.857	4.715	7.977	4.050	3.527	2.756	5.343	-2.807	.005**
	Total	6.431	6.200	5.387	7.474	4.535	4.708	3.429	5.642	-3.000	.003**
CDC CFS	Psychology	6.333	4.996	4.777	7.890	3.500	3.995	1.193	5.807	-1.965	.049*
Memory	Nutrition	9.409	7.183	7.225	11.593	8.667	7.681	5.628	11.705	-.338	.735
Problems	Combined	8.173	7.610	6.055	10.292	6.148	4.905	4.349	7.947	-1.446	.148

	Total	8.007	6.835	6.857	9.158	6.578	6.189	5.123	8.032	-2.053	.040*
CDC CFS	Psychology	8.500	6.094	6.601	10.399	5.143	5.559	1.933	8.353	-2.809	.005**
Difficulty	Nutrition	9.822	7.641	7.499	12.145	7.778	6.941	5.032	10.524	-1.196	.232
Concentrating	Combined	9.135	6.942	7.202	11.067	6.507	4.843	4.731	8.283	-1.899	.058
	Total	9.161	6.903	7.999	10.323	6.718	5.844	5.345	8.092	-3.440	.001***
CDC CFS	Psychology	3.476	4.845	1.966	4.986	2.286	2.946	.585	3.987	-.213	.832
Nausea	Nutrition	4.769	5.135	3.208	6.330	3.407	5.746	1.134	5.681	-1.686	.092
	Combined	3.327	4.902	1.962	4.692	3.458	3.585	2.144	4.773	-.855	.392
	Total	3.832	4.966	2.996	4.668	3.211	4.396	2.178	4.244	-.584	.559
CDC CFS	Psychology	2.548	3.270	1.529	3.567	2.786	4.003	.474	5.097	-.343	.732
Abdominal	Nutrition	5.064	5.165	3.493	6.634	3.593	3.905	2.048	5.137	-1.968	.049*
Pain	Combined	3.750	4.635	2.460	5.041	2.548	2.791	1.524	3.572	-.598	.550
	Total	3.803	4.535	3.040	4.566	2.986	3.470	2.171	3.801	-1.727	.084
CDC CFS	Psychology	3.524	4.702	2.059	4.989	2.357	2.437	.950	3.764	-.724	.469
Sinus Nasal	Nutrition	5.469	6.476	3.500	7.438	4.889	6.104	2.474	7.304	-1.400	.162
Symptoms	Combined	4.789	6.304	3.034	6.544	3.804	6.710	1.343	6.266	-2.482	.013*
	Total	4.620	5.931	3.622	5.619	3.930	5.882	2.547	5.312	-2.971	.003**
CDC CFS	Psychology	3.000	4.191	1.694	4.306	1.571	2.209	.296	2.847	-1.556	.120
Shortness Of	Nutrition	3.285	4.090	2.026	4.543	2.407	4.060	.801	4.013	-1.849	.064
Breath	Combined	3.392	4.788	2.046	4.739	2.526	3.631	1.194	3.858	-.976	.329
	Total	3.237	4.365	2.497	3.977	2.296	3.554	1.461	3.131	-2.538	.011*
CDC CFS	Psychology	3.429	5.347	1.762	5.095	1.214	2.517	-.239	2.668	-1.973	.049*
Sensitivity To	Nutrition	5.031	6.097	3.177	6.884	4.111	6.198	1.659	6.563	-2.136	.033*
Light	Combined	4.481	6.360	2.710	6.251	3.297	5.557	1.259	5.335	-.787	.431
	Total	4.336	5.975	3.330	5.342	3.197	5.419	1.924	4.471	-2.542	.011*

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CDC CFS	Psychology	3.952	3.938	2.725	5.180	1.571	3.228	-.292	3.435	-1.614	.106
Depression	Nutrition	4.477	5.450	2.821	6.134	3.333	4.883	1.402	5.265	-1.584	.113
	Combined	5.077	5.950	3.420	6.734	2.766	3.324	1.547	3.985	-1.304	.192
	Total	4.544	5.230	3.663	5.424	2.747	3.964	1.815	3.678	-2.297	.022*
CDC CFS	Psychology	94.381	16.836	89.134	99.628	78.571	18.434	67.928	89.215	-3.111	.002**
Maladaptive	Nutrition	96.386	21.946	89.714	103.059	85.259	27.665	74.315	96.203	-3.443	.001***
Stress Index	Combined	98.269	19.165	92.934	103.605	87.484	22.965	79.060	95.908	-2.215	.027*
Scale Score	Total	96.486	19.373	93.225	99.747	84.917	24.004	79.276	90.557	-5.123	.001***

<sup>a</sup> z-statistic for Wilcoxon Signed-Rank Test

Table 3. Change score comparisons between intervention groups

		% change over time for sig. results <sup>a</sup>	Mean	Std. Deviation	Std. Error	95% CI for Mean		<i>H</i> <sup>b</sup>	p-value
						Lower	Upper		
SF-36	Psychology	16.75	-13.629	14.990	4.006	-22.285	-4.974	3.215	.200
Physical Functioning	Nutrition		-.407	19.967	3.843	-8.306	7.492		
	Combined		-6.813	18.242	3.276	-13.505	-.122		
	Total	5.80	-5.736	18.744	2.209	-10.141	-1.332		
SF-36	Psychology	84.61	-33.929	39.960	10.680	-57.001	-10.856	1.558	.459

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5	Role limitations physical	Nutrition	61.05	-14.509	21.005	4.042	-22.818	-6.199		
6		Combined	57.02	-13.871	31.457	5.650	-25.409	-2.333		
7		Total	63.32	-18.010	30.564	3.602	-25.192	-10.828		
8	SF-36	Psychology		-6.071	15.588	4.166	-15.072	2.929	.163	.922
9	Bodily pain	Nutrition		-6.574	18.800	3.618	-14.011	.863		
10		Combined		-3.387	25.532	4.586	-12.752	5.978		
11		Total	5.17	-5.104	21.252	2.505	-10.098	-.110		
12	SF-36	Psychology	37.81	-24.107	24.741	6.612	-38.392	-9.822	3.301	.192
13	Social functioning	Nutrition	24.93	-10.648	20.423	3.931	-18.727	-2.569		
14		Combined	22.60	-11.290	24.013	4.313	-20.098	-2.482		
15		Total	26.17	-13.542	23.149	2.728	-18.981	-8.102		
16	SF-36	Psychology	19.15	-12.000	14.294	3.820	-20.253	-3.747	4.404	.111
17	General mental health	Nutrition		-3.259	15.963	3.072	-9.574	3.056		
18		Combined		-.645	16.911	3.037	-6.848	5.558		
19		Total	10.58	-3.833	16.409	1.934	-7.689	.022		
20	SF-36	Psychology		-9.527	49.664	13.273	-38.202	19.148	.573	.751
21	Role limitations	Nutrition		-18.561	55.759	10.731	-40.618	3.497		
22	emotional	Combined	29.47	-18.284	52.240	9.383	-37.446	.878		
23		Total	10.58	-16.685	52.496	6.187	-29.021	-4.349		
24	SF-36	Psychology	49.57	-17.500	15.902	4.250	-26.682	-8.318	4.988	.083
25	Vitality Energy or	Nutrition	35.35	-11.482	19.206	3.696	-19.079	-3.884		
26	Fatigue	Combined		-6.129	17.688	3.177	-12.617	.359		
27		Total	22.30	-10.347	18.219	2.147	-14.628	-6.066		
28	SF-36	Psychology	19.01	-11.429	14.335	3.831	-19.705	-3.152	.627	.731
29	General health	Nutrition	29.73	-6.852	15.201	2.925	-12.865	-.839		
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perceptions	Combined	26.45	-10.161	22.154	3.97	-18.288	-2.035		
	Total	36.49	-9.167	18.251	2.151	-13.455	-4.878		
MHLCS Internal	Psychology	17.56	-.146	.203	.054	-.263	-.029	3.402	.183
	Nutrition		-.573	3.028	.583	-1.771	.625		
	Combined		-.106	.315	.057	-.222	.010		
	Total	30.67	-.289	1.859	.219	-.726	.148		
MHLCS Chance	Psychology	4.67	.077	.098	.026	.021	.134	7.674	.022*
	Nutrition		-.570	3.019	.581	-1.765	.624		
	Combined		.001	.081	.015	-.029	.031		
	Total		-.198	1.852	.218	-.633	.237		
MHLCS Powerful Others	Psychology		-.054	.284	.076	-.218	.109	1.571	.456
	Nutrition		-.375	2.282	.439	-1.277	.528		
	Combined		-.030	.277	.050	-.132	.072		
	Total		-.164	1.408	.166	-.495	.167		
MHLCS Doctors	Psychology		.020	.058	.0155	-.014	.053	0.076	.963
	Nutrition		-.492	2.678	.515	-1.551	.568		
	Combined		.057	.199	.036	-.016	.130		
	Total	47.49	-.156	1.647	.194	-.543	.231		
MHLCS Other People	Psychology		-.032	.166	.044	-.128	.064	2.479	.290
	Nutrition		-.446	2.692	.518	-1.510	.619		
	Combined		-.012	.096	.017	-.047	.023		
	Total		-.178	1.645	.193	-.565	.208		

MFI	Psychology	13.58	2.571	2.766	.739	.975	4.168	6.790	.034*
General Fatigue	Nutrition	13.39	2.074	3.842	.740	.554	3.594		
	Combined		.419	2.233	.401	-.400	1.238		
	Total	8.55	1.458	3.126	.368	.724	2.193		
MFI	Psychology	17.74	2.857	2.797	.748	1.242	4.472	3.038	.219
Physical Fatigue	Nutrition	15.00	2.444	4.371	.841	.716	4.173		
	Combined	6.42	1.290	2.735	.491	.287	2.294		
	Total	10.98	2.028	3.468	.409	1.213	2.843		
MFI	Psychology	23.20	1.857	2.932	.784	.165	3.550	1.734	.420
Reduced Activity	Nutrition	13.28	1.148	2.685	.517	.086	2.210		
	Combined		.645	3.189	.572	-.525	1.815		
	Total	8.81	1.069	2.952	.348	.376	1.763		
MFI	Psychology	11.42	2.500	3.502	.936	.478	4.522	5.171	.075
Reduced Motivation	Nutrition	14.64	1.593	3.511	.676	.204	2.982		
	Combined		.129	3.471	.624	-1.144	1.402		
	Total	12.96	1.139	3.570	.421	.300	1.978		
MFI	Psychology	29.66	3.571	3.056	.817	1.807	5.336	4.551	.103
Mental Fatigue	Nutrition	12.83	1.519	3.631	.699	.082	2.955		
	Combined		1.161	4.267	.766	-.404	2.726		
	Total	12.79	1.764	3.880	.457	.852	2.676		
CDC CFS	Psychology		1.429	3.736	.998	-.728	3.586	1.298	.523
Sore Throat	Nutrition	56.23	1.185	2.661	.512	.133	2.238		
	Combined		.500	4.591	.825	-1.184	2.184		
	Total	46.26	.937	3.769	.444	.052	1.823		
CDC CFS Swollen Lymph	Psychology		-.143	2.932	.784	-1.835	1.550	0.462	.794

nodes Glands	Nutrition	10.09	1.247	2.700	.520	.179	2.316		
	Combined		.794	6.549	1.176	-1.608	3.197		
	Total		.782	4.756	.560	-.336	1.900		
CDC CFS Diarrhoea	Psychology		-.286	1.490	.398	-1.146	.575	3.619	.164
	Nutrition		.926	2.868	.552	-.209	2.060		
	Combined	47.97	1.272	3.789	.681	-.118	2.662		
	Total	42.47	.839	3.134	.369	.103	1.576		
CDC CFS Fatigue after exertion	Psychology		2.286	4.811	1.286	-.492	5.063	0.379	.827
	Nutrition	13.90	2.593	5.507	1.060	.414	4.771		
	Combined	19.20	2.532	5.578	1.002	-.486	4.578		
	Total	16.32	2.507	5.339	.629	1.252	3.761		
CDC CFS Muscle Aches or Muscle Pains	Psychology	10.34	2.500	4.034	1.078	.171	4.829	0.469	.791
	Nutrition	20.56	2.333	3.637	.700	.894	3.772		
	Combined		2.070	5.335	.958	.113	4.027		
	Total	21.01	2.253	4.459	.526	1.205	3.300		
CDC CFS Pain In Joints	Psychology		1.857	4.036	1.079	-.473	4.187	0.054	.973
	Nutrition	16.40	1.393	3.721	.716	-.079	2.865		
	Combined		1.978	5.622	1.010	-.084	4.040		
	Total	28.32	1.735	4.634	.546	.646	2.824		
CDC CFS Fever	Psychology		-.214	1.968	.526	-1.351	.922	0.399	.819
	Nutrition		.604	2.311	.445	-.310	1.519		
	Combined		1.245	4.816	.865	-.521	3.012		
	Total		.721	3.573	.421	-.118	1.561		
CDC CFS Chills	Psychology	23.40	1.571	2.738	.732	-.009	3.152	1.517	.468
	Nutrition	40.74	2.148	3.097	.596	.923	3.373		



	Combined	40.23	1.447	3.986	.716	-.015	2.909		
	Total	37.00	1.734	3.421	.403	.930	2.538		
CDC CFS Unrefreshing Sleep	Psychology		1.857	6.803	1.818	-2.071	5.785	0.160	.948
	Nutrition		2.148	6.904	1.329	-.583	4.879		
	Combined		1.581	5.726	1.029	-.520	3.681		
	Total	19.55	1.847	6.3123	.744	.364	3.331		
CDC CFS Sleeping Problems	Psychology		2.786	5.352	1.430	-.304	5.876	3.218	.200
	Nutrition		-.222	5.139	.989	-2.255	1.811		
	Combined		1.762	4.871	.875	-.025	3.548		
	Total	17.17	1.217	5.133	.605	.011	2.423		
CDC CFS Headaches	Psychology		-.7143	2.091	.559	-1.922	.493	6.625	.036*
	Nutrition	32.19	1.572	3.507	.675	.184	2.959		
	Combined	36.18	2.467	4.944	.888	.653	4.280		
	Total	29.32	1.512	4.124	.486	.543	2.482		
CDC CFS Memory Problems	Psychology	44.73	2.857	4.655	1.244	.169	5.545	2.316	.314
	Nutrition		-.111	4.925	.947	-2.059	1.837		
	Combined		1.949	6.011	1.080	-.256	4.154		
	Total	17.86	1.353	5.435	.641	.076	2.630		
CDC CFS Difficulty Concentrating	Psychology	39.50	4.643	4.534	1.212	2.025	7.261	5.945	.051
	Nutrition		.815	4.359	.839	-.910	2.539		
	Combined		2.170	5.877	1.056	.015	4.326		
	Total	26.66	2.143	5.217	.615	.917	3.369		
CDC CFS Nausea	Psychology		.143	2.770	.740	-1.456	1.742	4.773	.092
	Nutrition		.660	2.667	.513	-.395	1.716		
	Combined		.251	4.468	.803	-1.388	1.890		

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	Total		.384	3.535	.417	-.447	1.214		
CDC CFS Abdominal Pain	Psychology		.286	1.729	.462	-.713	1.284	1.082	.582
	Nutrition	29.05	.882	2.165	.417	.025	1.738		
	Combined		.839	4.390	.789	-.771	2.449		
	Total		.747	3.234	.381	-.013	1.507		
CDC CFS Sinus Nasal Symptoms	Psychology		.929	3.125	.835	-.876	2.733	1.255	.534
	Nutrition		1.060	4.193	.807	-.599	2.719		
	Combined	20.56	1.906	5.923	1.063	-.267	4.078		
	Total	14.95	1.399	4.822	.568	.266	2.532		
CDC CFS Shortness Of Breath	Psychology		1.500	3.459	.924	-.497	3.497	0.707	.702
	Nutrition	18.28	.779	2.057	.403	-.052	1.609		
	Combined		.690	3.972	.725	-.793	2.173		
	Total	29.08	.885	3.243	.388	.112	1.658		
CDC CFS Sensitivity To Light	Psychology	64.58	1.429	2.472	.661	.001	2.856	0.939	.625
	Nutrition		1.568	3.764	.725	.079	3.057		
	Combined		.961	5.178	.930	-.938	2.860		
	Total	26.26	1.280	4.209	.496	.291	2.269		
CDC CFS Depression	Psychology		1.429	3.502	.936	-.593	3.451	0.490	.783
	Nutrition		.704	3.268	.629	-.589	1.996		
	Combined		1.363	5.345	.960	-.598	3.323		
	Total	39.55	1.129	4.282	.505	.122	2.135		
CDC CFS Maladaptive Stress Index Scale Score	Psychology	16.75	16.286	13.234	3.537	8.645	23.927	4.379	.112
	Nutrition	11.54	12.815	17.802	3.426	5.772	19.857		
	Combined	10.98	9.613	26.424	4.746	-.080	19.305		
	Total	11.99	12.111	21.201	2.499	7.129	17.093		

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6<sup>a</sup> see table 2 for descriptive and inferential statistics

7<sup>b</sup> *H*-statistic for Kruskal-Wallis test, d.f. = 2

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9 \* significant at the .05 level

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For peer review only

**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\***  
**Checklist for cohort, case-control, and cross-sectional studies (combined)**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	Title and Abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Title and Abstract
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1-4
Objectives	3	State specific objectives, including any pre-specified hypotheses	3-4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	4
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	14
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	9-10

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	8-9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	8-9 9
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	6-7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	12-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

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**A preliminary prospective study of the comparative effectiveness of nutritional, psychological and combined therapies for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) in a private care setting.**

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2012-001079.R1
Article Type:	Research
Date Submitted by the Author:	24-May-2012
Complete List of Authors:	Arroll, Megan; The Optimum Health Clinic, Howard, Alex; The Optimum Health Clinic,
<b>Primary Subject Heading</b>:	Patient-centred medicine
Secondary Subject Heading:	Complementary medicine, Nutrition and metabolism
Keywords:	COMPLEMENTARY MEDICINE, SOCIAL MEDICINE, REHABILITATION MEDICINE

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## Abstract

Background: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a condition ~~characterised~~[characterized](#) by severe and persistent fatigue, neurological disturbances, autonomic and endocrine dysfunctions and sleep difficulties that have a pronounced and significant impact on individuals' lives. Current NICE guidelines within the United Kingdom suggest that this condition should be treated with cognitive ~~behavioural~~[behavioral](#) therapy and/or graded exercise therapy where appropriate. There is currently a lack of evidence base concerning other, more integrative interventions that may be beneficial to those with ME/CFS.

Objectives: This study aimed to evaluate whether three patient-centered treatment modalities of psychology, nutrition and combined treatment, [influenced symptom report measures in those with reduced symptomatology](#) of ME/CFS over a 3-month time period and whether there were significant differences in these changes between groups.

Design and setting: This is a ~~preliminary prospective longitudinal observational~~ study [with one follow-up point](#) conducted at ~~a one~~ private secondary health care facility in London, UK.

Participants: One-hundred and thirty-eight individuals (110 females, 79.7%; 42 participants in psychology, 44 in nutrition and 52 in combined) participated at baseline and 72 participants completed the battery of measures at follow-up (52.17% response rate; 14, 27, 31 participants in each group, respectively).

Outcome measures: Self-report measures of ME/CFS symptoms, functional ability, multidimensional fatigue, perceived control and maladaptive stress.

Results: Baseline comparisons showed those in the combined group had higher levels of fatigue. At follow-up, all groups saw improvements in fatigue, functional physical symptomatology and maladaptive stress; those within the psychology group also experienced a shift in perceived control over time. ~~The psychology group demonstrated a significantly greater change in fatigue and perceived control than the combined group; however, the opposite relationship was observed for headaches.~~

Conclusions: ~~This study provides early evidence that p~~ Patient-centered techniques for the treatment of ME/CFS ~~may influence appear promising in reducing~~ symptomatology, fatigue, ~~function, perceived control~~ and inappropriate responses to stressors, ~~and increasing function and perceived control~~. However, these results must be viewed with caution as the allocation to groups was not randomized, there was no control group and the study suffered from high drop-out rates. ~~The need for further studies of integrative treatment with robust designs appears warranted.~~

## Summary

### Article focus

- This ~~preliminary prospective observational~~ study investigated three (psychological, nutritional and combined) tailored patient-centered interventions for ME/CFS over time.
- Differences between the reported changes over time between groups were also assessed.

### Key messages

- Patient-centered approaches for the management of ME/CFS ~~reduce~~ ~~symptomatology influence symptomatology~~ over time ~~in some individuals with this disorder~~.
- ~~Self-reported f~~ Functional ability, ~~(-physical and social), are influenced increase with~~ following tailored interventions ~~lasting 3 months-~~
- ~~Psychological intervention can help individuals to regain a sense of control over their condition-~~
  - ~~This study provides preliminary evidence that tailored psychological, nutritional and~~ ~~Combined interventions may be effective treatments for some people with ME/CFS; however~~ ~~due to the study's methodological limitations, it is important that this potential treatment~~ ~~effect is investigated further in high quality randomized controlled studies.~~

### Strengths and limitations of this study

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- The findings here are an initial step to fill the gap in the extant literature regarding the utility of tailored, multidisciplinary and patient-centered treatments for ME/CFS.
- There is bias in this study as the participants were self-selected in the sense that they chose to attend the clinic and which treatment option they preferred (with advice), i.e. the study was not randomized.
  - There were low retention rates in this study which may constitute a bias in that those who remained in the study may have experienced benefits and those who experienced little or no benefits may have dropped out.

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### **Introduction**

Chronic Fatigue Syndrome or myalgic encephalomyelitis (ME/CFS) is a condition characterized by prolonged and debilitating fatigue, although the exact cause of this disorder is still under debate. Due to the lack of a definitive biological marker, diagnosis is made on the basis of the exclusion of other explanatory conditions. The most widely used case definition by the Centers for Disease Control <sup>1</sup> states that there must be at least six months severe fatigue of new and definite onset, not the result of ongoing exertion, not alleviated by rest and resulting in reduced levels of physical activity. The CDC definition also sets out a series of minor complaints that must accompany the fatigue (cognitive impairment, sore throat, tender cervical or axillary lymph nodes, muscle pain, multi-joint pain, headaches of a new type, pattern or severity at onset, unrefreshing sleep and post-exertion malaise), with individuals needing to have the occurrence of four or more symptoms to be diagnosed with

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7 ME/CFS. Estimates of the prevalence of ME/CFS have been made as low as 3 and as high as  
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9 2,800 per 100,000 <sup>2</sup>.

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12 The most widely researched strategies for alleviating the symptoms of ME/CFS are Cognitive  
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14 Behavior Therapy (CBT) and Graded Exercise Therapy (GET). Two reviews of studies on  
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16 CBT <sup>3,4</sup> found that it significantly improved physical functioning in adult out-patients as  
17  
18 compared with medical management, counseling, guided support, education and support or  
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20 relaxation. ~~However, the longitudinal evidence for CBT is inconsistent and there is a lack of~~  
21  
22 ~~evidence with regard to CBT in combination with other treatments~~<sup>4</sup>. Regarding GET, a  
23  
24 systematic review illustrated that this form of therapy was potentially beneficial for people  
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26 with ME/CFS, especially when combined with a patient education programme<sup>5</sup>. However,  
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28 drop-out rates were high in the GET groups suggesting that individuals with ME/CFS are  
29  
30 adverse to this type of therapy. Recently, a large scale, longitudinal study investigating CBT,  
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32 GET, Adaptive Pacing Therapy (APT) and specialist medical care (SMC) found that CBT  
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34 and GET (when added to SMC) were moderately effective outpatient treatments for this  
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36 patient group as opposed to APT or SMC alone <sup>6</sup>.

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39 Although CBT and GET studies have shown some promising outcomes, there is no known  
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41 cure for ME/CFS. Therefore the National Institute for Health and Clinical Excellence (NICE)  
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43 <sup>7,6</sup> recommends a number of symptom management strategies and interventions aimed at  
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45 helping individuals to cope with their condition and reduce physical deconditioning brought  
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47 about by the illness. Pharmacological interventions are, at times, suggested for patients with  
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49 poor sleep or pain, for instance, low-dose antidepressants, as these have been shown to be  
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51 effective <sup>8-14,13</sup>. However, patient expectations must be realistic as the drugs may help  
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53 elevate mood and psychological outlook but not reduce fatigue and other symptomatology  
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6 associated with ME/CFS<sup>1514</sup>. Numerous drugs such as thyroxin, hydrocortisone and antiviral  
7 agents are not advised by NICE due to contradictory findings<sup>16:1715;16</sup>.  
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12 In terms of function and quality of life management, NICE offers general advice concerning  
13 sleep management, appropriate rest periods, and pacing. Sleep hygiene instruction, together  
14 with pharmacological treatment tailored to the individual patient can be beneficial in  
15 combating fatigue<sup>1817</sup>. Dietary management may also reduce symptomatology for those with  
16 concurrent irritable bowel syndrome (IBS). Management approaches recommended for IBS,  
17 such as diet restriction, are thus also recommended for those with ME/CFS<sup>1918</sup>. Dietary  
18 supplementation has been investigated in relation to ME/CFS. Fatty acids<sup>2019</sup>, folic acid<sup>2120</sup>,  
19 vitamin C<sup>2221</sup>, co-enzyme Q10<sup>2322</sup>, magnesium<sup>2423</sup>, multivitamins<sup>2524</sup> and minerals<sup>2625</sup> have  
20 all been shown to reduce symptomatology in ME/CFS patients. However other studies have  
21 shown conflicting findings with regard to nutritional supplementation, therefore it is perhaps  
22 wise to treat with supplements on a case-by-case basis<sup>27:2826;27</sup>.  
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35 Due to the lack of clear and definitive treatment strategies, individuals often seek out  
36 Complementary and Alternative Medicines (CAM). Although NICE does not recommend the  
37 use of CAM they do acknowledge that many people with ME/CFS use such therapies and  
38 find them beneficial for symptom management. This view is due to the lack of published  
39 evidence for the effectiveness of these treatments. Examples of CAM treatments used by  
40 individuals with ME/CFS include religious healing, massage therapy, relaxation, meditation,  
41 homeopathy, acupuncture, naturopathy and herbal therapies<sup>29:3028;29</sup>; patient satisfaction with  
42 such approaches as CAM has been high, over 80% in some instances<sup>2928</sup>. A recent systematic  
43 review of such interventions identified 70 controlled clinical trials (randomized and non-  
44 randomized) and found that 86% of these studies illustrated at least one positive effect, with  
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7 74% showing a decrease of illness-related symptomatology <sup>3130</sup>. Meditative or mindfulness  
8 approaches warranted further investigation based on these results as did supplement programs  
9 of magnesium, l-carnitine, and S-adenosylmethionine. A subsequent review based solely on  
10 randomized controlled trials (RCTs) of CAM techniques identified 26 such studies and  
11 observed that qigong, massage and tuina (approaches based within Chinese Traditional  
12 Medicine and based upon relaxation and connection with the body) illustrated positive effects  
13 as did supplementation studies utilizing nicotinamide adenine dinucleotide (NADH) and  
14 magnesium <sup>3234</sup>. However, within both reviews it was noted that the methodological quality  
15 of reporting was poor and the sample sizes in these studies were small; hence ability to draw  
16 strong conclusions on the efficacy of CAM methods is limited. Porter et al. (2010) <sup>31</sup> did note  
17 that patient-centered, individualized treatment protocols which include a range of tailored  
18 strategies are a promising area for further investigation for this complex, multi-system illness.  
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### 35 Objectives

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37 There is still much debate and uncertainty regarding the most effective treatment for  
38 ME/CFS. Recent reviews of CAM techniques highlight the need for further exploration of  
39 patient-centered and individually tailored interventions for the alleviation of the condition's  
40 often debilitating and intrusive symptomatology. This study therefore aims to provide  
41 preliminary evidence for the utility ~~evaluate the effectiveness of three of three~~ types of  
42 patient-centered approaches to the management of ME/CFS over time (baseline and follow-  
43 up) offered at a private health-care center in the UK.  
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### 51 Methods

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### Study design and setting

This ~~preliminary prospective a longitudinal observational~~ study ~~which~~ aimed to [explore the effectiveness of evaluate](#) three treatment options offered to individuals with ME/CFS. The research was conducted at one private secondary health care facility. All ~~potential prospective~~ patients of the clinic are first asked to complete a comprehensive symptom profile and medical history, including questions relating to triggering factors, psychology sub-types and structural/biological sub-types (this is distinct from the research data collected). Subsequent to this, every individual receives a 15-minute screening with one of the practitioners ([please note, this was not either of the authors of the current study](#)) who recommends the best course of action for his/her needs; this will be the psychology-related interventions, nutritional advice and support or a combination of the two.

All individuals requesting treatment at the private care setting were offered the opportunity to participate in the study. Those that expressed an interest ([N = 145](#)) were emailed a spreadsheet that contained the questionnaires and asked to complete it at their convenience. Informed consent was obtained prior to the completion of the questionnaires and the study was approved by the University of East London Ethics Committee. Participants were told that they could withdraw from the study at any time and that withdrawal would not affect their care at the clinic. Participants were able to ask questions at any point in the study and no deception was used as the participants were informed of the nature of the research program before they agreed to participate. [Subsequently, participants were requested to complete the questionnaire pack on a second occasion, three months from the baseline measures.](#)

### *Psychology*

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7 The clinic offers a 3-month intervention which consists of a combination of Neuro-linguistic  
8 Programming (NLP), Emotional Freedom Technique (EFT), life coaching and  
9 hypnotherapy/self-hypnosis constructed in a manner specific to the needs of those with  
10 ME/CFS. The primary aim of this approach is to reduce the anxiety that is associated with  
11 having a debilitating and unpredictable condition, improve emotional well-being and help  
12 individuals slowly manage and increase their activity within their own limits (i.e. pacing).  
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14 The program is offered as a series of group sessions and the peer support is seen as an  
15 important component of the intervention, which is solidified via the use of moderated online  
16 support forums, narratives of previous clients' experiences and online materials that can be  
17 accessed as often as necessary. In addition to, or as an alternative to this course, individuals  
18 receive a series of one-to-one sessions and for the most severely affected ME/CFS patients,  
19 telephone sessions are arranged and support materials can be accessed in their own homes.

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22 Over the three-month period of this preliminary study, the participants experienced one of  
23 three treatment options. The first option included 13 hours of practitioner contact time in a  
24 mix of group training in person, group telephone conference calls and one-to-one telephone  
25 sessions, the second option was four hours of one-to-one telephone sessions and the final  
26 option was three hours of in person sessions. Participants all had access to various support  
27 materials which included CDs and online resources. The amount of time spent on these was  
28 patient-led, but was in the region of a further six hours. All the practitioners offering this  
29 option are qualified in hypnotherapy, NLP, life coaching and EFT and undergo an intensive  
30 period of training in the clinic's own integrative approach (please see Howard and Arroll <sup>33</sup>  
31 for more details of this approach) and ongoing supervision (individual and group supervision  
32 on a biweekly basis) from the department director, who is the only senior practitioner in the  
33 team.



### *Nutrition*

Tailored nutritional therapy is achieved via one-to-one consultations with individuals. To begin, a very detailed history is taken based upon the information given in the aforementioned symptom profile. Qualified nutritional therapists (who have been given specialist training regarding ME/CFS from the clinic) then suggest tests consistent with symptomatology, for instance the Adrenal Stress Index Test, comprehensive stool analysis/gastro-intestinal function, vitamin & mineral status, etc. Results from these tests are then used to compose an evidence-driven diet and supplement program. As most cases of ME/CFS are complex involving multiple body systems, this process is often iterative and follow-up consultations are necessary to check progress and make alterations to the protocol.

The nutritional therapy program consists of an initial one-hour evaluation (which includes the tailored advice) and follow-up approximately every six weeks; therefore, during the course of the present study, the participants received a minimum of two one-hour sessions with email support for any queries and detailed nutritional guidance. All the nutritional therapists are qualified to diploma level and members of (voluntary) regulatory bodies such as the British Association for Applied Nutrition and Nutritional Therapy (BANT) and the Complementary and Natural Healthcare Council (CNHC). Similar to the psychology department, the nutrition department is led by one senior practitioner who supervises the team with individual and group supervisory arrangements.

### *Combined*

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7 Within the combined program, a multidisciplinary approach is taken with practitioners  
8 discussing the patients in case meetings to ensure that the psychological and nutritional  
9 aspects complement each other in order to achieve the best outcome. [It should be noted that](#)  
10 [the interventions in the combined program are phased-in as it was found that asking](#)  
11 [individuals to engage in numerous therapeutic activities at the same time resulted in high](#)  
12 [drop-out rates.](#)  
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### 20 **[Primary Outcome Measures](#)**

#### 21 *Medical Outcomes Survey Short-Form 36 (SF-36)*

22 This 36-item measure is the short form of the original Medical Outcomes Survey [3432](#) to  
23 measure functional impairment and contains eight sub-sections: 1) physical activity  
24 limitations due to health problems; 2) social activity limitations due to physical or emotional  
25 problems; 3) usual role activity limitations due to physical health problems; 4) bodily pain; 5)  
26 general mental health; 6) role activity limitations due to emotional problems; 7) vitality  
27 (energy and fatigue); and 8) general health perceptions [3432](#). The items are scored so that  
28 higher scores indicate greater functional ability. In terms of the psychometric properties of  
29 this measure, reliability estimates for all sub-scales are good, exceeding a Cronbach's alpha  
30 coefficient value of 0.70 [3533](#). In terms of validity, the SF-36 correlates amply,  $r \geq 0.40$ , with  
31 the frequency and severity of numerous symptoms and general health conditions [36:37,34:35](#).  
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#### 49 *Multidimensional Health Locus of Control Scale (MHLCS)*

50 [Multidimensional Health Locus of Control](#) <sup>36-38</sup> ~~measures perceived control via three distinct~~  
51 ~~sub-scales: 'internal', 'chance' and 'powerful others' which has two dimensions, that of~~  
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~~'doctors' and 'other people'. The instrument contains 18 items in total (six items each for the internal and chance scales and three items for both the powerful others scales) and is scored on a 6 point Likert scale from 'strongly agree' to 'strongly disagree'. Internal reliability of the instrument is good with Cronbach's alpha coefficients ranging from 0.67 for 'powerful others' to 0.77 for 'internal'. The measure correlates positively and significantly with associated scales from Levenson's<sup>39</sup> locus of control measure from which the MHLOC was based upon, which demonstrates good convergent validity<sup>36</sup>.~~

### *Multidimensional Fatigue Inventory (MFI)*

This 20-item measure contains five fatigue dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity<sup>38,40</sup>. Items such as 'I tire easily' are rated on a 5-point scale (1 = yes, that is true; 5 = no, that is not true) with lower scores reflecting higher levels of fatigue. The MFI has good internal consistency with average Cronbach's alpha coefficient equaling 0.84 across the sub-scales. Convergent validity based on a sample of radiotherapy patients found correlations between the sub-scales and a visual analog fatigue scale to be 0.77 for general fatigue, 0.70 for physical fatigue, 0.61 for reduced activity, 0.56 for reduced motivation ( $p < 0.001$ ) to 0.23 for mental fatigue ( $p < 0.01$ )<sup>38,40</sup>.

### Secondary Outcome Measures (ME/CFS-specific)

#### *CDC CFS Symptom Inventory*

CDC CFS Symptom Inventory<sup>39,41</sup> was used to measure specific ME/CFS symptoms and confirm diagnosis. This instrument is based upon the CDC case definition<sup>1</sup> and includes a fatigue item and the eight distinct symptoms are also included in the CDC guidelines with an additional ten associated symptoms. The format of this self-report measure is a six-point scale of perceived frequency (0 = absent, 5 = all the time) and severity (0 = none, 5 = very severe). The psychometric properties of this instrument are good: Cronbach's alpha coefficient = 0.88;

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$r = .74$  convergent validity with the Chalder Fatigue Scale <sup>40,42</sup>;  $r = -.68$  and  $-.87$  convergent validity with the SF-36 'vitality' and 'bodily pain' sub-scales, respectively.

### **Secondary Outcome Measures (psychological)**

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#### *Multidimensional Health Locus of Control Scale (MHLCS)*

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Multidimensional Health Locus of Control <sup>41-43</sup> measures perceived control via three distinct sub-scales: 'internal', 'chance' and 'powerful others' which has two dimensions, that of 'doctors' and 'other people'. The instrument contains 18 items in total (six items each for the 'internal' and 'chance' scales and three items for both the 'powerful others' scales) and is scored on a 6-point Likert scale from 'strongly agree' to 'strongly disagree'. Internal reliability of the instrument is good with Cronbach's alpha coefficients ranging from 0.67 for 'powerful others' to 0.77 for 'internal'. The measure correlates positively and significantly with associated scales from Levenson's <sup>44</sup> locus of control measure from which the MHLOC was based, which demonstrates good convergent validity <sup>41</sup>.

#### *Maladaptive Stress Index*

This 32-item measure contains three sub-scales (cognitive/mood, sleep and ME/CFS symptoms) and was designed specifically for this population <sup>45,43</sup>. Items such as 'I constantly replay or pre-empt situations and conversations' are scored on a 5-point scale where 1 = never true and 5 = always true; higher scores illustrate a greater degree of disturbance.

### **Statistical methods**

The data was initially screened for missing data. Four cases contained substantial amounts of missing data; therefore these were excluded from the analysis (one individual from the nutrition group and three from the combined group). Once this was done, all the variables had

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6 less than 5% missing data, hence mean substitution was carried out in line with guidance <sup>4644</sup> .  
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9 The baseline data was subsequently of the quality for parametric tests, except for the  
10 variables CDC CFS swollen lymph nodes and glands, memory problems, abdominal pain and  
11 depression. However, the follow-up data suffered from high levels of skew and kurtosis  
12 which was not substantially alleviated by data transformation. This violated a key criterion  
13 for parametric testing, that of normality of distribution, so non-parametric tests were selected.  
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15 In addition, as the sample sizes in each individual treatment group were small, the more  
16 conservative non-parametric tests were the preferred choice as even though tests such as  
17 analysis of variance are generally robust against non-normality, this does not hold true with  
18 small sample sizes. ~~For baseline data, One-way analysis of variance tests and Kruskal-~~  
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20 ~~Wallis tests (the former for those variables that met the criteria for parametric tests, and the~~  
21 ~~latter that did not) were used to investigate baseline variation difference between groups;~~  
22 ~~Wilcoxon sign rank tests were employed to look for differences over time (baseline and 3-~~  
23 ~~month follow-up) and multivariate analysis of covariance (MANCOVA) tests were used to~~  
24 ~~account for this variation and test to for differences between the three groups. Kruskal-~~  
25 ~~Wallis tests were performed to investigate group differences in measures of change as~~  
26 ~~evaluated by mean change scores, with Bonferroni corrected Mann Whitney tests calculated~~  
27 ~~to identify post hoc differences between groups if the Kruskal Wallis tests were significant.~~  
28 ~~Wilcoxon sign-rank tests were employed to look for differences over time (baseline and 3-~~  
29 ~~month follow-up) and if differences were significant, percentage change was calculated.~~  
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31 ~~Please note, as this is an exploratory study with only one time-point and no control group,~~  
32 ~~any significant findings do not infer clinical significance, rather statistical significance, and as~~  
33 ~~such exact p-values are presented.~~  
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## 51 52 53 **Results** 54 55 56 57 58 59 60

## Participants

Of the 145 individuals who expressed an interest in the study, 142 time-one questionnaires were returned, equating to a 97.9% response rate at baseline (two participants from the psychology group and one from the combined group dropped out at this stage). Therefore, excluding the four cases deleted due to insufficient data, 138 ~~One hundred and thirty eight cases were used for baseline analysis; individuals completed the questionnaire battery at time one (excluding the four deleted cases);~~ 42 participants in the psychology group, 44 in the nutrition group and 52 in the combined group. There was no significant association between gender and group ( $\chi^2(2) = 0.179, p = .915 > .05$ ), all groups consisting of approximately one-fifth males (Table 1). There was not a significant difference in age ( $F(2,135) = 0.0010, p = 1.000 > .05$ ); in fact group means for age were near identical at 42.881, 42.864 and 42.843 for psychology, nutrition and combined groups, respectively. There was also a non-significant result for illness duration ( $F(2, 135) = 0.252, p = .778 > .05$ ). Therefore, in terms of demographics, the groups were comparable. With regard to the outcome measures, there were significant differences between the groups in terms of the MFI sub-scale 'general fatigue' ( $F(2, 135) = 3.219, p = .043 < .05$ ), MFI 'physical fatigue' ( $F(2, 135) = 3.343, p = .038 < .05$ ) and the CDC CFS symptom 'swollen lymph nodes and glands' ( $H(2) = 7.161, p = .028 < .05$ ). To investigate the source of these differences, post-hoc tests were conducted (unrelated t-tests for the fatigue variables and Mann-Whitney tests for swollen lymph glands as the former did not meet criteria for parametric tests, all with Bonferroni correction for multiple comparisons). A significant difference was observed between the psychology and combined groups with regards to general fatigue ( $t(92) = -2.449, p = .016 < .05$ ) and physical fatigue ( $t(92) = -2.658, p = .009 < .05$ ) and also between the nutrition and psychology group in terms of the degree of lymph node and gland swelling ( $U = 635.00, p = .009 < .05$ ). Within the fatigue measures, the combined group reported

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7 significantly higher levels of both general and physical fatigued than the psychology group  
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9 whereas those undertaking nutritional support stated a higher occurrence of swollen lymph  
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11 nodes and glands.

#### 12 13 14 *Retention analysis*

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16 Seventy-two of the original 138 participants ([14 participants in the psychology group, 27 in](#)  
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18 [the nutrition group and 31 in the combined group](#)) completed the battery of measures at the 3-  
19  
20 month follow-up, [resulting in retention rates of \(52.17% in the study overall, 33.33% in the](#)  
21  
22 [psychology group, 61.36% in the nutrition group and 59.62% in the combined group](#)). To  
23  
24 investigate whether the individuals who did not complete the time-two measures were  
25  
26 significantly different from those at baseline on demographic and outcome measures, a series  
27  
28 of t-tests and Mann-Whitney tests were performed. Those that dropped out of the research  
29  
30 (although still receiving treatment at the clinic) differed significantly in terms of age ( $t(136) =$   
31  
32  $-2.227, p = .028 < .05$ ) and illness duration ( $t(136) = -2.549, p = .012 < .05$ ). Those who  
33  
34 remained in the study were of significantly older age (mean age of those that remained in the  
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36 study = 45.056, SD = 11.535; mean age of drop-outs = 40.400, SD = 12.932) and longer  
37  
38 illness duration than those who dropped out (mean age of those that remained in the study =  
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40 10.836, SD = 7.383; mean illness duration of drop-outs = 7.571, SD = 7.472). Individuals who  
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42 did not remain in the study did not differ significantly in terms of gender ( $\chi^2(2) = 1.222, p =$   
43  
44 [.269 > .05](#)) or any of the outcome measures.

#### 45 46 47 Longitudinal data Comparison from time-one to time-two

##### 48 49 Primary outcomes

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51 [The following percentage change scores represent statistically significant changes, rather than](#)  
52  
53 [clinically significant shifts, as this was an exploratory study. \(Please see Table 2 for the exact](#)  
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7 p-value for each repeated measures comparison.) In the sample as a whole, there were  
8 improvements in all areas of the SF-36, with a 5.80% improvement in physical functioning, a  
9 63.32% improvement in role limitations due to physical difficulties, a 5.17% improvement in  
10 bodily pain, a 26.17% improvement in social functioning, a 10.58% improvement in role  
11 limitations due to emotional difficulties, a 22.30% improvement in vitality, energy or fatigue  
12 and a 36.49% improvement in general health perception. When looking at the fatigue sub-  
13 scales of the MFI, all five sub-scales showed significant reductions in fatigue; 8.55% in  
14 general fatigue, 10.98% in physical fatigue, 8.81% in reduced activity, 12.96% in reduced  
15 motivation and 12.79% in mental fatigue.

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26 Within the group of individuals who opted for a purely psychological intervention,  
27 improvements were seen in physical functioning (16.75%), role limitations due to physical  
28 problems (84.61%), social functioning (37.81%), general mental health (19.15%), vitality,  
29 energy or fatigue (49.57%) and general health perceptions (19.01%). Also, all the MFI  
30 fatigue scales decreased over a 3-month period, 13.58% in general fatigue, 17.74% in  
31 physical fatigue, 23.20% in reduced activity, 11.42% in reduced motivation and 29.66% in  
32 mental fatigue.

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41 The nutrition group saw improvements in role limitations due to physical problems (61.05%),  
42 social functioning (24.93%), vitality, energy or fatigue (35.35%). and general health  
43 perceptions (29.73%). Once again, all the MFI fatigue scales decreased over a 3-month  
44 period, 13.39% in general fatigue, 15.00% in physical fatigue, 13.28% in reduced activity,  
45 14.64% in reduced motivation and 12.83% in mental fatigue.



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7 In terms of general health as evaluated by the SF-36 measure, the group who received both  
8 psychological and nutritional intervention reported reductions in role limitations due to  
9 physical difficulties (57.02%), social functioning (22.61%), role limitations due to emotional  
10 difficulties (29.47%) and general health perceptions (26.45%). In the combined group, only  
11 one measure of fatigue, that of physical fatigue, saw significant improvements over time  
12 (6.42%).

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20 *Secondary outcomes (ME/CFS-specific)*

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22 Within the CFS Symptom Inventory, there were improvements in occurrence of sore throats  
23 (46.26%), diarrhea (42.47%), fatigue after exertion (16.32%), muscle aches or muscle pains  
24 (21.01%), pain in joints (28.32%) chills (37.00%), unrefreshing sleep (19.55%), sleeping  
25 problems (17.17%), headaches (29.47%), memory problems (17.86%), difficulty  
26 concentrating (26.66%), sinus and nasal symptoms (14.95%), shortness of breath (29.08%),  
27 sensitivity to light (26.26%) and depression (39.55%) in the merged sample. Within those  
28 taking part in the psychology intervention, ratings of muscle aches or muscle pains (10.34%),  
29 chills (23.40%), memory problems (44.73%), difficulty concentrating (39.50%) and  
30 sensitivity to light (64.58%) decreased. In the nutrition group, numerous symptom-related  
31 indices also showed improvements; sore throat (56.23%), swollen lymph glands (10.09%),  
32 fatigue after exertion (13.90%), muscle aches or muscle pains (20.56%), pain in joints  
33 (16.40%), chills (40.74%), headaches (32.19%), abdominal pain (29.05%), and sensitivity to  
34 light (18.28%). Those in the combined group saw significant reductions over the 3-month  
35 interval in diarrhea (47.97%), fatigue after exertion (19.20%), chills (40.23%), headaches  
36 (36.18%) and sinus and nasal symptoms (20.56%). (Please see Table 3 for the descriptive and  
37 inferential statistics associated with these findings and the exact p-value for each repeated  
38 measures comparison.)

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Secondary outcomes (psychological)

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There were no significant differences from time-one to time-two in the MHLCS sub-scale of 'chance', 'powerful others' and 'other people', however the MHLCS did illustrate significant increases in internal locus of control (30.67%) and that of doctors (47.49%) in the sample as a whole. Reductions were also observed in the Maladaptive Stress Response (11.99%) in the entire group. In the psychology group, a significant increase of 17.56% was observed in internal locus of control, a decrease of 4.67% in the perception that chance played an influential part in the individuals' lives and a significant reduction in the Maladaptive Stress Response of 16.75%. No significant differences were found from baseline to follow-up in perceived control in the nutrition group, however the way in which the individuals in this group responded to stress also decreased, by 11.54%. No significant differences were found from baseline to follow-up in perceived control as measured by the MHLCS in the combined treatment group although there was a statistically significant difference in the Maladaptive Stress Response (10.98%). (Please see Table 4 for the descriptive and inferential statistics associated with these findings and the exact p-value for each repeated measures comparison.)

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In the sample as a whole, there were significant differences from baseline to follow up within the internal and doctors sub-scale of the MHLCS and all the CDC-CFS Symptom Inventory items bar swollen lymph nodes and glands, fever and abdominal pain. There were also significant differences in all areas of the SF-36, all the fatigue sub-scales of the MFI with the five sub-scales illustrating significant reductions in fatigue and, finally, reductions were also observed in the Maladaptive Stress Response.

Within the psychology group significant differences were also found in the SF-36 sub-scales 'physical functioning', 'role limitations due to physical problem', 'social functioning',

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7 ~~'general mental health', 'vitality, energy or fatigue' and 'general health perceptions'.~~  
8 ~~Regarding perceived control, significant differences were found in internal locus of control~~  
9 ~~and the perception that chance played an influential part in the individuals' lives. Again, all~~  
10 ~~the MFI fatigue scales saw significant decreases over a 3 month period. Regarding ME/CFS~~  
11 ~~specific symptoms, ratings of muscle aches or muscle pains, chills, memory problems,~~  
12 ~~difficulty concentrating and sensitivity to light differed significantly from baseline to follow-~~  
13 ~~up in the expected direction. There was also a significant reduction in the Maladaptive Stress~~  
14 ~~Response over time.~~

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24 ~~The nutrition group saw significant improvements in role limitations due to physical~~  
25 ~~problems, social functioning, vitality, energy or fatigue and general health perceptions. No~~  
26 ~~significant differences were found from baseline to follow up in perceived control in the~~  
27 ~~nutrition group. Once again, all the MFI fatigue scales decreased over a 3 month period and~~  
28 ~~numerous symptom related indices also showed improvements; sore throat, swollen lymph~~  
29 ~~glands, fatigue after exertion, muscle aches or muscle pains, pain in joints, chills, headaches,~~  
30 ~~abdominal pain and sensitivity to light. The way in which the individuals in this group~~  
31 ~~responded to stress also decreased over the 3 month time period.~~

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41 ~~In terms of general health as evaluated by the SF-36 measure, the group who received both~~  
42 ~~psychological and nutritional intervention reported reductions in role limitations due to~~  
43 ~~physical difficulties, social functioning, role limitations due to emotional difficulties and~~  
44 ~~general health perceptions. No significant differences were found from baseline to follow up~~  
45 ~~in perceived control as measured by the MHLCS in the combined treatment group. Only one~~  
46 ~~measure of fatigue, that of physical fatigue, saw significant improvements over time.~~  
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49 ~~Diarrhea, fatigue after exertion, chills, headaches and sinus and nasal symptoms all illustrated~~  
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significant reductions over the 3 month interval, as did the Maladaptive Stress Response. (See Table 2 for descriptive and inferential statistics associated with these findings and Table 3 for percentage of change over time.)

### Comparisons across groups

Once correction for baseline variation was achieved, there were no significant differences between the three groups in terms of change scores.

As shown in Table 3, three of the outcome measures differed significantly in terms of change from baseline to follow up, namely the MHLCs 'chance' sub scale ( $H(2) = 7.674, p < .05$ ), the MFI 'general fatigue' sub scale ( $H(2) = 6.790, p < .05$ ) and the CDC-CFS symptom 'headaches' ( $H(2) = 6.625, p < .05$ ). In terms of perceived control and general fatigue, the psychology group differed significantly as compared to the combined group ( $U = 110.500, p < .05$ ) and ( $U = 118.000, p < .05$ ), respectively, with the psychology group seeing a greater change over time as compared to the combined group on both measures. Regarding headaches, the combined group ( $U = 118.000, p < .05$ ) improved significantly more than the psychology group. No other comparisons reached statistical significance with a Bonferroni correction for multiple comparisons.

## Discussion

### Key results

There was statistically significant (rather than known clinically significant) change over time of numerous measures in all groups investigated. However, this is not to say that these changes were due to the interventions as the design of this study was exploratory, rather than experimental (please see below for a further critique of the design). The psychology group contained the most significant findings, including those concerned with daily functioning,

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7 fatigue, locus of control, the cognitive CDC CFS specific symptoms and the Maladaptive  
8 Stress Response. As expected, changes in perceived control were not observed in the  
9 nutrition group as this is not an area that is targeted in this program. However, the more  
10 immune-type symptoms such as sore throat, swollen lymph nodes or glands and pain in joints  
11 did see significant reductions over time as would be envisaged in treatment protocols based  
12 upon nutritional expertise. The group that exhibited the least significant findings was the  
13 combined group and, as noted below, this may be due to the greater general severity of  
14 symptoms in this group and the need for a more lengthy intervention. Nevertheless,  
15 considering the small sample sizes in the groups at follow-up, these results are very  
16 promising and warrant further attention. ~~In terms of these preliminary findings, the~~  
17 ~~psychology group performed better with regard to lowering the belief that chance influences~~  
18 ~~the course of the condition. This is an important observation as the unpredictable nature of~~  
19 ~~ME/CFS can be one of the most difficult components for individuals to cope with<sup>45</sup> and~~  
20 ~~helping patients gain an improved sense of control over the illness is of great potential~~  
21 ~~benefit. The psychology group also demonstrated a significantly greater change score in~~  
22 ~~general fatigue as compared with the combined group which may infer that in the short term,~~  
23 ~~guiding individuals through the complex nature of the disorder, helping them to understand it~~  
24 ~~and accept that the condition itself gives rise to stresses and psychological distress may be a~~  
25 ~~good starting point for intervention (i.e. a stepped program could be developed).~~

### 45 Interpretation

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47 As noted previously <sup>3130</sup> patient-centered, individualized treatment protocols which include a  
48 range of tailored strategies is a favorable direction for dealing with a complex and multi-  
49 system disorder such as ME/CFS. The present study has demonstrated that such interventions  
50 may be ~~are~~ useful in lowering symptomatology, improving functioning and helping  
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7 individuals gain a greater sense of control over their health status. ~~Considering that the~~  
8 ~~options available on the National Health Service, mainly CBT and GET, are often perceived~~  
9 ~~as coping strategies at best, and physically damaging at worst~~<sup>46</sup>, ~~tailored treatments such as~~  
10 ~~described here may be more palatable, and hence effective.~~

### 16 **Limitations and Generalisability**

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18 This study ~~was a preliminary study in a naturalistic setting and as such did not have a robust~~  
19 ~~design. There was not a~~ ~~did not have a~~ control group ~~and the participants were not randomly~~  
20 ~~assigned to groups, therefore so~~ the results should be treated with caution. ~~In order to~~  
21 ~~ascertain whether the changes in symptom and functional reports were due to the~~  
22 ~~interventions, a randomized control trial should be conducted (RCT). Also, the participants~~  
23 ~~were not randomly assigned to groups as this was a naturalistic, observational study. Also,~~  
24 ~~there was a high drop-out rate from time-one to time-two and this rate differed across groups.~~  
25 ~~The highest drop-out rate was in the psychology group; whilst we cannot be sure why this~~  
26 ~~occurred, it is postulated that the retention was poor in the group as the individuals in the~~  
27 ~~psychology program had more activities to engage in and may have felt overburdened with~~  
28 ~~the research questionnaires in addition to their session and homework (this would not be the~~  
29 ~~case in the combined group as the therapeutic activities are phased-in as mentioned above).~~

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43 In this study, ~~e~~Each individual was guided to appropriate treatment within an initial screening  
44 with clinic staff; therefore the group was dependent on the nature of the individual's  
45 symptoms and their personal choice as the programs on offer were privately funded.

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49 ~~However, as can be seen in the baseline comparisons, the groups did not differ in terms of~~  
50 ~~gender, age, illness duration or the majority of outcome measures.~~ Notably, the groups did  
51 differ in general and physical fatigue with participants in the combined groups reporting  
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7 greater fatigue than those in the psychology group which suggests that this group's general  
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9 symptomatology was more severe. The combined group illustrated less ~~change~~improvement  
10 over time compared to the psychology and nutrition groups and it is feasible to infer that  
11 individuals with a greater number and degree of complaints are referred to the combined  
12 group within the clinic. ~~Also, it should be noted that the interventions in the combined~~  
13 ~~program are phased in as it was found that asking individuals to engage in numerous~~  
14 ~~therapeutic activities resulted in high drop-out rates. Also, those in the combined group will~~  
15 ~~not experience the intensity of each intervention as this has been demonstrated to result in~~  
16 ~~non-compliance;~~ therefore, changes in outcome measures in this group may not be noted at  
17 an interval of three months ~~for that group~~. Further studies underway presently will investigate  
18 follow-ups at 6- and 12-months to identify whether the findings here are maintained over  
19 time and also whether those with greater symptom severity benefit with a longer intervention.  
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21 As the participants were self-selected onto these programs, the findings lack generalizability;  
22 future work should sample from the overall ME/CFS population and be randomly-assigned to  
23 groups in order to make valid assumptions regarding the illness-group as a whole.  
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### 37 Funding

38 No external funding was obtained for this research; the work was accomplished in-house at  
39 the clinic in question.  
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### 47 Data Sharing

48 Dataset available from the corresponding author at [m.a.arroll@sa.uel.ac.uk](mailto:m.a.arroll@sa.uel.ac.uk). Consent was not  
49 obtained for data sharing but the presented data are anonymised and risk of identification is  
50 low.  
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### Contributorship

Alex Howard made substantial contributions to the conception and design and acquisition of data, whilst Megan Arroll made a substantial contribution to the analysis and interpretation of data. Both authors made a substantial contribution to the drafting of the article and revisions for the critical review of important intellectual content. Final approval of the version to be published was also granted by both authors.

### Acknowledgements

We would like to thank Tomas Ros for preparing the questionnaire spreadsheet, Niki Gratrix for helping in setting-up the study and Andy McLellan and Val Duschinsky for proof-reading and editing.

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### Competing Interests

Alex Howard is the founder and CEO of The Optimum Health Clinic and Megan Arroll is the Director of Research at the Optimum Health Clinic, where this study was conducted.



## List of abbreviations

ME: myalgic encephalomyelitis

CFS: Chronic Fatigue Syndrome

NICE: National Institute for Health and Clinical Excellence

CBT: Cognitive Behavioral Therapy

GET: Graded Exercise Therapy

[APT: Adaptive Pacing Therapy](#)

[SMC: specialist medical care](#)

CAM: Complementary and Alternative Medicine

NLP: Neuro-linguistic Programming

EFT: Emotional Freedom Technique

SF-36: Medical Outcomes Survey Short-Form 36

MHLCS: Multidimensional Health Locus of Control Scale

MFI: Multidimensional Fatigue Inventory

[RCT: randomized controlled trial](#)

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Table 1. Baseline comparisons of sample demographics and outcome variables

		Mean	SD	95% CI for Mean		Test statistic	p-value
				Lower	Upper		
Gender	Psychology	9 (21.4%) <sup>d</sup>				.179 <sup>e</sup>	.915
	Nutrition	8 (18.2%) <sup>d</sup>					
	Combined	11 (21.2%) <sup>d</sup>					
	Total	28 (20.3%) <sup>d</sup>					
Age	Psychology	42.881	13.986	38.523	47.239	.000 <sup>a</sup>	1.000
	Nutrition	42.864	12.504	39.062	46.665		
	Combined	42.843	11.125	39.714	45.972		
	Total	42.861	12.406	40.765	44.957		
Illness duration	Psychology	8.874	8.252	6.302	11.445	.252 <sup>a</sup>	.778
	Nutrition	10.023	7.375	7.781	12.265		
	Combined	9.625	7.291	7.595	11.655		
	Total	9.523	7.580	8.247	10.800		
SF-36 Physical Functioning	Psychology	49.339	22.698	42.266	56.413	.319 <sup>a</sup>	.727
	Nutrition	47.855	26.226	39.882	55.829		
	Combined	45.299	25.479	38.206	52.393		
	Total	47.344	24.792	43.171	51.517		
SF-36 Role limitations physical	Psychology	7.143	15.894	2.190	12.096	.281 <sup>a</sup>	.755
	Nutrition	7.574	17.500	2.254	12.895		
	Combined	9.774	21.051	3.914	15.635		
	Total	8.272	18.387	5.177	11.367		
SF-36	Psychology	61.548	25.614	53.566	69.530	1.002 <sup>a</sup>	.370

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Bodily pain	Nutrition	55.625	30.242	46.431	64.819		
	Combined	53.606	27.019	46.084	61.128		
	Total	56.667	27.683	52.007	61.327		
SF-36	Psychology	37.202	21.824	30.402	44.003	-.536 <sup>a</sup>	-.586
Social functioning	Nutrition	32.671	25.888	24.800	40.541		
	Combined	32.452	24.786	25.552	39.352		
	Total	33.967	24.212	29.892	38.043		
SF-36 General mental health	Psychology	60.286	19.584	54.183	66.389	-.124 <sup>a</sup>	-.884
	Nutrition	59.727	19.355	53.843	65.612		
	Combined	58.308	20.948	52.476	64.140		
	Total	59.362	19.911	56.011	62.714		
SF-36 Role limitations emotional	Psychology	55.554	46.368	41.104	70.004	-.390 <sup>a</sup>	-.678
	Nutrition	48.482	47.390	34.074	62.890		
	Combined	47.780	43.924	35.551	60.008		
	Total	50.370	45.590	42.695	58.044		
SF-36 Vitality Energy or Fatigue	Psychology	20.714	16.1386	15.685	25.743	-.129 <sup>a</sup>	-.879
	Nutrition	20.114	14.570	15.685	24.542		
	Combined	19.039	17.658	14.123	23.955		
	Total	19.891	16.159	17.171	22.611		
SF-36 General health perceptions	Psychology	37.024	17.945	31.432	42.616	2.769 <sup>a</sup>	-.066
	Nutrition	28.636	15.528	23.915	33.357		
	Combined	30.962	17.575	26.069	35.854		
	Total	32.065	17.286	29.156	34.975		
MHLCs Internal	Psychology	-.677	-.159	-.627	-.726	1.216 <sup>a</sup>	-.300
	Nutrition	-.622	-.177	-.568	-.675		

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	Combined	-.662	-.174	-.613	-.710		
	Total	-.653	-.171	-.625	-.682		
MHLCS-Chance	Psychology	-.368	-.156	-.320	-.417	.395 <sup>a</sup>	-.674
	Nutrition	-.340	-.133	-.299	-.380		
	Combined	-.354	-.155	-.311	-.397		
	Total	-.354	-.148	-.329	-.379		
MHLCS-Powerful Others	Psychology	-.404	-.134	-.362	-.446	.119 <sup>a</sup>	-.888
	Nutrition	-.417	-.141	-.374	-.460		
	Combined	-.407	-.101	-.379	-.436		
	Total	-.409	-.124	-.388	-.430		
MHLCS-Doctors	Psychology	-.169	-.082	-.143	-.194	.575 <sup>a</sup>	-.564
	Nutrition	-.171	-.089	-.144	-.197		
	Combined	-.191	-.147	-.150	-.232		
	Total	-.178	-.112	-.159	-.196		
MHLCS-Other People	Psychology	-.235	-.075	-.212	-.259	1.051 <sup>a</sup>	-.352
	Nutrition	-.264	-.129	-.225	-.304		
	Combined	-.245	-.074	-.224	-.265		
	Total	-.248	-.095	-.232	-.264		
MFI-General Fatigue	Psychology	15.952	2.845	15.066	16.839	3.219 <sup>a</sup>	-.043 <sup>*</sup>
	Nutrition	16.977	2.601	16.186	17.768		
	Combined	17.327	2.587	16.607	18.047		
	Total	16.797	2.716	16.340	17.254		
MFI-Physical Fatigue	Psychology	15.929	3.331	14.891	16.966	3.343 <sup>a</sup>	-.038 <sup>*</sup>
	Nutrition	16.727	3.358	15.707	17.748		
	Combined	17.615	2.823	16.830	18.401		

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	Total	16.819	3.211	16.278	17.359		
MFI	Psychology	13.857	4.112	12.576	15.138	1.030 <sup>a</sup>	-.360
Reduced Activity	Nutrition	14.136	4.027	12.912	15.361		
	Combined	14.962	3.662	13.942	15.981		
	Total	14.362	3.921	13.702	15.022		
MFI	Psychology	10.357	4.287	9.021	11.693	1.324 <sup>a</sup>	-.270
Reduced Motivation	Nutrition	10.500	3.474	9.444	11.556		
	Combined	11.462	3.153	10.584	12.339		
	Total	10.819	3.639	10.206	11.431		
MFI	Psychology	13.524	4.363	12.164	14.883	.064 <sup>a</sup>	-.938
Mental Fatigue	Nutrition	13.682	4.328	12.366	14.998		
	Combined	13.846	4.345	12.637	15.056		
	Total	13.696	4.315	12.969	14.422		
CDC-CFS	Psychology	2.571	3.109	1.603	3.540	1.414 <sup>a</sup>	-.247
Sore Throat	Nutrition	3.977	3.776	2.829	5.125		
	Combined	3.202	4.494	1.951	4.454		
	Total	3.257	3.898	2.601	3.914		
CDC-CFS Swollen Lymph nodes Glands	Psychology	1.976	3.382	.922	3.030	7.161 <sup>b</sup>	-.028*
	Nutrition	5.561	6.491	3.587	7.534		
	Combined	3.462	4.881	2.103	4.820		
	Total	3.679	5.250	2.795	4.563		
CDC-CFS	Psychology	2.071	3.249	1.059	3.084	.850 <sup>a</sup>	-.430
Diarrhoea/Diarrhea	Nutrition	2.841	4.832	1.372	4.310		
	Combined	3.135	3.773	2.084	4.185		
	Total	2.717	3.998	2.044	3.390		

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CDC-CFS Fatigue after exertion	Psychology	13.286	6.271	11.331	15.240	.219 <sup>a</sup>	-.803
	Nutrition	13.722	6.450	11.761	15.682		
	Combined	14.154	6.270	12.408	15.899		
	Total	13.752	6.292	12.693	14.811		
CDC-CFS Muscle Aches or Muscle Pains	Psychology	8.286	6.747	6.183	10.388	-.166 <sup>a</sup>	-.847
	Nutrition	9.091	6.383	7.151	11.031		
	Combined	8.519	6.932	6.589	10.449		
	Total	8.630	6.664	7.509	9.752		
CDC-CFS Pain In Joints	Psychology	3.476	5.334	1.814	5.138	1.373 <sup>a</sup>	-.257
	Nutrition	4.696	5.560	3.006	6.386		
	Combined	5.474	6.386	3.696	7.251		
	Total	4.618	5.837	3.635	5.600		
CDC-CFS Fever	Psychology	1.238	2.516	-.454	2.022	.027 <sup>a</sup>	-.973
	Nutrition	1.394	2.562	-.615	2.173		
	Combined	1.333	3.909	-.245	2.421		
	Total	1.324	3.106	-.801	1.846		
CDC-CFS Chills	Psychology	3.357	4.637	1.912	4.802	-.206 <sup>a</sup>	-.814
	Nutrition	3.750	3.924	2.557	4.943		
	Combined	3.192	4.343	1.983	4.402		
	Total	3.420	4.283	2.699	4.141		
CDC-CFS Unrefreshing Sleep	Psychology	12.905	6.792	10.788	15.021	.150 <sup>a</sup>	-.861
	Nutrition	12.250	7.088	10.095	14.405		
	Combined	12.154	7.147	10.164	14.144		
	Total	12.413	6.978	11.238	13.588		
CDC-CFS Sleeping	Psychology	9.286	7.658	6.899	11.672	.085 <sup>a</sup>	-.918

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Problems	Nutrition	8.614	7.317	6.389	10.838		
	Combined	8.904	7.684	6.766	11.042		
	Total	8.928	7.509	7.664	10.192		
CDC-CFS Headaches	Psychology	5.262	5.548	3.533	6.991	1.611 <sup>a</sup>	-.203
	Nutrition	7.646	7.040	5.506	9.786		
	Combined	6.346	5.857	4.715	7.977		
	Total	6.431	6.200	5.3871	7.474		
CDC-CFS Memory Problems	Psychology	6.333	4.996	4.777	7.890	3.403 <sup>b</sup>	-.182
	Nutrition	9.409	7.183	7.225	11.593		
	Combined	8.173	7.610	6.055	10.292		
	Total	8.007	6.835	6.857	9.158		
CDC-CFS Difficulty Concentrating	Psychology	8.500	6.094	6.601	10.399	.391 <sup>a</sup>	-.677
	Nutrition	9.822	7.641	7.499	12.145		
	Combined	9.135	6.942	7.202	11.067		
	Total	9.161	6.903	7.999	10.323		
CDC-CFS Nausea	Psychology	3.476	4.845	1.966	4.986	1.162 <sup>a</sup>	-.316
	Nutrition	4.769	5.135	3.208	6.330		
	Combined	3.327	4.902	1.962	4.692		
	Total	3.832	4.966	2.996	4.668		
CDC-CFS Abdominal Pain	Psychology	2.548	3.270	1.529	3.567	5.971 <sup>b</sup>	-.051
	Nutrition	5.064	5.165	3.493	6.634		
	Combined	3.750	4.635	2.460	5.041		
	Total	3.803	4.535	3.040	4.566		
CDC-CFS Sinus Nasal Symptoms	Psychology	3.524	4.702	2.059	4.989	1.192 <sup>a</sup>	-.307
	Nutrition	5.469	6.476	3.500	7.438		

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	Combined	4.789	6.304	3.034	6.544		
	Total	4.620	5.932	3.622	5.619		
CDC-CFS Shortness Of Breath	Psychology	3.000	4.191	1.694	4.306	.095 <sup>a</sup>	.909
	Nutrition	3.285	4.090	2.026	4.543		
	Combined	3.392	4.788	2.046	4.739		
	Total	3.237	4.365	2.497	3.977		
CDC-CFS Sensitivity To Light	Psychology	3.429	5.347	1.762	5.095	.794 <sup>a</sup>	.454
	Nutrition	5.031	6.097	3.177	6.884		
	Combined	4.481	6.360	2.710	6.251		
	Total	4.336	5.975	3.330	5.342		
CDC-CFS Depression	Psychology	3.952	3.938	2.725	5.180	.160 <sup>b</sup>	.923
	Nutrition	4.477	5.450	2.821	6.134		
	Combined	5.077	5.950	3.420	6.734		
	Total	4.544	5.231	3.663	5.424		
CDC-CFS Maladaptive Stress Index Scale Score	Psychology	94.381	16.836	89.134	99.628	.465 <sup>a</sup>	.629
	Nutrition	96.386	21.946	89.714	103.059		
	Combined	98.269	19.165	92.934	103.605		
	Total	96.486	19.373	93.225	99.747		

<sup>a</sup>F-statistic for one-way analysis of variance, d.f.=2,134

<sup>b</sup>H-statistic for Kruskal-Wallis test, d.f.=2

<sup>c</sup> $\chi^2$ -statistic for comparison of nominal level data, d.f.=2

<sup>d</sup>number of males

\* test is significant at the  $p < .05$  level

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Table 2. Outcome variable comparisons across time

		Baseline				3-month follow-up				Comparisons	
		Mean	SD	95% CI for Mean		Mean	SD	95% CI for Mean		z-statistic	p-value
				Lower	Upper			Lower	Upper		
SF-36	Psychology	49.339	22.698	42.266	56.413	59.267	30.346	41.745	76.788	-2.707	.007**
Physical Functioning	Nutrition	47.855	26.226	39.882	55.829	46.706	30.744	34.544	58.868	-1.136	.256
	Combined	45.299	25.479	38.206	52.393	49.288	26.403	39.604	58.973	-1.850	.064
	Total	47.344	24.791	43.171	51.517	50.260	28.818	43.488	57.032	-3.120	.002**
SF-36	Psychology	7.143	15.894	2.190	12.096	46.429	39.048	23.883	68.974	-2.379	.017*
Role limitations physical	Nutrition	7.574	17.500	2.254	12.895	19.444	20.016	11.526	27.363	-2.907	.004**
	Combined	9.774	21.051	3.914	15.635	22.742	25.161	13.513	31.971	-2.225	.026*
	Total	8.272	18.387	5.177	11.367	26.111	28.225	19.479	32.744	-4.354	.001***
SF-36	Psychology	61.548	25.614	53.566	69.530	63.929	29.786	46.731	81.127	-1.196	.232
Bodily pain	Nutrition	55.625	30.242	46.434	64.819	58.889	32.943	45.857	71.921	-1.800	.072
	Combined	53.606	27.019	46.084	61.128	58.629	27.301	48.615	68.643	-1.048	.294
	Total	56.667	27.683	52.007	61.327	59.757	29.649	52.790	66.724	-2.240	.025*
SF-36	Psychology	37.202	21.824	30.402	44.003	59.821	33.318	40.584	79.058	-2.689	.007**
Social functioning	Nutrition	32.671	25.888	24.800	40.541	43.519	33.679	30.196	56.841	-2.476	.013*
	Combined	32.452	24.786	25.551	39.352	41.936	28.604	31.443	52.428	-2.426	.015*
	Total	33.967	24.212	29.892	38.043	46.007	31.805	38.533	53.481	-4.504	.001***
SF-36	Psychology	60.286	19.584	54.183	66.389	74.571	13.276	66.906	82.237	-2.497	.013*
General mental health	Nutrition	59.727	19.355	53.843	65.612	64.741	20.548	56.612	72.869	-1.696	.090
	Combined	58.308	20.948	52.476	64.140	64.129	16.637	58.027	70.232	-.524	.600

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	Total	59.362	19.911	56.011	62.714	66.389	17.897	62.183	70.594	-2.665	-.008**
SF-36	Psychology	55.554	46.368	41.105	70.004	76.191	33.150	57.051	95.331	-.842	-.400
Role	Nutrition	48.482	47.390	34.074	62.890	55.594	38.130	40.510	70.678	-1.788	-.074
limitations	Combined	47.780	43.924	35.551	60.008	67.742	32.756	55.727	79.757	-2.313	-.021*
emotional	Total	50.370	45.590	42.695	58.044	64.829	35.335	56.526	73.133	-3.159	-.002**
SF-36	Psychology	20.714	16.139	15.685	25.743	41.071	20.586	29.186	52.957	-3.066	-.002**
Vitality-Energy	Nutrition	20.114	14.5670	15.685	24.542	31.111	23.588	21.780	40.442	-2.734	-.006**
or-Fatigue	Combined	19.039	17.658	14.123	23.955	27.097	19.527	19.934	34.259	-1.558	-.119
	Total	19.891	16.159	17.171	22.611	31.319	21.657	26.230	36.409	-4.205	-.001***
SF-36	Psychology	37.024	17.945	31.432	42.616	45.714	21.109	33.526	57.903	-2.561	-.010*
General health	Nutrition	28.636	15.528	23.915	33.357	36.482	18.903	29.004	43.959	-2.157	-.031*
perceptions	Combined	30.962	17.575	26.069	35.854	42.097	21.632	34.162	50.032	-2.423	-.015*
	Total	32.065	17.286	29.156	34.975	40.694	20.561	-35.863	45.526	-3.996	-.001***
MHLCS	Psychology	-.677	-.159	-.627	-.726	-.821	-.251	-.676	-.966	-2.983	-.003**
Internal	Nutrition	-.622	-.177	-.568	-.675	1.193	2.969	-.019	2.368	-.687	-.492
	Combined	-.662	-.174	-.613	-.710	-.779	-.318	-.662	-.896	-1.755	-.079
	Total	-.653	-.171	-.624	-.682	-.942	1.822	-.514	1.371	-2.962	-.003**
MHLCS	Psychology	-.368	-.156	-.320	-.417	-.351	-.152	-.263	-.439	-2.594	-.009**
Chance	Nutrition	-.340	-.133	-.299	-.380	-.911	3.020	-.284	2.105	-.143	-.886
	Combined	-.354	-.155	-.311	-.397	-.314	-.133	-.265	-.363	-.672	-.501
	Total	-.354	-.148	-.329	-.379	-.545	1.853	-.109	-.980	-1.552	-.121
MHLCS	Psychology	-.404	-.134	-.362	-.446	-.441	-.315	-.259	-.624	-.000	1.000
Powerful	Nutrition	-.418	-.141	-.374	-.460	-.804	2.244	-.084	1.691	-1.843	-.065
Others	Combined	-.407	-.101	-.379	-.436	-.434	-.279	-.331	-.536	-.577	-.564
	Total	-.409	-.124	-.388	-.430	-.574	1.3880	-.248	-.900	-1.601	-.109

MHLCS	Psychology	-.169	-.082	-.143	-.194	-.131	-.093	-.077	-.185	-.122	-.262
Doctors	Nutrition	-.171	-.089	-.144	-.197	-.657	2.668	-.398	1.713	-.686	-.092
	Combined	-.191	-.147	-.150	-.232	-.153	-.070	-.128	-.179	-.1384	-.166
	Total	-.178	-.112	-.159	-.196	-.338	1.635	-.0462	-.722	-.2381	-.017*
MHLCS	Psychology	-.235	-.075	-.212	-.259	-.268	-.189	-.159	-.377	-.118	-.906
Other People	Nutrition	-.264	-.129	-.225	-.304	-.739	2.652	-.311	1.788	-.697	-.090
	Combined	-.245	-.074	-.224	-.265	-.252	-.118	-.209	-.295	-.213	-.831
	Total	-.248	-.095	-.232	-.264	-.438	1.626	-.055	-.820	-.1186	-.236
MFI	Psychology	15.952	2.845	15.066	16.839	13.786	4.441	11.222	16.350	-2.657	-.008**
General	Nutrition	16.977	2.601	16.186	17.768	14.704	4.898	12.766	16.641	-2.548	-.011*
Fatigue	Combined	17.327	2.588	16.607	18.047	16.645	2.811	15.614	17.676	-.854	-.393
	Total	16.797	2.716	16.340	17.254	15.361	4.136	14.389	16.333	-3.692	-.001***
MFI	Psychology	15.929	3.331	14.891	16.966	13.071	4.632	10.397	15.746	-2.810	-.005**
Physical	Nutrition	16.727	3.358	15.707	17.748	14.222	4.987	12.249	16.195	-2.791	-.005**
Fatigue	Combined	17.615	2.823	16.830	18.401	16.484	3.395	15.239	17.729	-2.364	-.018*
	Total	16.819	3.211	16.278	17.359	14.972	4.453	13.926	16.019	-4.591	-.001***
MFI	Psychology	13.857	4.112	12.576	15.138	10.643	5.153	7.668	13.618	-2.142	-.032*
Reduced	Nutrition	14.136	4.027	12.912	15.361	12.259	5.012	10.277	14.242	-2.164	-.030*
Activity	Combined	14.962	3.662	13.942	15.981	14.936	3.777	13.550	16.321	-.070	-.944
	Total	14.362	3.921	13.702	15.022	13.097	4.798	11.970	14.225	-2.421	-.015*
MFI	Psychology	10.357	4.287	9.021	11.693	7.286	4.214	4.853	9.719	-2.131	-.033*
Reduced	Nutrition	10.500	3.474	9.444	11.556	8.963	3.736	7.485	10.441	-1.985	-.047*
Motivation	Combined	11.462	3.153	10.584	12.339	10.774	3.095	9.639	11.910	-1.082	-.279
	Total	10.819	3.639	10.206	11.431	9.417	3.767	8.532	10.302	-2.986	-.003**
MFI	Psychology	13.524	4.363	12.164	14.883	10.500	4.468	7.920	13.080	-2.950	-.003*

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Mental-Fatigue	Nutrition	13.682	4.328	12.366	14.998	11.926	5.334	9.816	14.036	-2.082	.037*
	Combined	13.846	4.345	12.637	15.056	12.613	3.827	11.209	14.017	-1.586	.113
	Total	13.696	4.315	12.969	14.422	11.944	4.568	10.871	13.018	-3.661	.001***
CDC-CFS	Psychology	2.571	3.109	1.603	3.540	1.429	2.278	.114	2.744	-1.365	.172
Sore-Throat	Nutrition	3.977	3.776	2.829	5.125	1.741	2.087	.915	2.566	-2.211	.027*
	Combined	3.202	4.494	1.951	4.454	1.904	2.821	.870	2.939	-.804	.422
	Total	3.257	3.898	2.601	3.914	1.750	2.437	1.178	2.323	-2.387	.017*
CDC-CFS	Psychology	1.976	3.382	.922	3.030	1.786	3.378	-.165	3.736	-.341	.733
Swollen	Nutrition	5.561	6.491	3.587	7.534	5.000	6.760	2.326	7.674	-2.212	.027*
Lymph-nodes	Combined	3.462	4.881	2.103	4.820	2.690	4.477	1.0458	4.332	-.725	.468
Glands	Total	3.679	5.250	2.795	4.563	3.380	5.385	2.115	4.646	-1.684	.092
CDC-CFS	Psychology	2.071	3.249	1.059	3.084	1.643	2.818	.016	3.270	-.730	.465
DiarrhoeaDiarr hea	Nutrition	2.841	4.832	1.372	4.310	1.444	3.274	.149	2.740	-1.649	.099
	Combined	3.135	3.773	2.084	4.185	1.631	2.483	.720	2.542	-1.996	.046*
	Total	2.717	3.998	2.044	3.390	1.563	2.827	-.899	2.228	-2.481	.013*
CDC-CFS	Psychology	13.286	6.271	11.331	15.240	11.071	6.673	7.218	14.925	-1.550	.121
Fatigue after exertion	Nutrition	13.722	6.450	11.761	15.682	11.815	7.217	8.960	14.670	-2.209	.027*
	Combined	14.154	6.270	12.408	15.899	11.436	6.275	9.134	13.738	-2.392	.017*
	Total	13.752	6.292	12.693	14.811	11.507	6.629	9.949	13.065	-3.574	.001***
CDC-CFS	Psychology	8.286	6.747	6.183	10.388	7.429	6.892	3.450	11.408	-2.145	.032*
Muscle-Aches or-Muscle Pains	Nutrition	9.091	6.383	7.151	11.031	7.222	6.278	4.739	9.706	-2.901	.004**
	Combined	8.519	6.932	6.589	10.449	6.188	5.528	4.160	8.215	-1.908	.056
	Total	8.630	6.664	7.509	9.752	6.817	6.029	5.400	8.234	-3.995	.001***
CDC-CFS	Psychology	3.476	5.334	1.814	5.138	2.786	4.458	.212	5.360	-1.778	.075
Pain-In-Joints	Nutrition	4.696	5.560	3.006	6.386	3.926	5.099	1.909	5.943	-2.022	.043*



	Combined	5.474	6.386	3.696	7.251	3.010	4.140	1.492	4.528	-1.840	.066
	Total	4.618	5.837	3.635	5.600	3.310	4.543	2.242	4.377	-3.141	.002**
CDC-CFS	Psychology	1.238	2.516	.454	2.022	1.643	4.181	-.771	4.057	-.135	.892
Fever	Nutrition	1.394	2.562	-.615	2.173	-.630	2.041	-.178	1.437	-1.487	-.137
	Combined	1.333	3.909	-.245	2.421	-.378	.709	-.118	.638	-1.517	-.129
	Total	1.324	3.106	-.801	1.846	-.718	2.272	-.185	1.252	-1.876	-.061
CDC-CFS	Psychology	3.357	4.637	1.912	4.802	2.571	4.398	.032	5.111	-1.970	.049*
Chills	Nutrition	3.750	3.924	2.557	4.943	2.222	4.098	-.601	3.843	-3.401	.001***
	Combined	3.192	4.343	1.983	4.402	1.908	2.797	-.882	2.934	-2.049	.040*
	Total	3.420	4.283	2.699	4.141	2.155	3.614	-1.306	3.004	-4.206	.001***
CDC-CFS	Psychology	12.905	6.792	10.788	15.021	10.643	6.698	6.776	14.510	-.802	.422
Unrefreshing	Nutrition	12.250	7.088	10.095	14.405	9.444	7.738	6.384	12.505	-1.421	.155
Sleep	Combined	12.154	7.147	10.164	14.143	10.161	7.959	7.242	13.080	-1.513	.130
	Total	12.413	6.978	11.238	13.588	9.986	7.557	8.210	11.762	-2.295	.022*
CDC-CFS	Psychology	9.286	7.658	6.899	11.672	5.286	4.921	2.444	8.127	-1.738	.082
Sleeping	Nutrition	8.614	7.317	6.389	10.838	9.482	9.200	5.842	13.121	-.190	.849
Problems	Combined	8.904	7.681	6.766	11.042	6.529	6.749	4.053	9.004	-1.794	.073
	Total	8.928	7.509	7.664	10.192	7.394	7.585	5.612	9.177	-1.983	.047*
CDC-CFS	Psychology	5.262	5.548	3.533	6.991	4.357	3.411	2.388	6.326	-1.200	.230
Headaches	Nutrition	7.646	7.040	5.506	9.786	5.185	6.294	2.695	7.675	-2.084	.037*
	Combined	6.346	5.857	4.715	7.977	4.050	3.527	2.756	5.343	-2.807	.005**
	Total	6.431	6.200	5.387	7.474	4.535	4.708	3.429	5.642	-3.000	.003**
CDC-CFS	Psychology	6.333	4.996	4.777	7.890	3.500	3.995	1.193	5.807	-1.965	.049*
Memory	Nutrition	9.409	7.183	7.225	11.593	8.667	7.681	5.628	11.705	-.338	.735
Problems	Combined	8.173	7.610	6.055	10.292	6.148	4.905	4.349	7.947	-1.446	.148

	Total	8.007	6.835	6.857	9.158	6.578	6.189	5.123	8.032	-2.053	.040*
CDC-CFS	Psychology	8.500	6.094	6.601	10.399	5.143	5.559	1.933	8.353	-2.809	.005**
Difficulty	Nutrition	9.822	7.641	7.499	12.145	7.778	6.941	5.032	10.524	-1.196	.232
Concentrating	Combined	9.135	6.942	7.202	11.067	6.507	4.843	4.731	8.283	-1.899	.058
	Total	9.161	6.903	7.999	10.323	6.718	5.844	5.345	8.092	-3.440	.001***
CDC-CFS	Psychology	3.476	4.845	1.966	4.986	2.286	2.946	.585	3.987	-.213	.832
Nausea	Nutrition	4.769	5.135	3.208	6.330	3.407	5.746	1.134	5.681	-1.686	.092
	Combined	3.327	4.902	1.962	4.692	3.458	3.585	2.144	4.773	-.855	.392
	Total	3.832	4.966	2.996	4.668	3.211	4.396	2.178	4.244	-.584	.559
CDC-CFS	Psychology	2.548	3.270	1.529	3.567	2.786	4.003	-.474	5.097	-.343	.732
Abdominal	Nutrition	5.064	5.165	3.493	6.634	3.593	3.905	2.048	5.137	-1.968	.049*
Pain	Combined	3.750	4.635	2.460	5.041	2.548	2.791	1.524	3.572	-.598	.550
	Total	3.803	4.535	3.040	4.566	2.986	3.470	2.171	3.801	-1.727	.084
CDC-CFS	Psychology	3.524	4.702	2.059	4.989	2.357	2.437	.950	3.764	-.724	.469
Sinus-Nasal	Nutrition	5.469	6.476	3.500	7.438	4.889	6.104	2.474	7.304	-1.400	.162
Symptoms	Combined	4.789	6.304	3.034	6.544	3.804	6.710	1.343	6.266	-2.482	.013*
	Total	4.620	5.931	3.622	5.619	3.930	5.882	2.547	5.312	-2.971	.003**
CDC-CFS	Psychology	3.000	4.191	1.694	4.306	1.571	2.209	.296	2.847	-1.556	.120
Shortness-Of	Nutrition	3.285	4.090	2.026	4.543	2.407	4.060	.801	4.013	-1.849	.064
Breath	Combined	3.392	4.788	2.046	4.739	2.526	3.631	1.194	3.858	-.976	.329
	Total	3.237	4.365	2.497	3.977	2.296	3.554	1.461	3.131	-2.538	.011*
CDC-CFS	Psychology	3.429	5.347	1.762	5.095	1.214	2.517	-.239	2.668	-1.973	.049*
Sensitivity-To	Nutrition	5.031	6.097	3.177	6.884	4.111	6.198	1.659	6.563	-2.136	.033*
Light	Combined	4.481	6.360	2.710	6.251	3.297	5.557	1.259	5.335	-.787	.431
	Total	4.336	5.975	3.330	5.342	3.197	5.419	1.924	4.471	-2.542	.011*

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CDC-CFS	Psychology	3.952	3.938	2.725	5.180	1.571	3.228	-.292	3.435	-1.614	-.106
Depression	Nutrition	4.477	5.450	2.821	6.134	3.333	4.883	1.402	5.265	-1.584	-.113
	Combined	5.077	5.950	3.420	6.734	2.766	3.324	1.547	3.985	-1.304	-.192
	Total	4.544	5.230	3.663	5.424	2.747	3.964	1.815	3.678	-2.297	.022*
CDC-CFS	Psychology	94.381	16.836	89.134	99.628	78.571	18.434	67.928	89.215	-3.111	.002**
Maladaptive	Nutrition	96.386	21.946	89.714	103.059	85.259	27.665	74.315	96.203	-3.443	.001***
Stress-Index	Combined	98.269	19.165	92.934	103.605	87.484	22.965	79.060	95.908	-2.215	.027*
Scale-Score	Total	96.486	19.373	93.225	99.747	84.917	24.004	79.276	90.557	-5.123	.001***

\*z-statistic for Wilcoxon Signed-Rank Test

Table 3. Change score comparisons between intervention groups

		% change over time for sig. results <sup>a</sup>	Mean	Std. Deviation	Std. Error	95% CI for Mean		H <sup>b</sup>	p-value
						Lower	Upper		
SF-36 Physical Functioning	Psychology	16.75	-13.629	14.990	4.006	-22.285	-4.974	3.215	.200
	Nutrition		-.407	19.967	3.843	-8.306	7.492		
	Combined		-6.813	18.242	3.276	-13.505	-.122		
	Total	5.80	-5.736	18.744	2.209	-10.141	-1.332		
SF-36	Psychology	84.61	-33.929	39.960	10.680	-57.001	-10.856	1.558	.459

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Role limitations physical	Nutrition	61.05	-14.509	21.005	4.042	-22.818	-6.199		
	Combined	57.02	-13.871	31.457	5.650	-25.409	-2.333		
	Total	63.32	-18.010	30.564	3.602	-25.192	-10.828		
SF-36	Psychology		-6.071	15.588	4.166	-15.072	2.929	.163	-.922
Bodily pain	Nutrition		-6.574	18.800	3.618	-14.011	.863		
	Combined		-3.387	25.532	4.586	-12.752	5.978		
	Total	5.17	-5.104	21.252	2.505	-10.098	-1.10		
SF-36	Psychology	37.81	-24.107	24.741	6.612	-38.392	-9.822	3.301	-.192
Social functioning	Nutrition	24.93	-10.648	20.423	3.931	-18.727	-2.569		
	Combined	22.60	-11.290	24.013	4.313	-20.098	-2.482		
	Total	26.17	-13.542	23.149	2.728	-18.981	-8.102		
SF-36	Psychology	19.15	-12.000	14.294	3.820	-20.253	-3.747	4.404	-.111
General mental health	Nutrition		-3.259	15.963	3.072	-9.574	3.056		
	Combined		-.645	16.911	3.037	-6.848	5.558		
	Total	10.58	-3.833	16.409	1.934	-7.689	-.022		
SF-36	Psychology		-9.527	49.664	13.273	-38.202	19.148	-.573	-.751
Role limitations emotional	Nutrition		-18.561	55.759	10.731	-40.618	3.497		
	Combined	29.47	-18.284	52.240	9.383	-37.446	.878		
	Total	10.58	-16.685	52.496	6.187	-29.021	-4.349		
SF-36	Psychology	49.57	-17.500	15.902	4.250	-26.682	-8.318	4.988	-.083
Vitality Energy or Fatigue	Nutrition	35.35	-11.482	19.206	3.696	-19.079	-3.884		
	Combined		-6.129	17.688	3.177	-12.617	.359		
	Total	22.30	-10.347	18.219	2.147	-14.628	-6.066		
SF-36	Psychology	19.01	-11.429	14.335	3.831	-19.705	-3.152	-.627	-.731
General health	Nutrition	29.73	-6.852	15.201	2.925	-12.865	-.839		

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perceptions	Combined	26.45	-10.161	22.154	3.97	-18.288	-2.035		
	Total	36.49	-9.167	18.251	2.151	-13.455	-4.878		
MHLCS Internal	Psychology	17.56	-.146	-.203	-.054	-.263	-.029	3.402	-.183
	Nutrition		-.573	3.028	-.583	-1.771	-.625		
	Combined		-.106	-.315	-.057	-.222	.010		
	Total	30.67	-.289	1.859	-.219	-.726	-.148		
MHLCS Chance	Psychology	4.67	.077	-.098	-.026	.021	-.134	7.674	.022*
	Nutrition		-.570	3.019	-.581	-1.765	-.624		
	Combined		-.001	-.081	-.015	-.029	.031		
	Total		-.198	1.852	-.218	-.633	-.237		
MHLCS Powerful Others	Psychology		-.054	-.284	-.076	-.218	-.109	1.571	-.456
	Nutrition		-.375	2.282	-.439	-1.277	-.528		
	Combined		-.030	-.277	-.050	-.132	.072		
	Total		-.164	1.408	-.166	-.495	-.167		
MHLCS Doctors	Psychology		.020	-.058	-.0155	-.014	-.053	0.076	-.963
	Nutrition		-.492	2.678	-.515	-1.551	-.568		
	Combined		-.057	-.199	-.036	-.016	-.130		
	Total	47.49	-.156	1.647	-.194	-.543	-.231		
MHLCS Other People	Psychology		-.032	-.166	-.044	-.128	-.064	2.479	-.290
	Nutrition		-.446	2.692	-.518	-1.510	-.619		
	Combined		-.012	-.096	-.017	-.047	.023		
	Total		-.178	1.645	-.193	-.565	-.208		

MFI	Psychology	13.58	2.571	2.766	.739	.975	4.168	6.790	.034*
General Fatigue	Nutrition	13.39	2.074	3.842	.740	.554	3.594		
	Combined		.419	2.233	.401	-.400	1.238		
	Total	8.55	1.458	3.126	.368	.724	2.193		
MFI	Psychology	17.74	2.857	2.797	.748	1.242	4.472	3.038	.219
Physical Fatigue	Nutrition	15.00	2.444	4.371	.841	.716	4.173		
	Combined	6.42	1.290	2.735	.491	.287	2.294		
	Total	10.98	2.028	3.468	.409	1.213	2.843		
MFI	Psychology	23.20	1.857	2.932	.784	.165	3.550	1.734	.420
Reduced Activity	Nutrition	13.28	1.148	2.685	.517	.086	2.210		
	Combined		.645	3.189	.572	-.525	1.815		
	Total	8.81	1.069	2.952	.348	.376	1.763		
MFI	Psychology	11.42	2.500	3.502	.936	.478	4.522	5.171	.075
Reduced Motivation	Nutrition	14.64	1.593	3.511	.676	.204	2.982		
	Combined		.129	3.471	.624	-1.144	1.402		
	Total	12.96	1.139	3.570	.421	.300	1.978		
MFI	Psychology	29.66	3.571	3.056	.817	1.807	5.336	4.551	.103
Mental Fatigue	Nutrition	12.83	1.519	3.631	.699	.082	2.955		
	Combined		1.161	4.267	.766	-.404	2.726		
	Total	12.79	1.764	3.880	.457	.852	2.676		
CDC-CFS	Psychology		1.429	3.736	.998	.728	3.586	1.298	.523
Sore Throat	Nutrition	56.23	1.185	2.661	.512	.133	2.238		
	Combined		.500	4.591	.825	-1.184	2.184		
	Total	46.26	.937	3.769	.444	.052	1.823		
CDC-CFS Swollen Lymph	Psychology		-.143	2.932	.784	-1.835	1.550	0.462	.794

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Lymph Nodes-Glands	Nutrition	10.09	1.247	2.700	-.520	-.179	2.316		
	Combined		-.794	6.549	1.176	-1.608	3.197		
	Total		-.782	4.756	-.560	-.336	1.900		
CDC-CFS Diarrhoea/Diarrhea	Psychology		-.286	1.490	-.398	-1.146	-.575	3.619	-.164
	Nutrition		-.926	2.868	-.552	-.209	2.060		
	Combined	47.97	1.272	3.789	-.681	-.118	2.662		
	Total	42.47	-.839	3.134	-.369	-.103	1.576		
CDC-CFS Fatigue after exertion	Psychology		2.286	4.811	1.286	-.492	5.063	0.379	-.827
	Nutrition	13.90	2.593	5.507	1.060	-.414	4.771		
	Combined	19.20	2.532	5.578	1.002	-.486	4.578		
	Total	16.32	2.507	5.339	-.629	1.252	3.761		
CDC-CFS Muscle Aches or Muscle Pains	Psychology	10.34	2.500	4.034	1.078	-.171	4.829	0.469	-.791
	Nutrition	20.56	2.333	3.637	-.700	-.894	3.772		
	Combined		2.070	5.335	-.958	-.113	4.027		
	Total	21.01	2.253	4.459	-.526	1.205	3.300		
CDC-CFS Pain In Joints	Psychology		1.857	4.036	1.079	-.473	4.187	0.054	-.973
	Nutrition	16.40	1.393	3.721	-.716	-.079	2.865		
	Combined		1.978	5.622	1.010	-.084	4.040		
	Total	28.32	1.735	4.634	-.546	-.646	2.824		
CDC-CFS Fever	Psychology		-.214	1.968	-.526	-1.351	-.922	0.399	-.819
	Nutrition		-.604	2.311	-.445	-.310	1.519		
	Combined		1.245	4.816	-.865	-.521	3.012		
	Total		-.721	3.573	-.421	-.118	1.561		
CDC-CFS Chills	Psychology	23.40	1.571	2.738	-.732	-.009	3.152	1.517	-.468
	Nutrition	40.74	2.148	3.097	-.596	-.923	3.373		

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	Combined	40.23	1.447	3.986	.716	-.015	2.909		
	Total	37.00	1.734	3.421	-.403	-.930	2.538		
CDC-CFS Unrefreshing Sleep	Psychology		1.857	6.803	1.818	-2.071	5.785	0.160	.948
	Nutrition		2.148	6.904	1.329	-.583	4.879		
	Combined		1.581	5.726	1.029	-.520	3.681		
	Total	19.55	1.847	6.3123	-.744	-.364	3.331		
CDC-CFS Sleeping Problems	Psychology		2.786	5.352	1.430	-.304	5.876	3.218	.200
	Nutrition		-.222	5.139	-.989	-2.255	1.811		
	Combined		1.762	4.871	-.875	-.025	3.548		
	Total	17.17	1.217	5.133	-.605	-.011	2.423		
CDC-CFS Headaches	Psychology		-.7143	2.091	-.559	-1.922	-.493	6.625	-.036*
	Nutrition	32.19	1.572	3.507	-.675	-.184	2.959		
	Combined	36.18	2.467	4.944	-.888	-.653	4.280		
	Total	29.32	1.512	4.124	-.486	-.543	2.482		
CDC-CFS Memory Problems	Psychology	44.73	2.857	4.655	1.244	-.169	5.545	2.316	-.314
	Nutrition		-.111	4.925	-.947	-2.059	1.837		
	Combined		1.949	6.011	1.080	-.256	4.154		
	Total	17.86	1.353	5.435	-.641	-.076	2.630		
CDC-CFS Difficulty Concentrating	Psychology	39.50	4.643	4.534	1.212	2.025	7.261	5.945	-.051
	Nutrition		-.815	4.359	-.839	-.910	2.539		
	Combined		2.170	5.877	1.056	-.015	4.326		
	Total	26.66	2.143	5.217	-.615	-.917	3.369		
CDC-CFS Nausea	Psychology		-.143	2.770	-.740	-1.456	1.742	4.773	-.092
	Nutrition		-.660	2.667	-.513	-.395	1.716		
	Combined		-.251	4.468	-.803	-1.388	1.890		



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	Total			.384	3.535	.417	-.447	1.214		
CDC-CFS-Abdominal Pain	Psychology			-.286	1.729	-.462	-.713	1.284	1.082	-.582
	Nutrition	29.05		-.882	2.165	-.417	-.025	1.738		
	Combined			-.839	4.390	-.789	-.771	2.449		
	Total			-.747	3.234	-.381	-.013	1.507		
CDC-CFS-Sinus-Nasal Symptoms	Psychology			-.929	3.125	-.835	-.876	2.733	1.255	-.534
	Nutrition			1.060	4.193	-.807	-.599	2.719		
	Combined	20.56		1.906	5.923	1.063	-.267	4.078		
	Total	14.95		1.399	4.822	-.568	-.266	2.532		
CDC-CFS-Shortness-Of-Breath	Psychology			1.500	3.459	-.924	-.497	3.497	0.707	-.702
	Nutrition	18.28		-.779	2.057	-.403	-.052	1.609		
	Combined			-.690	3.972	-.725	-.793	2.173		
	Total	29.08		-.885	3.243	-.388	-.112	1.658		
CDC-CFS-Sensitivity-To-Light	Psychology	64.58		1.429	2.472	-.661	-.001	2.856	0.939	-.625
	Nutrition			1.568	3.764	-.725	-.079	3.057		
	Combined			-.961	5.178	-.930	-.938	2.860		
	Total	26.26		1.280	4.209	-.496	-.291	2.269		
CDC-CFS-Depression	Psychology			1.429	3.502	-.936	-.593	3.451	0.490	-.783
	Nutrition			-.704	3.268	-.629	-.589	1.996		
	Combined			1.363	5.345	-.960	-.598	3.323		
	Total	39.55		1.129	4.282	-.505	-.122	2.135		
CDC-CFS-Maladaptive Stress-Index-Scale-Score	Psychology	16.75		16.286	13.234	3.537	8.645	23.927	4.379	-.112
	Nutrition	11.54		12.815	17.802	3.426	5.772	19.857		
	Combined	10.98		9.613	26.424	4.746	-.080	19.305		
	Total	11.99		12.111	21.201	2.499	7.129	17.093		

<sup>a</sup>see table 2 for descriptive and inferential statistics

<sup>b</sup>H-statistic for Kruskal-Wallis test, d.f. = 2

\* significant at the .05 level

**Table 1. Demographics for gender, age and illness duration across the three treatment groups**

		Mean	SD	95% CI for Mean		Test statistic	p-value
				Lower	Upper		
Gender	Psychology	9 (21.4%) <sup>d</sup>				.179 <sup>c</sup>	.915
	Nutrition	8 (18.2%) <sup>d</sup>					
	Combined	11 (21.2%) <sup>d</sup>					
	Total	28 (20.3%) <sup>d</sup>					
Age	Psychology	42.881	13.986	38.523	47.239	.000 <sup>a</sup>	1.000
	Nutrition	42.864	12.504	39.062	46.665		
	Combined	42.843	11.125	39.714	45.972		
	Total	42.861	12.406	40.765	44.957		
Illness duration	Psychology	8.874	8.252	6.302	11.445	.252 <sup>a</sup>	.778
	Nutrition	10.023	7.375	7.781	12.265		
	Combined	9.625	7.291	7.595	11.655		
	Total	9.523	7.580	8.247	10.800		

**Table 2. Comparisons across time within the primary outcome measures**

		Baseline				3-month follow-up				Comparisons	
		Mean	SD	95% CI for Mean		Mean	SD	95% CI for Mean		z-statistic	p-value
				Lower	Upper			Lower	Upper		
SF-36	Psychology	49.339	22.698	42.266	56.413	59.267	30.346	41.745	76.788	-2.707	.007**
Physical	Nutrition	47.855	26.226	39.882	55.829	46.706	30.744	34.544	58.868	-1.136	.256
Functioning	Combined	45.299	25.479	38.206	52.393	49.288	26.403	39.604	58.973	-1.850	.064
	Total	47.344	24.791	43.171	51.517	50.260	28.818	43.488	57.032	-3.120	.002**
SF-36	Psychology	7.143	15.894	2.190	12.096	46.429	39.048	23.883	68.974	-2.379	.017*
Role	Nutrition	7.574	17.500	2.254	12.895	19.444	20.016	11.526	27.363	-2.907	.004**
limitations	Combined	9.774	21.051	3.914	15.635	22.742	25.161	13.513	31.971	-2.225	.026*
physical	Total	8.272	18.387	5.177	11.367	26.111	28.225	19.479	32.744	-4.354	.001***
SF-36	Psychology	61.548	25.614	53.566	69.530	63.929	29.786	46.731	81.127	-1.196	.232
Bodily pain	Nutrition	55.625	30.242	46.434	64.819	58.889	32.943	45.857	71.921	-1.800	.072
	Combined	53.606	27.019	46.084	61.128	58.629	27.301	48.615	68.643	-1.048	.294
	Total	56.667	27.683	52.007	61.327	59.757	29.649	52.790	66.724	-2.240	.025*
SF-36	Psychology	37.202	21.824	30.402	44.003	59.821	33.318	40.584	79.058	-2.689	.007**
Social	Nutrition	32.671	25.888	24.800	40.541	43.519	33.679	30.196	56.841	-2.476	.013*
functioning	Combined	32.452	24.786	25.551	39.352	41.936	28.604	31.443	52.428	-2.426	.015*
	Total	33.967	24.212	29.892	38.043	46.007	31.805	38.533	53.481	-4.504	.001***
SF-36	Psychology	60.286	19.584	54.183	66.389	74.571	13.276	66.906	82.237	-2.497	.013*
General mental	Nutrition	59.727	19.355	53.843	65.612	64.741	20.548	56.612	72.869	-1.696	.090
health	Combined	58.308	20.948	52.476	64.140	64.129	16.637	58.027	70.232	-.524	.600
	Total	59.362	19.911	56.011	62.714	66.389	17.897	62.183	70.594	-2.665	.008**
SF-36	Psychology	55.554	46.368	41.105	70.004	76.191	33.150	57.051	95.331	-.842	.400

Role	Nutrition	48.482	47.390	34.074	62.890	55.594	38.130	40.510	70.678	-1.788	.074
limitations	Combined	47.780	43.924	35.551	60.008	67.742	32.756	55.727	79.757	-2.313	.021*
emotional	Total	50.370	45.590	42.695	58.044	64.829	35.335	56.526	73.133	-3.159	.002**
SF-36	Psychology	20.714	16.139	15.685	25.743	41.071	20.586	29.186	52.957	-3.066	.002**
Vitality Energy	Nutrition	20.114	14.5670	15.685	24.542	31.111	23.588	21.780	40.442	-2.734	.006**
or Fatigue	Combined	19.039	17.658	14.123	23.955	27.097	19.527	19.934	34.259	-1.558	.119
	Total	19.891	16.159	17.171	22.611	31.319	21.657	26.230	36.409	-4.205	.001***
SF-36	Psychology	37.024	17.945	31.432	42.616	45.714	21.109	33.526	57.903	-2.561	.010*
General health	Nutrition	28.636	15.528	23.915	33.357	36.482	18.903	29.004	43.959	-2.157	.031*
perceptions	Combined	30.962	17.575	26.069	35.854	42.097	21.632	34.162	50.032	-2.423	.015*
	Total	32.065	17.286	29.156	34.975	40.694	20.561	35.863	45.526	-3.996	.001***
MFI	Psychology	15.952	2.845	15.066	16.839	13.786	4.441	11.222	16.350	-2.657	.008**
General	Nutrition	16.977	2.601	16.186	17.768	14.704	4.898	12.766	16.641	-2.548	.011*
Fatigue	Combined	17.327	2.588	16.607	18.047	16.645	2.811	15.614	17.676	-.854	.393
	Total	16.797	2.716	16.340	17.254	15.361	4.136	14.389	16.333	-3.692	.001***
MFI	Psychology	15.929	3.331	14.891	16.966	13.071	4.632	10.397	15.746	-2.810	.005**
Physical	Nutrition	16.727	3.358	15.707	17.748	14.222	4.987	12.249	16.195	-2.791	.005**
Fatigue	Combined	17.615	2.823	16.830	18.401	16.484	3.395	15.239	17.729	-2.364	.018*
	Total	16.819	3.211	16.278	17.359	14.972	4.453	13.926	16.019	-4.591	.001***
MFI	Psychology	13.857	4.112	12.576	15.138	10.643	5.153	7.668	13.618	-2.142	.032*
Reduced	Nutrition	14.136	4.027	12.912	15.361	12.259	5.012	10.277	14.242	-2.164	.030*
Activity	Combined	14.962	3.662	13.942	15.981	14.936	3.777	13.550	16.321	-.070	.944
	Total	14.362	3.921	13.702	15.022	13.097	4.798	11.970	14.225	-2.421	.015*
MFI	Psychology	10.357	4.287	9.021	11.693	7.286	4.214	4.853	9.719	-2.131	.033*
Reduced	Nutrition	10.500	3.474	9.444	11.556	8.963	3.736	7.485	10.441	-1.985	.047*

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<u>Motivation</u>	<u>Combined</u>	<u>11.462</u>	<u>3.153</u>	<u>10.584</u>	<u>12.339</u>	<u>10.774</u>	<u>3.095</u>	<u>9.639</u>	<u>11.910</u>	<u>-1.082</u>	<u>.279</u>
	<u>Total</u>	<u>10.819</u>	<u>3.639</u>	<u>10.206</u>	<u>11.431</u>	<u>9.417</u>	<u>3.767</u>	<u>8.532</u>	<u>10.302</u>	<u>-2.986</u>	<u>.003**</u>
<u>MFI</u>	<u>Psychology</u>	<u>13.524</u>	<u>4.363</u>	<u>12.164</u>	<u>14.883</u>	<u>10.500</u>	<u>4.468</u>	<u>7.920</u>	<u>13.080</u>	<u>-2.950</u>	<u>.003*</u>
<u>Mental Fatigue</u>	<u>Nutrition</u>	<u>13.682</u>	<u>4.328</u>	<u>12.366</u>	<u>14.998</u>	<u>11.926</u>	<u>5.334</u>	<u>9.816</u>	<u>14.036</u>	<u>-2.082</u>	<u>.037*</u>
	<u>Combined</u>	<u>13.846</u>	<u>4.345</u>	<u>12.637</u>	<u>15.056</u>	<u>12.613</u>	<u>3.827</u>	<u>11.209</u>	<u>14.017</u>	<u>-1.586</u>	<u>.113</u>
	<u>Total</u>	<u>13.696</u>	<u>4.315</u>	<u>12.969</u>	<u>14.422</u>	<u>11.944</u>	<u>4.568</u>	<u>10.871</u>	<u>13.018</u>	<u>-3.661</u>	<u>.001***</u>

<sup>a</sup>z-statistic for Wilcoxon Signed-Rank Test

**Table 3. Comparisons across time within the secondary outcome measures (ME/CFS-specific)**

		<u>Baseline</u>				<u>3-month follow-up</u>				<u>Comparisons</u>	
		<u>Mean</u>	<u>SD</u>	<u>95% CI for Mean</u>		<u>Mean</u>	<u>SD</u>	<u>95% CI for Mean</u>		<u>z-statistic</u>	<u>p-value</u>
				<u>Lower</u>	<u>Upper</u>			<u>Lower</u>	<u>Upper</u>		
<u>CDC CFS</u>	<u>Psychology</u>	<u>2.571</u>	<u>3.109</u>	<u>1.603</u>	<u>3.540</u>	<u>1.429</u>	<u>2.278</u>	<u>.114</u>	<u>2.744</u>	<u>-1.365</u>	<u>.172</u>
<u>Sore Throat</u>	<u>Nutrition</u>	<u>3.977</u>	<u>3.776</u>	<u>2.829</u>	<u>5.125</u>	<u>1.741</u>	<u>2.087</u>	<u>.915</u>	<u>2.566</u>	<u>-2.211</u>	<u>.027*</u>
	<u>Combined</u>	<u>3.202</u>	<u>4.494</u>	<u>1.951</u>	<u>4.454</u>	<u>1.904</u>	<u>2.821</u>	<u>.870</u>	<u>2.939</u>	<u>-.804</u>	<u>.422</u>
	<u>Total</u>	<u>3.257</u>	<u>3.898</u>	<u>2.601</u>	<u>3.914</u>	<u>1.750</u>	<u>2.437</u>	<u>1.178</u>	<u>2.323</u>	<u>-2.387</u>	<u>.017*</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>1.976</u>	<u>3.382</u>	<u>.922</u>	<u>3.030</u>	<u>1.786</u>	<u>3.378</u>	<u>-.165</u>	<u>3.736</u>	<u>-.341</u>	<u>.733</u>
<u>Swollen</u>	<u>Nutrition</u>	<u>5.561</u>	<u>6.491</u>	<u>3.587</u>	<u>7.534</u>	<u>5.000</u>	<u>6.760</u>	<u>2.326</u>	<u>7.674</u>	<u>-2.212</u>	<u>.027*</u>
<u>Lymph nodes</u>	<u>Combined</u>	<u>3.462</u>	<u>4.881</u>	<u>2.103</u>	<u>4.820</u>	<u>2.690</u>	<u>4.477</u>	<u>1.0458</u>	<u>4.332</u>	<u>-.725</u>	<u>.468</u>
<u>Glands</u>	<u>Total</u>	<u>3.679</u>	<u>5.250</u>	<u>2.795</u>	<u>4.563</u>	<u>3.380</u>	<u>5.385</u>	<u>2.115</u>	<u>4.646</u>	<u>-1.684</u>	<u>.092</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>2.071</u>	<u>3.249</u>	<u>1.059</u>	<u>3.084</u>	<u>1.643</u>	<u>2.818</u>	<u>.016</u>	<u>3.270</u>	<u>-.730</u>	<u>.465</u>

<a href="#">Diarrhea</a>	<a href="#">Nutrition</a>	<a href="#">2.841</a>	<a href="#">4.832</a>	<a href="#">1.372</a>	<a href="#">4.310</a>	<a href="#">1.444</a>	<a href="#">3.274</a>	<a href="#">.149</a>	<a href="#">2.740</a>	<a href="#">-1.649</a>	<a href="#">.099</a>
	<a href="#">Combined</a>	<a href="#">3.135</a>	<a href="#">3.773</a>	<a href="#">2.084</a>	<a href="#">4.185</a>	<a href="#">1.631</a>	<a href="#">2.483</a>	<a href="#">.720</a>	<a href="#">2.542</a>	<a href="#">-1.996</a>	<a href="#">.046*</a>
	<a href="#">Total</a>	<a href="#">2.717</a>	<a href="#">3.998</a>	<a href="#">2.044</a>	<a href="#">3.390</a>	<a href="#">1.563</a>	<a href="#">2.827</a>	<a href="#">.899</a>	<a href="#">2.228</a>	<a href="#">-2.481</a>	<a href="#">.013*</a>
<a href="#">CDC CFS</a>	<a href="#">Psychology</a>	<a href="#">13.286</a>	<a href="#">6.271</a>	<a href="#">11.331</a>	<a href="#">15.240</a>	<a href="#">11.071</a>	<a href="#">6.673</a>	<a href="#">7.218</a>	<a href="#">14.925</a>	<a href="#">-1.550</a>	<a href="#">.121</a>
<a href="#">Fatigue after exertion</a>	<a href="#">Nutrition</a>	<a href="#">13.722</a>	<a href="#">6.450</a>	<a href="#">11.761</a>	<a href="#">15.682</a>	<a href="#">11.815</a>	<a href="#">7.217</a>	<a href="#">8.960</a>	<a href="#">14.670</a>	<a href="#">-2.209</a>	<a href="#">.027*</a>
	<a href="#">Combined</a>	<a href="#">14.154</a>	<a href="#">6.270</a>	<a href="#">12.408</a>	<a href="#">15.899</a>	<a href="#">11.436</a>	<a href="#">6.275</a>	<a href="#">9.134</a>	<a href="#">13.738</a>	<a href="#">-2.392</a>	<a href="#">.017*</a>
	<a href="#">Total</a>	<a href="#">13.752</a>	<a href="#">6.292</a>	<a href="#">12.693</a>	<a href="#">14.811</a>	<a href="#">11.507</a>	<a href="#">6.629</a>	<a href="#">9.949</a>	<a href="#">13.065</a>	<a href="#">-3.574</a>	<a href="#">.001***</a>
<a href="#">CDC CFS</a>	<a href="#">Psychology</a>	<a href="#">8.286</a>	<a href="#">6.747</a>	<a href="#">6.183</a>	<a href="#">10.388</a>	<a href="#">7.429</a>	<a href="#">6.892</a>	<a href="#">3.450</a>	<a href="#">11.408</a>	<a href="#">-2.145</a>	<a href="#">.032*</a>
<a href="#">Muscle Aches or Muscle Pains</a>	<a href="#">Nutrition</a>	<a href="#">9.091</a>	<a href="#">6.383</a>	<a href="#">7.151</a>	<a href="#">11.031</a>	<a href="#">7.222</a>	<a href="#">6.278</a>	<a href="#">4.739</a>	<a href="#">9.706</a>	<a href="#">-2.901</a>	<a href="#">.004**</a>
	<a href="#">Combined</a>	<a href="#">8.519</a>	<a href="#">6.932</a>	<a href="#">6.589</a>	<a href="#">10.449</a>	<a href="#">6.188</a>	<a href="#">5.528</a>	<a href="#">4.160</a>	<a href="#">8.215</a>	<a href="#">-1.908</a>	<a href="#">.056</a>
	<a href="#">Total</a>	<a href="#">8.630</a>	<a href="#">6.664</a>	<a href="#">7.509</a>	<a href="#">9.752</a>	<a href="#">6.817</a>	<a href="#">6.029</a>	<a href="#">5.400</a>	<a href="#">8.234</a>	<a href="#">-3.995</a>	<a href="#">.001***</a>
<a href="#">CDC CFS</a>	<a href="#">Psychology</a>	<a href="#">3.476</a>	<a href="#">5.334</a>	<a href="#">1.814</a>	<a href="#">5.138</a>	<a href="#">2.786</a>	<a href="#">4.458</a>	<a href="#">.212</a>	<a href="#">5.360</a>	<a href="#">-1.778</a>	<a href="#">.075</a>
<a href="#">Pain In Joints</a>	<a href="#">Nutrition</a>	<a href="#">4.696</a>	<a href="#">5.560</a>	<a href="#">3.006</a>	<a href="#">6.386</a>	<a href="#">3.926</a>	<a href="#">5.099</a>	<a href="#">1.909</a>	<a href="#">5.943</a>	<a href="#">-2.022</a>	<a href="#">.043*</a>
	<a href="#">Combined</a>	<a href="#">5.474</a>	<a href="#">6.386</a>	<a href="#">3.696</a>	<a href="#">7.251</a>	<a href="#">3.010</a>	<a href="#">4.140</a>	<a href="#">1.492</a>	<a href="#">4.528</a>	<a href="#">-1.840</a>	<a href="#">.066</a>
	<a href="#">Total</a>	<a href="#">4.618</a>	<a href="#">5.837</a>	<a href="#">3.635</a>	<a href="#">5.600</a>	<a href="#">3.310</a>	<a href="#">4.543</a>	<a href="#">2.242</a>	<a href="#">4.377</a>	<a href="#">-3.141</a>	<a href="#">.002**</a>
<a href="#">CDC CFS</a>	<a href="#">Psychology</a>	<a href="#">1.238</a>	<a href="#">2.516</a>	<a href="#">.454</a>	<a href="#">2.022</a>	<a href="#">1.643</a>	<a href="#">4.181</a>	<a href="#">-.771</a>	<a href="#">4.057</a>	<a href="#">-.135</a>	<a href="#">.892</a>
<a href="#">Fever</a>	<a href="#">Nutrition</a>	<a href="#">1.394</a>	<a href="#">2.562</a>	<a href="#">.615</a>	<a href="#">2.173</a>	<a href="#">.630</a>	<a href="#">2.041</a>	<a href="#">-.178</a>	<a href="#">1.437</a>	<a href="#">-1.487</a>	<a href="#">.137</a>
	<a href="#">Combined</a>	<a href="#">1.333</a>	<a href="#">3.909</a>	<a href="#">.245</a>	<a href="#">2.421</a>	<a href="#">.378</a>	<a href="#">.709</a>	<a href="#">.118</a>	<a href="#">.638</a>	<a href="#">-1.517</a>	<a href="#">.129</a>
	<a href="#">Total</a>	<a href="#">1.324</a>	<a href="#">3.106</a>	<a href="#">.801</a>	<a href="#">1.846</a>	<a href="#">.718</a>	<a href="#">2.272</a>	<a href="#">.185</a>	<a href="#">1.252</a>	<a href="#">-1.876</a>	<a href="#">.061</a>
<a href="#">CDC CFS</a>	<a href="#">Psychology</a>	<a href="#">3.357</a>	<a href="#">4.637</a>	<a href="#">1.912</a>	<a href="#">4.802</a>	<a href="#">2.571</a>	<a href="#">4.398</a>	<a href="#">.032</a>	<a href="#">5.111</a>	<a href="#">-1.970</a>	<a href="#">.049*</a>
<a href="#">Chills</a>	<a href="#">Nutrition</a>	<a href="#">3.750</a>	<a href="#">3.924</a>	<a href="#">2.557</a>	<a href="#">4.943</a>	<a href="#">2.222</a>	<a href="#">4.098</a>	<a href="#">.601</a>	<a href="#">3.843</a>	<a href="#">-3.401</a>	<a href="#">.001***</a>
	<a href="#">Combined</a>	<a href="#">3.192</a>	<a href="#">4.343</a>	<a href="#">1.983</a>	<a href="#">4.402</a>	<a href="#">1.908</a>	<a href="#">2.797</a>	<a href="#">.882</a>	<a href="#">2.934</a>	<a href="#">-2.049</a>	<a href="#">.040*</a>
	<a href="#">Total</a>	<a href="#">3.420</a>	<a href="#">4.283</a>	<a href="#">2.699</a>	<a href="#">4.141</a>	<a href="#">2.155</a>	<a href="#">3.614</a>	<a href="#">1.306</a>	<a href="#">3.004</a>	<a href="#">-4.206</a>	<a href="#">.001***</a>
<a href="#">CDC CFS</a>	<a href="#">Psychology</a>	<a href="#">12.905</a>	<a href="#">6.792</a>	<a href="#">10.788</a>	<a href="#">15.021</a>	<a href="#">10.643</a>	<a href="#">6.698</a>	<a href="#">6.776</a>	<a href="#">14.510</a>	<a href="#">-.802</a>	<a href="#">.422</a>
<a href="#">UnrefreshingSl</a>	<a href="#">Nutrition</a>	<a href="#">12.250</a>	<a href="#">7.088</a>	<a href="#">10.095</a>	<a href="#">14.405</a>	<a href="#">9.444</a>	<a href="#">7.738</a>	<a href="#">6.384</a>	<a href="#">12.505</a>	<a href="#">-1.421</a>	<a href="#">.155</a>

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<u>cep</u>	<u>Combined</u>	<u>12.154</u>	<u>7.147</u>	<u>10.164</u>	<u>14.143</u>	<u>10.161</u>	<u>7.959</u>	<u>7.242</u>	<u>13.080</u>	<u>-1.513</u>	<u>.130</u>
	<u>Total</u>	<u>12.413</u>	<u>6.978</u>	<u>11.238</u>	<u>13.588</u>	<u>9.986</u>	<u>7.557</u>	<u>8.210</u>	<u>11.762</u>	<u>-2.295</u>	<u>.022*</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>9.286</u>	<u>7.658</u>	<u>6.899</u>	<u>11.672</u>	<u>5.286</u>	<u>4.921</u>	<u>2.444</u>	<u>8.127</u>	<u>-1.738</u>	<u>.082</u>
<u>Sleeping</u>	<u>Nutrition</u>	<u>8.614</u>	<u>7.317</u>	<u>6.389</u>	<u>10.838</u>	<u>9.482</u>	<u>9.200</u>	<u>5.842</u>	<u>13.121</u>	<u>-.190</u>	<u>.849</u>
<u>Problems</u>	<u>Combined</u>	<u>8.904</u>	<u>7.681</u>	<u>6.766</u>	<u>11.042</u>	<u>6.529</u>	<u>6.749</u>	<u>4.053</u>	<u>9.004</u>	<u>-1.794</u>	<u>.073</u>
	<u>Total</u>	<u>8.928</u>	<u>7.509</u>	<u>7.664</u>	<u>10.192</u>	<u>7.394</u>	<u>7.585</u>	<u>5.612</u>	<u>9.177</u>	<u>-1.983</u>	<u>.047*</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>5.262</u>	<u>5.548</u>	<u>3.533</u>	<u>6.991</u>	<u>4.357</u>	<u>3.411</u>	<u>2.388</u>	<u>6.326</u>	<u>-1.200</u>	<u>.230</u>
<u>Headaches</u>	<u>Nutrition</u>	<u>7.646</u>	<u>7.040</u>	<u>5.506</u>	<u>9.786</u>	<u>5.185</u>	<u>6.294</u>	<u>2.695</u>	<u>7.675</u>	<u>-2.084</u>	<u>.037*</u>
	<u>Combined</u>	<u>6.346</u>	<u>5.857</u>	<u>4.715</u>	<u>7.977</u>	<u>4.050</u>	<u>3.527</u>	<u>2.756</u>	<u>5.343</u>	<u>-2.807</u>	<u>.005**</u>
	<u>Total</u>	<u>6.431</u>	<u>6.200</u>	<u>5.387</u>	<u>7.474</u>	<u>4.535</u>	<u>4.708</u>	<u>3.429</u>	<u>5.642</u>	<u>-3.000</u>	<u>.003**</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>6.333</u>	<u>4.996</u>	<u>4.777</u>	<u>7.890</u>	<u>3.500</u>	<u>3.995</u>	<u>1.193</u>	<u>5.807</u>	<u>-1.965</u>	<u>.049*</u>
<u>Memory</u>	<u>Nutrition</u>	<u>9.409</u>	<u>7.183</u>	<u>7.225</u>	<u>11.593</u>	<u>8.667</u>	<u>7.681</u>	<u>5.628</u>	<u>11.705</u>	<u>-.338</u>	<u>.735</u>
<u>Problems</u>	<u>Combined</u>	<u>8.173</u>	<u>7.610</u>	<u>6.055</u>	<u>10.292</u>	<u>6.148</u>	<u>4.905</u>	<u>4.349</u>	<u>7.947</u>	<u>-1.446</u>	<u>.148</u>
	<u>Total</u>	<u>8.007</u>	<u>6.835</u>	<u>6.857</u>	<u>9.158</u>	<u>6.578</u>	<u>6.189</u>	<u>5.123</u>	<u>8.032</u>	<u>-2.053</u>	<u>.040*</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>8.500</u>	<u>6.094</u>	<u>6.601</u>	<u>10.399</u>	<u>5.143</u>	<u>5.559</u>	<u>1.933</u>	<u>8.353</u>	<u>-2.809</u>	<u>.005**</u>
<u>Difficulty</u>	<u>Nutrition</u>	<u>9.822</u>	<u>7.641</u>	<u>7.499</u>	<u>12.145</u>	<u>7.778</u>	<u>6.941</u>	<u>5.032</u>	<u>10.524</u>	<u>-1.196</u>	<u>.232</u>
<u>Concentrating</u>	<u>Combined</u>	<u>9.135</u>	<u>6.942</u>	<u>7.202</u>	<u>11.067</u>	<u>6.507</u>	<u>4.843</u>	<u>4.731</u>	<u>8.283</u>	<u>-1.899</u>	<u>.058</u>
	<u>Total</u>	<u>9.161</u>	<u>6.903</u>	<u>7.999</u>	<u>10.323</u>	<u>6.718</u>	<u>5.844</u>	<u>5.345</u>	<u>8.092</u>	<u>-3.440</u>	<u>.001***</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>3.476</u>	<u>4.845</u>	<u>1.966</u>	<u>4.986</u>	<u>2.286</u>	<u>2.946</u>	<u>.585</u>	<u>3.987</u>	<u>-.213</u>	<u>.832</u>
<u>Nausea</u>	<u>Nutrition</u>	<u>4.769</u>	<u>5.135</u>	<u>3.208</u>	<u>6.330</u>	<u>3.407</u>	<u>5.746</u>	<u>1.134</u>	<u>5.681</u>	<u>-1.686</u>	<u>.092</u>
	<u>Combined</u>	<u>3.327</u>	<u>4.902</u>	<u>1.962</u>	<u>4.692</u>	<u>3.458</u>	<u>3.585</u>	<u>2.144</u>	<u>4.773</u>	<u>-.855</u>	<u>.392</u>
	<u>Total</u>	<u>3.832</u>	<u>4.966</u>	<u>2.996</u>	<u>4.668</u>	<u>3.211</u>	<u>4.396</u>	<u>2.178</u>	<u>4.244</u>	<u>-.584</u>	<u>.559</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>2.548</u>	<u>3.270</u>	<u>1.529</u>	<u>3.567</u>	<u>2.786</u>	<u>4.003</u>	<u>.474</u>	<u>5.097</u>	<u>-.343</u>	<u>.732</u>
<u>Abdominal</u>	<u>Nutrition</u>	<u>5.064</u>	<u>5.165</u>	<u>3.493</u>	<u>6.634</u>	<u>3.593</u>	<u>3.905</u>	<u>2.048</u>	<u>5.137</u>	<u>-1.968</u>	<u>.049*</u>
<u>Pain</u>	<u>Combined</u>	<u>3.750</u>	<u>4.635</u>	<u>2.460</u>	<u>5.041</u>	<u>2.548</u>	<u>2.791</u>	<u>1.524</u>	<u>3.572</u>	<u>-.598</u>	<u>.550</u>

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	<u>Total</u>	<u>3.803</u>	<u>4.535</u>	<u>3.040</u>	<u>4.566</u>	<u>2.986</u>	<u>3.470</u>	<u>2.171</u>	<u>3.801</u>	<u>-1.727</u>	<u>.084</u>
CDC CFS	Psychology	3.524	4.702	2.059	4.989	2.357	2.437	.950	3.764	-.724	.469
Sinus Nasal	Nutrition	5.469	6.476	3.500	7.438	4.889	6.104	2.474	7.304	-1.400	.162
Symptoms	Combined	4.789	6.304	3.034	6.544	3.804	6.710	1.343	6.266	-2.482	.013*
	<u>Total</u>	<u>4.620</u>	<u>5.931</u>	<u>3.622</u>	<u>5.619</u>	<u>3.930</u>	<u>5.882</u>	<u>2.547</u>	<u>5.312</u>	<u>-2.971</u>	<u>.003**</u>
CDC CFS	Psychology	3.000	4.191	1.694	4.306	1.571	2.209	.296	2.847	-1.556	.120
Shortness Of	Nutrition	3.285	4.090	2.026	4.543	2.407	4.060	.801	4.013	-1.849	.064
Breath	Combined	3.392	4.788	2.046	4.739	2.526	3.631	1.194	3.858	-.976	.329
	<u>Total</u>	<u>3.237</u>	<u>4.365</u>	<u>2.497</u>	<u>3.977</u>	<u>2.296</u>	<u>3.554</u>	<u>1.461</u>	<u>3.131</u>	<u>-2.538</u>	<u>.011*</u>
CDC CFS	Psychology	3.429	5.347	1.762	5.095	1.214	2.517	-.239	2.668	-1.973	.049*
Sensitivity To	Nutrition	5.031	6.097	3.177	6.884	4.111	6.198	1.659	6.563	-2.136	.033*
Light	Combined	4.481	6.360	2.710	6.251	3.297	5.557	1.259	5.335	-.787	.431
	<u>Total</u>	<u>4.336</u>	<u>5.975</u>	<u>3.330</u>	<u>5.342</u>	<u>3.197</u>	<u>5.419</u>	<u>1.924</u>	<u>4.471</u>	<u>-2.542</u>	<u>.011*</u>
CDC CFS	Psychology	3.952	3.938	2.725	5.180	1.571	3.228	-.292	3.435	-1.614	.106
Depression	Nutrition	4.477	5.450	2.821	6.134	3.333	4.883	1.402	5.265	-1.584	.113
	Combined	5.077	5.950	3.420	6.734	2.766	3.324	1.547	3.985	-1.304	.192
	<u>Total</u>	<u>4.544</u>	<u>5.230</u>	<u>3.663</u>	<u>5.424</u>	<u>2.747</u>	<u>3.964</u>	<u>1.815</u>	<u>3.678</u>	<u>-2.297</u>	<u>.022*</u>

<sup>a</sup>z-statistic for Wilcoxon Signed-Rank Test

**Table 4. Comparisons across time within the secondary outcome measures (psychological)**

	<u>Baseline</u>				<u>3-month follow-up</u>				<u>Comparisons</u>	
	<u>Mean</u>	<u>SD</u>	<u>95% CI for Mean</u>		<u>Mean</u>	<u>SD</u>	<u>95% CI for Mean</u>		<u>z-statistic</u>	<u>p-value</u>
			<u>Lower</u>	<u>Upper</u>			<u>Lower</u>	<u>Upper</u>		



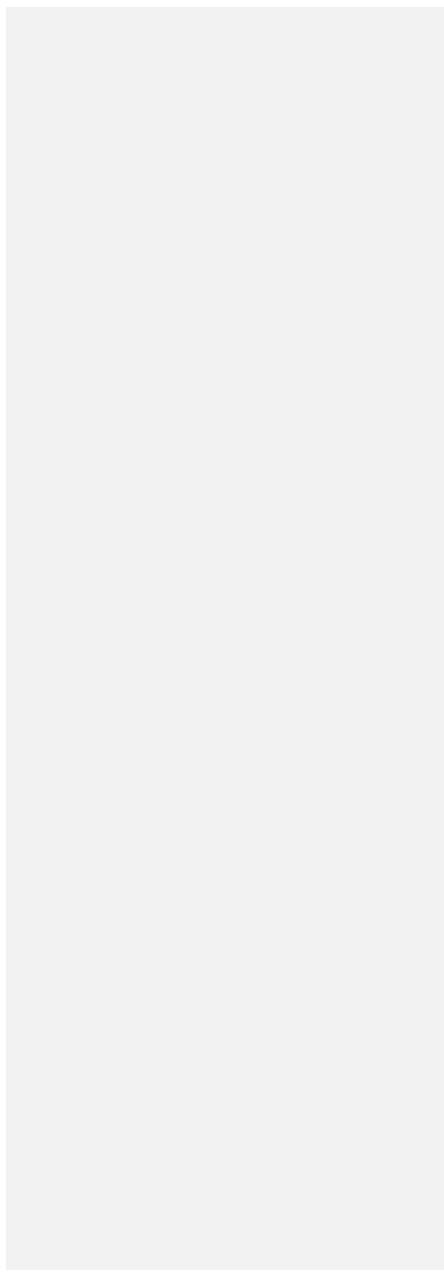
MHLCS	Psychology	.677	.159	.627	.726	.821	.251	.676	.966	-2.983	.003**
Internal	Nutrition	.622	.177	.568	.675	1.193	2.969	.019	2.368	-.687	.492
	Combined	.662	.174	.613	.710	.779	.318	.662	.896	-1.755	.079
	Total	.653	.171	.624	.682	.942	1.822	.514	1.371	-2.962	.003**
MHLCS	Psychology	.368	.156	.320	.417	.351	.152	.263	.439	-2.594	.009**
Chance	Nutrition	.340	.133	.299	.380	.911	3.020	-.284	2.105	-.143	.886
	Combined	.354	.155	.311	.397	.314	.133	.265	.363	-.672	.501
	Total	.354	.148	.329	.379	.545	1.853	.109	.980	-1.552	.121
MHLCS	Psychology	.404	.134	.362	.446	.441	.315	.259	.624	.000	1.000
Powerful	Nutrition	.418	.141	.374	.460	.804	2.244	-.084	1.691	-1.843	.065
Others	Combined	.407	.101	.379	.436	.434	.279	.331	.536	-.577	.564
	Total	.409	.124	.388	.430	.574	1.3880	.248	.900	-1.601	.109
MHLCS	Psychology	.169	.082	.143	.194	.131	.093	.077	.185	-1.122	.262
Doctors	Nutrition	.171	.089	.144	.197	.657	2.668	-.398	1.713	-1.686	.092
	Combined	.191	.147	.150	.232	.153	.070	.128	.179	-1.384	.166
	Total	.178	.112	.159	.196	.338	1.635	-.0462	.722	-2.381	.017*
MHLCS	Psychology	.235	.075	.212	.259	.268	.189	.159	.377	-.118	.906
Other People	Nutrition	.264	.129	.225	.304	.739	2.652	-.311	1.788	-1.697	.090
	Combined	.245	.074	.224	.265	.252	.118	.209	.295	-.213	.831
	Total	.248	.095	.232	.264	.438	1.626	.055	.820	-1.186	.236
CDC CFS	Psychology	94.381	16.836	89.134	99.628	78.571	18.434	67.928	89.215	-3.111	.002**
Maladaptive	Nutrition	96.386	21.946	89.714	103.059	85.259	27.665	74.315	96.203	-3.443	.001***
Stress Index	Combined	98.269	19.165	92.934	103.605	87.484	22.965	79.060	95.908	-2.215	.027*
Scale Score	Total	96.486	19.373	93.225	99.747	84.917	24.004	79.276	90.557	-5.123	.001***

<sup>a</sup>z-statistic for Wilcoxon Signed-Rank Test

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For peer review only



**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\***  
**Checklist for cohort, case-control, and cross-sectional studies (combined)**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Title and Abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Title and Abstract
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1-4
Objectives	3	State specific objectives, including any pre-specified hypotheses	3-4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	4
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	14
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	9-10

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	8-9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	8-9 9
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	6-7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	12-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

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**A preliminary prospective study of nutritional, psychological and combined therapies for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) in a private care setting.**

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2012-001079.R2
Article Type:	Research
Date Submitted by the Author:	19-Jul-2012
Complete List of Authors:	Arroll, Megan; The Optimum Health Clinic, Howard, Alex; The Optimum Health Clinic,
<b>Primary Subject Heading</b>:	Patient-centred medicine
Secondary Subject Heading:	Complementary medicine, Nutrition and metabolism
Keywords:	COMPLEMENTARY MEDICINE, SOCIAL MEDICINE, REHABILITATION MEDICINE

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## Abstract

Background: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a condition ~~characterised~~[characterized](#) by severe and persistent fatigue, neurological disturbances, autonomic and endocrine dysfunctions and sleep difficulties that have a pronounced and significant impact on individuals' lives. Current NICE guidelines within the United Kingdom suggest that this condition should be treated with cognitive ~~behavioural~~[behavioral](#) therapy and/or graded exercise therapy where appropriate. There is currently a lack of evidence base concerning other, more integrative interventions that may be beneficial to those with ME/CFS.

Objectives: This study aimed to evaluate whether three patient-centered treatment modalities of psychology, nutrition and combined treatment, [influenced symptom report measures in those with reduced symptomatology](#) of ME/CFS over a 3-month time period and whether there were significant differences in these changes between groups.

Design and setting: This is a ~~preliminary prospective longitudinal observational~~ study [with one follow-up point](#) conducted at ~~a one~~ private secondary health care facility in London, UK.

Participants: One-hundred and thirty-eight individuals (110 females, 79.7%; 42 participants in psychology, 44 in nutrition and 52 in combined) participated at baseline and 72 participants completed the battery of measures at follow-up (52.17% response rate; 14, 27, 31 participants in each group, respectively).

Outcome measures: Self-report measures of ME/CFS symptoms, functional ability, multidimensional fatigue, perceived control and maladaptive stress.

Results: Baseline comparisons showed those in the combined group had higher levels of fatigue. At follow-up, all groups saw improvements in fatigue, functional physical symptomatology and maladaptive stress; those within the psychology group also experienced a shift in perceived control over time. ~~The psychology group demonstrated a significantly greater change in fatigue and perceived control than the combined group; however, the opposite relationship was observed for headaches.~~



Conclusions: This study provides early evidence that patient-centered techniques for the treatment of ME/CFS may influence appear promising in reducing symptomatology, fatigue, function, perceived control and inappropriate responses to stressors, and increasing function and perceived control. However, these results must be viewed with caution as the allocation to groups was not randomized, there was no control group and the study suffered from high drop-out rates. The need for further studies of integrative treatment with robust designs appears warranted.

## **Summary**

### **Article focus**

- This preliminary prospective observational study investigated three (psychological, nutritional and combined) tailored patient-centered interventions for ME/CFS over time.
- Differences between the reported changes over time between groups were also assessed.

### **Key messages**

- Patient-centered approaches for the management of ME/CFS reduce symptomatology influence symptomatology over time in some individuals with this disorder.
- Self-reported (Functional ability, (-physical and social), are influenced increase with following tailored interventions lasting 3 months-
- Psychological intervention can help individuals to regain a sense of control over their condition-
- This study provides preliminary evidence that tailored psychological, nutritional and Combined interventions may be effective treatments for some people with ME/CFS; however due to the study's methodological limitations, it is important that this potential treatment effect is investigated further in high quality randomized controlled studies.

### **Strengths and limitations of this study**

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- The findings here are an initial step to fill the gap in the extant literature regarding the utility of tailored, multidisciplinary and patient-centered treatments for ME/CFS.
- There is bias in this study as the participants were self-selected in the sense that they chose to attend the clinic and which treatment option they preferred (with advice), i.e. the study was not randomized.
  - There were low retention rates in this study which may constitute a bias in that those who remained in the study may have experienced benefits and those who experienced little or no benefits may have dropped out.

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### **Introduction**

Chronic Fatigue Syndrome or myalgic encephalomyelitis (ME/CFS) is a condition characterized by prolonged and debilitating fatigue, although the exact cause of this disorder is still under debate. Due to the lack of a definitive biological marker, diagnosis is made on the basis of the exclusion of other explanatory conditions. The most widely used case definition by the Centers for Disease Control <sup>1</sup> states that there must be at least six months severe fatigue of new and definite onset, not the result of ongoing exertion, not alleviated by rest and resulting in reduced levels of physical activity. The CDC definition also sets out a series of minor complaints that must accompany the fatigue (cognitive impairment, sore throat, tender cervical or axillary lymph nodes, muscle pain, multi-joint pain, headaches of a new type, pattern or severity at onset, unrefreshing sleep and post-exertion malaise), with individuals needing to have the occurrence of four or more symptoms to be diagnosed with

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7 ME/CFS. Estimates of the prevalence of ME/CFS have been made as low as 3 and as high as  
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9 2,800 per 100,000 <sup>2</sup>.

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12 The most widely researched strategies for alleviating the symptoms of ME/CFS are Cognitive  
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14 Behavior Therapy (CBT) and Graded Exercise Therapy (GET). Two reviews of studies on  
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16 CBT <sup>3,4</sup> found that it significantly improved physical functioning in adult out-patients as  
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18 compared with medical management, counseling, guided support, education and support or  
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20 relaxation. ~~However, the longitudinal evidence for CBT is inconsistent and there is a lack of~~  
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22 ~~evidence with regard to CBT in combination with other treatments~~<sup>4</sup>. Regarding GET, a  
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24 systematic review illustrated that this form of therapy was potentially beneficial for people  
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26 with ME/CFS, especially when combined with a patient education programme<sup>5</sup>. However,  
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28 drop-out rates were high in the GET groups suggesting that individuals with ME/CFS are  
29  
30 adverse to this type of therapy. Recently, a large scale, longitudinal study investigating CBT,  
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32 GET, Adaptive Pacing Therapy (APT) and specialist medical care (SMC) found that CBT  
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34 and GET (when added to SMC) were moderately effective outpatient treatments for this  
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36 patient group as opposed to APT or SMC alone <sup>6</sup>.

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39 Although CBT and GET studies have shown some promising outcomes, there is no known  
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41 cure for ME/CFS. Therefore the National Institute for Health and Clinical Excellence (NICE)  
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43 <sup>7,6</sup> recommends a number of symptom management strategies and interventions aimed at  
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45 helping individuals to cope with their condition and reduce physical deconditioning brought  
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47 about by the illness. Pharmacological interventions are, at times, suggested for patients with  
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49 poor sleep or pain, for instance, low-dose antidepressants, as these have been shown to be  
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51 effective <sup>8-14,13</sup>. However, patient expectations must be realistic as the drugs may help  
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53 elevate mood and psychological outlook but not reduce fatigue and other symptomatology  
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6 associated with ME/CFS<sup>1514</sup>. Numerous drugs such as thyroxin, hydrocortisone and antiviral  
7 agents are not advised by NICE due to contradictory findings<sup>16:1715;16</sup>.  
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12 In terms of function and quality of life management, NICE offers general advice concerning  
13 sleep management, appropriate rest periods, and pacing. Sleep hygiene instruction, together  
14 with pharmacological treatment tailored to the individual patient can be beneficial in  
15 combating fatigue<sup>1817</sup>. Dietary management may also reduce symptomatology for those with  
16 concurrent irritable bowel syndrome (IBS). Management approaches recommended for IBS,  
17 such as diet restriction, are thus also recommended for those with ME/CFS<sup>1918</sup>. Dietary  
18 supplementation has been investigated in relation to ME/CFS. Fatty acids<sup>2019</sup>, folic acid<sup>2120</sup>,  
19 vitamin C<sup>2221</sup>, co-enzyme Q10<sup>2322</sup>, magnesium<sup>2423</sup>, multivitamins<sup>2524</sup> and minerals<sup>2625</sup> have  
20 all been shown to reduce symptomatology in ME/CFS patients. However other studies have  
21 shown conflicting findings with regard to nutritional supplementation, therefore it is perhaps  
22 wise to treat with supplements on a case-by-case basis<sup>27:2826;27</sup>.  
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35 Due to the lack of clear and definitive treatment strategies, individuals often seek out  
36 Complementary and Alternative Medicines (CAM). Although NICE does not recommend the  
37 use of CAM they do acknowledge that many people with ME/CFS use such therapies and  
38 find them beneficial for symptom management. This view is due to the lack of published  
39 evidence for the effectiveness of these treatments. Examples of CAM treatments used by  
40 individuals with ME/CFS include religious healing, massage therapy, relaxation, meditation,  
41 homeopathy, acupuncture, naturopathy and herbal therapies<sup>29:3028;29</sup>; patient satisfaction with  
42 such approaches as CAM has been high, over 80% in some instances<sup>2928</sup>. A recent systematic  
43 review of such interventions identified 70 controlled clinical trials (randomized and non-  
44 randomized) and found that 86% of these studies illustrated at least one positive effect, with  
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7 74% showing a decrease of illness-related symptomatology <sup>3130</sup>. Meditative or mindfulness  
8 approaches warranted further investigation based on these results as did supplement programs  
9 of magnesium, l-carnitine, and S-adenosylmethionine. A subsequent review based solely on  
10 randomized controlled trials (RCTs) of CAM techniques identified 26 such studies and  
11 observed that qigong, massage and tuina (approaches based within Chinese Traditional  
12 Medicine and based upon relaxation and connection with the body) illustrated positive effects  
13 as did supplementation studies utilizing nicotinamide adenine dinucleotide (NADH) and  
14 magnesium <sup>3234</sup>. However, within both reviews it was noted that the methodological quality  
15 of reporting was poor and the sample sizes in these studies were small; hence ability to draw  
16 strong conclusions on the efficacy of CAM methods is limited. Porter et al. (2010) <sup>31</sup> did note  
17 that patient-centered, individualized treatment protocols which include a range of tailored  
18 strategies are a promising area for further investigation for this complex, multi-system illness.  
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### 35 Objectives

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37 There is still much debate and uncertainty regarding the most effective treatment for  
38 ME/CFS. Recent reviews of CAM techniques highlight the need for further exploration of  
39 patient-centered and individually tailored interventions for the alleviation of the condition's  
40 often debilitating and intrusive symptomatology. This study therefore aims to provide  
41 preliminary evidence for the utility ~~evaluate the effectiveness of three of three~~ types of  
42 patient-centered approaches to the management of ME/CFS over time (baseline and follow-  
43 up) offered at a private health-care center in the UK.  
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### 51 Methods

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### Study design and setting

This ~~preliminary prospective a longitudinal observational~~ study ~~which~~ aimed to [explore the effectiveness of evaluate](#) three treatment options offered to individuals with ME/CFS. The research was conducted at one private secondary health care facility. All ~~potential prospective~~ patients of the clinic are first asked to complete a comprehensive symptom profile and medical history, including questions relating to triggering factors, psychology sub-types and structural/biological sub-types (this is distinct from the research data collected). Subsequent to this, every individual receives a 15-minute screening with one of the practitioners ([please note, this was not either of the authors of the current study](#)) who recommends the best course of action for his/her needs; this will be the psychology-related interventions, nutritional advice and support or a combination of the two.

All individuals requesting treatment at the private care setting were offered the opportunity to participate in the study. Those that expressed an interest ([N = 145](#)) were emailed a spreadsheet that contained the questionnaires and asked to complete it at their convenience. Informed consent was obtained prior to the completion of the questionnaires and the study was approved by the University of East London Ethics Committee. Participants were told that they could withdraw from the study at any time and that withdrawal would not affect their care at the clinic. Participants were able to ask questions at any point in the study and no deception was used as the participants were informed of the nature of the research program before they agreed to participate. [Subsequently, participants were requested to complete the questionnaire pack on a second occasion, three months from the baseline measures.](#)

*Psychology*

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7 The clinic offers a 3-month intervention which consists of a combination of Neuro-linguistic  
8 Programming (NLP), Emotional Freedom Technique (EFT), life coaching and  
9 hypnotherapy/self-hypnosis constructed in a manner specific to the needs of those with  
10 ME/CFS. The primary aim of this approach is to reduce the anxiety that is associated with  
11 having a debilitating and unpredictable condition, improve emotional well-being and help  
12 individuals slowly manage and increase their activity within their own limits (i.e. pacing).  
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14 The program is offered as a series of group sessions and the peer support is seen as an  
15 important component of the intervention, which is solidified via the use of moderated online  
16 support forums, narratives of previous clients' experiences and online materials that can be  
17 accessed as often as necessary. In addition to, or as an alternative to this course, individuals  
18 receive a series of one-to-one sessions and for the most severely affected ME/CFS patients,  
19 telephone sessions are arranged and support materials can be accessed in their own homes.

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22 Over the three-month period of this preliminary study, the participants experienced one of  
23 three treatment options. The first option included 13 hours of practitioner contact time in a  
24 mix of group training in person, group telephone conference calls and one-to-one telephone  
25 sessions, the second option was four hours of one-to-one telephone sessions and the final  
26 option was three hours of in person sessions. Participants all had access to various support  
27 materials which included CDs and online resources. The amount of time spent on these was  
28 patient-led, but was in the region of a further six hours. All the practitioners offering this  
29 option are qualified in hypnotherapy, NLP, life coaching and EFT and undergo an intensive  
30 period of training in the clinic's own integrative approach (please see Howard and Arroll <sup>33</sup>  
31 for more details of this approach) and ongoing supervision (individual and group supervision  
32 on a biweekly basis) from the department director, who is the only senior practitioner in the  
33 team.

### *Nutrition*

Tailored nutritional therapy is achieved via one-to-one consultations with individuals. To begin, a very detailed history is taken based upon the information given in the aforementioned symptom profile. Qualified nutritional therapists (who have been given specialist training regarding ME/CFS from the clinic) then suggest tests consistent with symptomatology, for instance the Adrenal Stress Index Test, comprehensive stool analysis/gastro-intestinal function, vitamin & mineral status, etc. Results from these tests are then used to compose an evidence-driven diet and supplement program. As most cases of ME/CFS are complex involving multiple body systems, this process is often iterative and follow-up consultations are necessary to check progress and make alterations to the protocol.

The nutritional therapy program consists of an initial one-hour evaluation (which includes the tailored advice) and follow-up approximately every six weeks; therefore, during the course of the present study, the participants received a minimum of two one-hour sessions with email support for any queries and detailed nutritional guidance. All the nutritional therapists are qualified to diploma level and members of (voluntary) regulatory bodies such as the British Association for Applied Nutrition and Nutritional Therapy (BANT) and the Complementary and Natural Healthcare Council (CNHC). Similar to the psychology department, the nutrition department is led by one senior practitioner who supervises the team with individual and group supervisory arrangements.

### *Combined*



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7 Within the combined program, a multidisciplinary approach is taken with practitioners  
8 discussing the patients in case meetings to ensure that the psychological and nutritional  
9 aspects complement each other in order to achieve the best outcome. [It should be noted that](#)  
10 [the interventions in the combined program are phased-in as it was found that asking](#)  
11 [individuals to engage in numerous therapeutic activities at the same time resulted in high](#)  
12 [drop-out rates.](#)  
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### 20 **[Primary Outcome Measures](#)**

#### 21 *Medical Outcomes Survey Short-Form 36 (SF-36)*

22 This 36-item measure is the short form of the original Medical Outcomes Survey [3432](#) to  
23 measure functional impairment and contains eight sub-sections: 1) physical activity  
24 limitations due to health problems; 2) social activity limitations due to physical or emotional  
25 problems; 3) usual role activity limitations due to physical health problems; 4) bodily pain; 5)  
26 general mental health; 6) role activity limitations due to emotional problems; 7) vitality  
27 (energy and fatigue); and 8) general health perceptions [3432](#). The items are scored so that  
28 higher scores indicate greater functional ability. In terms of the psychometric properties of  
29 this measure, reliability estimates for all sub-scales are good, exceeding a Cronbach's alpha  
30 coefficient value of 0.70 [3533](#). In terms of validity, the SF-36 correlates amply,  $r \geq 0.40$ , with  
31 the frequency and severity of numerous symptoms and general health conditions [36:37,34:35](#).  
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#### 49 *Multidimensional Health Locus of Control Scale (MHLCS)*

50 [Multidimensional Health Locus of Control](#) <sup>36-38</sup> ~~measures perceived control via three distinct~~  
51 ~~sub-scales: 'internal', 'chance' and 'powerful others' which has two dimensions, that of~~  
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~~'doctors' and 'other people'. The instrument contains 18 items in total (six items each for the internal and chance scales and three items for both the powerful others scales) and is scored on a 6 point Likert scale from 'strongly agree' to 'strongly disagree'. Internal reliability of the instrument is good with Cronbach's alpha coefficients ranging from 0.67 for 'powerful others' to 0.77 for 'internal'. The measure correlates positively and significantly with associated scales from Levenson's<sup>39</sup> locus of control measure from which the MHLOC was based upon, which demonstrates good convergent validity<sup>36</sup>.~~

### *Multidimensional Fatigue Inventory (MFI)*

This 20-item measure contains five fatigue dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity<sup>38,40</sup>. Items such as 'I tire easily' are rated on a 5-point scale (1 = yes, that is true; 5 = no, that is not true) with lower scores reflecting higher levels of fatigue. The MFI has good internal consistency with average Cronbach's alpha coefficient equaling 0.84 across the sub-scales. Convergent validity based on a sample of radiotherapy patients found correlations between the sub-scales and a visual analog fatigue scale to be 0.77 for general fatigue, 0.70 for physical fatigue, 0.61 for reduced activity, 0.56 for reduced motivation ( $p < 0.001$ ) to 0.23 for mental fatigue ( $p < 0.01$ )<sup>38,40</sup>.

### Secondary Outcome Measures (ME/CFS-specific)

#### *CDC CFS Symptom Inventory*

CDC CFS Symptom Inventory<sup>39,41</sup> was used to measure specific ME/CFS symptoms and confirm diagnosis. This instrument is based upon the CDC case definition<sup>1</sup> and includes a fatigue item and the eight distinct symptoms are also included in the CDC guidelines with an additional ten associated symptoms. The format of this self-report measure is a six-point scale of perceived frequency (0 = absent, 5 = all the time) and severity (0 = none, 5 = very severe). The psychometric properties of this instrument are good: Cronbach's alpha coefficient = 0.88;

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$r = .74$  convergent validity with the Chalder Fatigue Scale <sup>40,42</sup>;  $r = -.68$  and  $-.87$  convergent validity with the SF-36 'vitality' and 'bodily pain' sub-scales, respectively.

### **Secondary Outcome Measures (psychological)**

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#### *Multidimensional Health Locus of Control Scale (MHLCS)*

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Multidimensional Health Locus of Control <sup>41-43</sup> measures perceived control via three distinct sub-scales: 'internal', 'chance' and 'powerful others' which has two dimensions, that of 'doctors' and 'other people'. The instrument contains 18 items in total (six items each for the 'internal' and 'chance' scales and three items for both the 'powerful others' scales) and is scored on a 6-point Likert scale from 'strongly agree' to 'strongly disagree'. Internal reliability of the instrument is good with Cronbach's alpha coefficients ranging from 0.67 for 'powerful others' to 0.77 for 'internal'. The measure correlates positively and significantly with associated scales from Levenson's <sup>44</sup> locus of control measure from which the MHLOC was based, which demonstrates good convergent validity <sup>41</sup>.

#### *Maladaptive Stress Index*

This 32-item measure contains three sub-scales (cognitive/mood, sleep and ME/CFS symptoms) and was designed specifically for this population <sup>45,43</sup>. Items such as 'I constantly replay or pre-empt situations and conversations' are scored on a 5-point scale where 1 = never true and 5 = always true; higher scores illustrate a greater degree of disturbance.

### **Statistical methods**

The data was initially screened for missing data. Four cases contained substantial amounts of missing data; therefore these were excluded from the analysis (one individual from the nutrition group and three from the combined group). Once this was done, all the variables had

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7 less than 5% missing data, hence mean substitution was carried out in line with guidance <sup>4644</sup> .  
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9 The baseline data was subsequently of the quality for parametric tests, except for the  
10 variables CDC CFS swollen lymph nodes and glands, memory problems, abdominal pain and  
11 depression. However, the follow-up data suffered from high levels of skew and kurtosis  
12 which was not substantially alleviated by data transformation. This violated a key criterion  
13 for parametric testing, that of normality of distribution, so non-parametric tests were selected.  
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15 In addition, as the sample sizes in each individual treatment group were small, the more  
16 conservative non-parametric tests were the preferred choice as even though tests such as  
17 analysis of variance are generally robust against non-normality, this does not hold true with  
18 small sample sizes. ~~For baseline data, One-way analysis of variance tests and Kruskal-~~  
19 ~~Wallis tests (the former for those variables that met the criteria for parametric tests, and the~~  
20 ~~latter that did not) were used to investigate baseline variation difference between groups;~~  
21 ~~Wilcoxon sign rank tests were employed to look for differences over time (baseline and 3-~~  
22 ~~month follow up) and analysis of covariance (ANCOVA) tests were used to account for this~~  
23 ~~variation and test to for differences between the three groups. Kruskal Wallis tests were~~  
24 ~~performed to investigate group differences in measures of change as evaluated by mean~~  
25 ~~change scores, with Bonferroni corrected Mann Whitney tests calculated to identify post hoc~~  
26 ~~differences between groups if the Kruskal Wallis tests were significant. Wilcoxon sign-rank~~  
27 ~~tests were employed to look for differences over time (baseline and 3-month follow-up) and~~  
28 ~~if differences were significant, percentage change was calculated. Please note, as this is an~~  
29 ~~exploratory study with only one time-point and no control group, any significant findings do~~  
30 ~~not infer clinical significance, rather statistical significance, and as such exact p-values are~~  
31 ~~presented.~~  
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## 51 52 53 **Results** 54 55 56 57 58 59 60

## Participants

Of the 145 individuals who expressed an interest in the study, 142 time-one questionnaires were returned, equating to a 97.9% response rate at baseline (two participants from the psychology group and one from the combined group dropped out at this stage). Therefore, excluding the four cases deleted due to insufficient data, 138 ~~One hundred and thirty eight cases were used for baseline analysis; individuals completed the questionnaire battery at time one (excluding the four deleted cases);~~ 42 participants in the psychology group, 44 in the nutrition group and 52 in the combined group. There was no significant association between gender and group ( $\chi^2(2) = 0.179, p = .915 > .05$ ), all groups consisting of approximately one-fifth males (Table 1). There was not a significant difference in age ( $F(2,135) = 0.0010, p = 1.000 > .05$ ); in fact group means for age were near identical at 42.881, 42.864 and 42.843 for psychology, nutrition and combined groups, respectively. There was also a non-significant result for illness duration ( $F(2, 135) = 0.252, p = .778 > .05$ ). Therefore, in terms of demographics, the groups were comparable. With regard to the outcome measures, there were significant differences between the groups in terms of the MFI sub-scale 'general fatigue' ( $F(2, 135) = 3.219, p = .043 < .05$ ), MFI 'physical fatigue' ( $F(2, 135) = 3.343, p = .038 < .05$ ) and the CDC CFS symptom 'swollen lymph nodes and glands' ( $H(2) = 7.161, p = .028 < .05$ ). To investigate the source of these differences, post-hoc tests were conducted (unrelated t-tests for the fatigue variables and Mann-Whitney tests for swollen lymph glands as the former did not meet criteria for parametric tests, all with Bonferroni correction for multiple comparisons). A significant difference was observed between the psychology and combined groups with regards to general fatigue ( $t(92) = -2.449, p = .016 < .05$ ) and physical fatigue ( $t(92) = -2.658, p = .009 < .05$ ) and also between the nutrition and psychology group in terms of the degree of lymph node and gland swelling ( $U = 635.00, p = .009 < .05$ ). Within the fatigue measures, the combined group reported

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7 significantly higher levels of both general and physical fatigued than the psychology group  
8 whereas those undertaking nutritional support stated a higher occurrence of swollen lymph  
9 nodes and glands.  
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#### 12 13 14 *Retention analysis*

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16 Seventy-two of the original 138 participants ([14 participants in the psychology group, 27 in](#)  
17 [the nutrition group and 31 in the combined group](#)) completed the battery of measures at the 3-  
18 month follow-up, [resulting in retention rates of \(52.17% in the study overall, 33.33% in the](#)  
19 [psychology group, 61.36% in the nutrition group and 59.62% in the combined group](#)). To  
20 investigate whether the individuals who did not complete the time-two measures were  
21 significantly different from those at baseline on demographic and outcome measures, a series  
22 of t-tests and Mann-Whitney tests were performed. Those that dropped out of the research  
23 (although still receiving treatment at the clinic) differed significantly in terms of age ( $t(136) =$   
24  $-2.227, p = .028 < .05$ ) and illness duration ( $t(136) = -2.549, p = .012 < .05$ ). Those who  
25 remained in the study were of significantly older age (mean age of those that remained in the  
26 study = 45.056, SD = 11.535; mean age of drop-outs = 40.400, SD = 12.932) and longer  
27 illness duration than those who dropped out (mean age of those that remained in the study =  
28 10.836, SD = 7.383; mean illness duration of drop-outs = 7.571, SD = 7.472). Individuals who  
29 did not remain in the study did not differ significantly in terms of gender ( $\chi^2(2) = 1.222, p =$   
30 [.269 > .05](#)) or any of the outcome measures.  
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#### 45 46 47 Longitudinal data Comparisons within-groups across time

##### 48 49 Primary outcomes

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51 [The following percentage change scores represent statistically significant changes, rather than](#)  
52 [clinically significant shifts, as this was an exploratory study. \(Please see Table 2 for the exact](#)  
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7 p-value for each repeated measures comparison.) In the sample as a whole, there were  
8 improvements in all areas of the SF-36, with a 5.80% improvement in physical functioning, a  
9 63.32% improvement in role limitations due to physical difficulties, a 5.17% improvement in  
10 bodily pain, a 26.17% improvement in social functioning, a 10.58% improvement in role  
11 limitations due to emotional difficulties, a 22.30% improvement in vitality, energy or fatigue  
12 and a 36.49% improvement in general health perception. When looking at the fatigue sub-  
13 scales of the MFI, all five sub-scales showed significant reductions in fatigue; 8.55% in  
14 general fatigue, 10.98% in physical fatigue, 8.81% in reduced activity, 12.96% in reduced  
15 motivation and 12.79% in mental fatigue.

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26 Within the group of individuals who opted for a purely psychological intervention,  
27 improvements were seen in physical functioning (16.75%), role limitations due to physical  
28 problems (84.61%), social functioning (37.81%), general mental health (19.15%), vitality,  
29 energy or fatigue (49.57%) and general health perceptions (19.01%). Also, all the MFI  
30 fatigue scales decreased over a 3-month period, 13.58% in general fatigue, 17.74% in  
31 physical fatigue, 23.20% in reduced activity, 11.42% in reduced motivation and 29.66% in  
32 mental fatigue.

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41 The nutrition group saw improvements in role limitations due to physical problems (61.05%),  
42 social functioning (24.93%), vitality, energy or fatigue (35.35%), and general health  
43 perceptions (29.73%). Once again, all the MFI fatigue scales decreased over a 3-month  
44 period, 13.39% in general fatigue, 15.00% in physical fatigue, 13.28% in reduced activity,  
45 14.64% in reduced motivation and 12.83% in mental fatigue.

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7 In terms of general health as evaluated by the SF-36 measure, the group who received both  
8 psychological and nutritional intervention reported reductions in role limitations due to  
9 physical difficulties (57.02%), social functioning (22.61%), role limitations due to emotional  
10 difficulties (29.47%) and general health perceptions (26.45%). In the combined group, only  
11 one measure of fatigue, that of physical fatigue, saw significant improvements over time  
12 (6.42%).

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20 *Secondary outcomes (ME/CFS-specific)*

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22 Within the CFS Symptom Inventory, there were improvements in occurrence of sore throats  
23 (46.26%), diarrhea (42.47%), fatigue after exertion (16.32%), muscle aches or muscle pains  
24 (21.01%), pain in joints (28.32%) chills (37.00%), unrefreshing sleep (19.55%), sleeping  
25 problems (17.17%), headaches (29.47%), memory problems (17.86%), difficulty  
26 concentrating (26.66%), sinus and nasal symptoms (14.95%), shortness of breath (29.08%),  
27 sensitivity to light (26.26%) and depression (39.55%) in the merged sample. Within those  
28 taking part in the psychology intervention, ratings of muscle aches or muscle pains (10.34%),  
29 chills (23.40%), memory problems (44.73%), difficulty concentrating (39.50%) and  
30 sensitivity to light (64.58%) decreased. In the nutrition group, numerous symptom-related  
31 indices also showed improvements; sore throat (56.23%), swollen lymph glands (10.09%),  
32 fatigue after exertion (13.90%), muscle aches or muscle pains (20.56%), pain in joints  
33 (16.40%), chills (40.74%), headaches (32.19%), abdominal pain (29.05%), and sensitivity to  
34 light (18.28%). Those in the combined group saw significant reductions over the 3-month  
35 interval in diarrhea (47.97%), fatigue after exertion (19.20%), chills (40.23%), headaches  
36 (36.18%) and sinus and nasal symptoms (20.56%). (Please see Table 3 for the descriptive and  
37 inferential statistics associated with these findings and the exact p-value for each repeated  
38 measures comparison.)

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Secondary outcomes (psychological)

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There were no significant differences from time-one to time-two in the MHLCS sub-scale of 'chance', 'powerful others' and 'other people', however the MHLCS did illustrate significant increases in internal locus of control (30.67%) and that of doctors (47.49%) in the sample as a whole. Reductions were also observed in the Maladaptive Stress Response (11.99%) in the entire group. In the psychology group, a significant increase of 17.56% was observed in internal locus of control, a decrease of 4.67% in the perception that chance played an influential part in the individuals' lives and a significant reduction in the Maladaptive Stress Response of 16.75%. No significant differences were found from baseline to follow-up in perceived control in the nutrition group, however the way in which the individuals in this group responded to stress also decreased, by 11.54%. No significant differences were found from baseline to follow-up in perceived control as measured by the MHLCS in the combined treatment group although there was a statistically significant difference in the Maladaptive Stress Response (10.98%). (Please see Table 4 for the descriptive and inferential statistics associated with these findings and the exact p-value for each repeated measures comparison.)

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In the sample as a whole, there were significant differences from baseline to follow up within the internal and doctors sub-scale of the MHLCS and all the CDC-CFS Symptom Inventory items bar swollen lymph nodes and glands, fever and abdominal pain. There were also significant differences in all areas of the SF-36, all the fatigue sub-scales of the MFI with the five sub-scales illustrating significant reductions in fatigue and, finally, reductions were also observed in the Maladaptive Stress Response.

Within the psychology group significant differences were also found in the SF-36 sub-scales 'physical functioning', 'role limitations due to physical problem', 'social functioning',

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7 ~~‘general mental health’, ‘vitality, energy or fatigue’ and ‘general health perceptions’.~~  
8 ~~Regarding perceived control, significant differences were found in internal locus of control~~  
9 ~~and the perception that chance played an influential part in the individuals’ lives. Again, all~~  
10 ~~the MFI fatigue scales saw significant decreases over a 3 month period. Regarding ME/CFS~~  
11 ~~specific symptoms, ratings of muscle aches or muscle pains, chills, memory problems,~~  
12 ~~difficulty concentrating and sensitivity to light differed significantly from baseline to follow-~~  
13 ~~up in the expected direction. There was also a significant reduction in the Maladaptive Stress~~  
14 ~~Response over time.~~

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24 ~~The nutrition group saw significant improvements in role limitations due to physical~~  
25 ~~problems, social functioning, vitality, energy or fatigue and general health perceptions. No~~  
26 ~~significant differences were found from baseline to follow up in perceived control in the~~  
27 ~~nutrition group. Once again, all the MFI fatigue scales decreased over a 3 month period and~~  
28 ~~numerous symptom related indices also showed improvements; sore throat, swollen lymph~~  
29 ~~glands, fatigue after exertion, muscle aches or muscle pains, pain in joints, chills, headaches,~~  
30 ~~abdominal pain and sensitivity to light. The way in which the individuals in this group~~  
31 ~~responded to stress also decreased over the 3 month time period.~~

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41 ~~In terms of general health as evaluated by the SF 36 measure, the group who received both~~  
42 ~~psychological and nutritional intervention reported reductions in role limitations due to~~  
43 ~~physical difficulties, social functioning, role limitations due to emotional difficulties and~~  
44 ~~general health perceptions. No significant differences were found from baseline to follow up~~  
45 ~~in perceived control as measured by the MHLCS in the combined treatment group. Only one~~  
46 ~~measure of fatigue, that of physical fatigue, saw significant improvements over time.~~  
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49 ~~Diarrhea, fatigue after exertion, chills, headaches and sinus and nasal symptoms all illustrated~~  
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significant reductions over the 3 month interval, as did the Maladaptive Stress Response. (See Table 2 for descriptive and inferential statistics associated with these findings and Table 3 for percentage of change over time.)

### Comparisons across groups

With correction for baseline variation, there were no significant differences between the three groups in terms of change scores.

As shown in Table 3, three of the outcome measures differed significantly in terms of change from baseline to follow up, namely the MHLCs 'chance' sub scale ( $H(2) = 7.674, p < .05$ ), the MFI 'general fatigue' sub scale ( $H(2) = 6.790, p < .05$ ) and the CDC-CFS symptom 'headaches' ( $H(2) = 6.625, p < .05$ ). In terms of perceived control and general fatigue, the psychology group differed significantly as compared to the combined group ( $U = 110.500, p < .05$ ) and ( $U = 118.000, p < .05$ ), respectively, with the psychology group seeing a greater change over time as compared to the combined group on both measures. Regarding headaches, the combined group ( $U = 118.000, p < .05$ ) improved significantly more than the psychology group. No other comparisons reached statistical significance with a Bonferroni correction for multiple comparisons.

### Discussion

#### Key results

There was statistically significant (rather than known clinically significant) change over time of numerous measures in all groups investigated. However, this is not to say that these changes were due to the interventions as the design of this study was exploratory, rather than experimental (please see below for a further critique of the design). The psychology group contained the most significant findings, including those concerned with daily functioning,

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7 fatigue, locus of control, the cognitive CDC CFS specific symptoms and the Maladaptive  
8 Stress Response. [These findings appear consistent with outcomes from other psychological](#)  
9 [interventions](#) <sup>3;4;6</sup>. As expected, changes in perceived control were not observed in the  
10 nutrition group as this is not an area that is targeted in this program. However, the more  
11 immune-type symptoms such as sore throat, swollen lymph nodes or glands and pain in joints  
12 did see significant reductions over time as would be envisaged in treatment protocols based  
13 upon nutritional expertise. The group that exhibited the least significant findings was the  
14 combined group and, as noted below, this may be due to the greater general severity [of](#)  
15 [symptoms](#) in this group and the need for a more lengthy intervention. Nevertheless,  
16 considering the small sample sizes in the groups at follow-up, these results are very  
17 promising and warrant further attention. ~~In terms of these preliminary findings, the~~  
18 ~~psychology group performed better with regard to lowering the belief that chance influences~~  
19 ~~the course of the condition. This is an important observation as the unpredictable nature of~~  
20 ~~ME/CFS can be one of the most difficult components for individuals to cope with~~ <sup>45</sup> ~~and~~  
21 ~~helping patients gain an improved sense of control over the illness is of great potential~~  
22 ~~benefit. The psychology group also demonstrated a significantly greater change score in~~  
23 ~~general fatigue as compared with the combined group which may infer that in the short term,~~  
24 ~~guiding individuals through the complex nature of the disorder, helping them to understand it~~  
25 ~~and accept that the condition itself gives rise to stresses and psychological distress may be a~~  
26 ~~good starting point for intervention (i.e. a stepped program could be developed).~~

### 47 Interpretation

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49 As noted previously <sup>31;30</sup> patient-centered, individualized treatment protocols which include a  
50 range of tailored strategies is a favorable direction for dealing with a complex and multi-  
51 system disorder such as ME/CFS. The present study has demonstrated that such interventions  
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7 may be ~~are~~ useful in lowering symptomatology, improving functioning and helping  
8 individuals gain a greater sense of control over their health status. ~~Considering that the~~  
9 ~~options available on the National Health Service, mainly CBT and GET, are often perceived~~  
10 ~~as coping strategies at best, and physically damaging at worst~~<sup>46</sup>; ~~tailored treatments such as~~  
11 ~~described here may be more palatable, and hence effective.~~

### 17 18 **Limitations and Generalisability**

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20 This study ~~was a preliminary study in a naturalistic setting and as such did not have a robust~~  
21 ~~design. There was not~~ ~~did not have a~~ control group ~~and the participants were not randomly~~  
22 ~~assigned to groups, therefore~~ ~~so~~ the results should be treated with caution. ~~In order to~~  
23 ~~ascertain whether the changes in symptom and functional reports were due to the~~  
24 ~~interventions, a randomized control trial should be conducted (RCT). Also, the participants~~  
25 ~~were not randomly assigned to groups as this was a naturalistic, observational study. Also,~~  
26 ~~there was a high drop-out rate from time-one to time-two and this rate differed across groups.~~  
27 ~~The highest drop-out rate was in the psychology group; whilst we cannot be sure why this~~  
28 ~~occurred, it is postulated that the retention was poor in the group as the individuals in the~~  
29 ~~psychology program had more activities to engage in and may have felt overburdened with~~  
30 ~~the research questionnaires in addition to their session and homework (this would not be the~~  
31 ~~case in the combined group as the therapeutic activities are phased-in as mentioned above).~~

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45 In this study, ~~e~~Each individual was guided to appropriate treatment within an initial screening  
46 with clinic staff; therefore the group was dependent on the nature of the individual's  
47 symptoms and their personal choice as the programs on offer were privately funded.

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51 ~~However, as can be seen in the baseline comparisons, the groups did not differ in terms of~~  
52 ~~gender, age, illness duration or the majority of outcome measures.~~ Notably, the groups did  
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7 differ in general and physical fatigue with participants in the combined groups reporting  
8 greater fatigue than those in the psychology group which suggests that this group's general  
9 symptomatology was more severe. The combined group illustrated less ~~change~~improvement  
10 over time compared to the psychology and nutrition groups and it is feasible to infer that  
11 individuals with a greater number and degree of complaints are referred to the combined  
12 group within the clinic. ~~Also, it should be noted that the interventions in the combined~~  
13 ~~program are phased in as it was found that asking individuals to engage in numerous~~  
14 ~~therapeutic activities resulted in high drop out rates. Also, those in the combined group will~~  
15 ~~not experience the intensity of each intervention as this has been demonstrated to result in~~  
16 ~~non-compliance;~~ therefore, changes in outcome measures in this group may not be noted at  
17 an interval of three months ~~for that group~~. Further studies underway presently will investigate  
18 follow-ups at 6- and 12-months to identify whether the findings here are maintained over  
19 time and also whether those with greater symptom severity benefit with a longer intervention.  
20 The results from this study will then inform plans for an RCT of the clinic's practices. As the  
21 participants were self-selected onto these programs, the findings lack generalizability; future  
22 work should sample from the overall ME/CFS population and be randomly-assigned to  
23 groups in order to make valid assumptions regarding the illness-group as a whole.  
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#### 41 **Funding**

42 No external funding was obtained for this research; the work was accomplished in-house at  
43 the clinic in question.  
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#### 51 **Data Sharing**

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7 Dataset available from the corresponding author at [m.a.arroll@sa.uel.ac.uk](mailto:m.a.arroll@sa.uel.ac.uk). Consent was not  
8 obtained for data sharing but the presented data are anonymised and risk of identification is  
9 low.  
10

### 11 12 13 14 **Contributorship**

15 Alex Howard made substantial contributions to the conception and design and acquisition of  
16 data, whilst Megan Arroll made a substantial contribution to the analysis and interpretation of  
17 data. Both authors made a substantial contribution to the drafting of the article and revisions  
18 for the critical review of important intellectual content. Final approval of the version to be  
19 published was also granted by both authors.  
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### 26 27 **Acknowledgements**

28 We would like to thank Tomas Ros for preparing the questionnaire spreadsheet, Niki Gratrix  
29 for helping in setting-up the study and Andy McLellan and Val Duschinsky for proof-reading  
30 and editing.  
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### 36 37 **Competing Interests**

38 Alex Howard is the founder and CEO of The Optimum Health Clinic and Megan Arroll is the  
39 Director of Research at the Optimum Health Clinic, where this study was conducted.  
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## List of abbreviations

ME: myalgic encephalomyelitis

CFS: Chronic Fatigue Syndrome

NICE: National Institute for Health and Clinical Excellence

CBT: Cognitive Behavioral Therapy

GET: Graded Exercise Therapy

[APT: Adaptive Pacing Therapy](#)

[SMC: specialist medical care](#)

CAM: Complementary and Alternative Medicine

NLP: Neuro-linguistic Programming

EFT: Emotional Freedom Technique

SF-36: Medical Outcomes Survey Short-Form 36

MHLCS: Multidimensional Health Locus of Control Scale

MFI: Multidimensional Fatigue Inventory

[RCT: randomized controlled trial](#)

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Table 1. Baseline comparisons of sample demographics and outcome variables

		Mean	SD	95% CI for Mean		Test statistic	p-value
				Lower	Upper		
Gender	Psychology	9 (21.4%) <sup>d</sup>				.179 <sup>e</sup>	.915
	Nutrition	8 (18.2%) <sup>d</sup>					
	Combined	11 (21.2%) <sup>d</sup>					
	Total	28 (20.3%) <sup>d</sup>					
Age	Psychology	42.881	13.986	38.523	47.239	.000 <sup>a</sup>	1.000
	Nutrition	42.864	12.504	39.062	46.665		
	Combined	42.843	11.125	39.714	45.972		
	Total	42.861	12.406	40.765	44.957		
Illness duration	Psychology	8.874	8.252	6.302	11.445	.252 <sup>a</sup>	.778
	Nutrition	10.023	7.375	7.781	12.265		
	Combined	9.625	7.291	7.595	11.655		
	Total	9.523	7.580	8.247	10.800		
SF-36 Physical Functioning	Psychology	49.339	22.698	42.266	56.413	.319 <sup>a</sup>	.727
	Nutrition	47.855	26.226	39.882	55.829		
	Combined	45.299	25.479	38.206	52.393		
	Total	47.344	24.792	43.171	51.517		
SF-36 Role limitations physical	Psychology	7.143	15.894	2.190	12.096	.281 <sup>a</sup>	.755
	Nutrition	7.574	17.500	2.254	12.895		
	Combined	9.774	21.051	3.914	15.635		
	Total	8.272	18.387	5.177	11.367		
SF-36	Psychology	61.548	25.614	53.566	69.530	1.002 <sup>a</sup>	.370

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Bodily pain	Nutrition	55.625	30.242	46.431	64.819		
	Combined	53.606	27.019	46.084	61.128		
	Total	56.667	27.683	52.007	61.327		
SF-36	Psychology	37.202	21.824	30.402	44.003	-.536 <sup>a</sup>	-.586
Social functioning	Nutrition	32.671	25.888	24.800	40.541		
	Combined	32.452	24.786	25.552	39.352		
	Total	33.967	24.212	29.892	38.043		
SF-36 General mental health	Psychology	60.286	19.584	54.183	66.389	-.124 <sup>a</sup>	-.884
	Nutrition	59.727	19.355	53.843	65.612		
	Combined	58.308	20.948	52.476	64.140		
	Total	59.362	19.911	56.011	62.714		
SF-36 Role limitations emotional	Psychology	55.554	46.368	41.104	70.004	-.390 <sup>a</sup>	-.678
	Nutrition	48.482	47.390	34.074	62.890		
	Combined	47.780	43.924	35.551	60.008		
	Total	50.370	45.590	42.695	58.044		
SF-36 Vitality Energy or Fatigue	Psychology	20.714	16.1386	15.685	25.743	-.129 <sup>a</sup>	-.879
	Nutrition	20.114	14.570	15.685	24.542		
	Combined	19.039	17.658	14.123	23.955		
	Total	19.891	16.159	17.171	22.611		
SF-36 General health perceptions	Psychology	37.024	17.945	31.432	42.616	2.769 <sup>a</sup>	-.066
	Nutrition	28.636	15.528	23.915	33.357		
	Combined	30.962	17.575	26.069	35.854		
	Total	32.065	17.286	29.156	34.975		
MHLCs Internal	Psychology	-.677	-.159	-.627	-.726	1.216 <sup>a</sup>	-.300
	Nutrition	-.622	-.177	-.568	-.675		

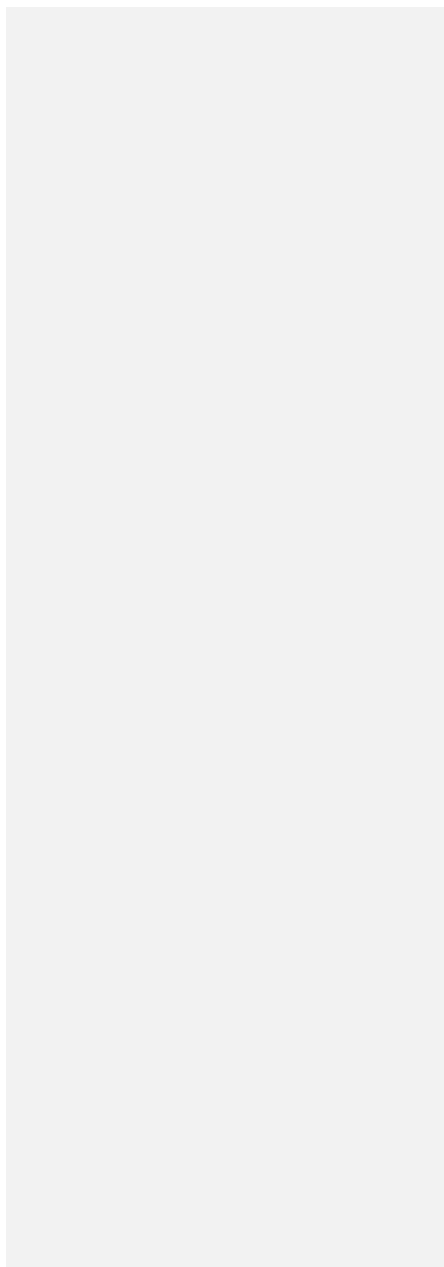
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	Combined	-.662	-.174	-.613	-.710		
	Total	-.653	-.171	-.625	-.682		
MHLCS-Chance	Psychology	-.368	-.156	-.320	-.417	.395 <sup>a</sup>	-.674
	Nutrition	-.340	-.133	-.299	-.380		
	Combined	-.354	-.155	-.311	-.397		
	Total	-.354	-.148	-.329	-.379		
MHLCS-Powerful Others	Psychology	-.404	-.134	-.362	-.446	.119 <sup>a</sup>	-.888
	Nutrition	-.417	-.141	-.374	-.460		
	Combined	-.407	-.101	-.379	-.436		
	Total	-.409	-.124	-.388	-.430		
MHLCS-Doctors	Psychology	-.169	-.082	-.143	-.194	.575 <sup>a</sup>	-.564
	Nutrition	-.171	-.089	-.144	-.197		
	Combined	-.191	-.147	-.150	-.232		
	Total	-.178	-.112	-.159	-.196		
MHLCS-Other People	Psychology	-.235	-.075	-.212	-.259	1.051 <sup>a</sup>	-.352
	Nutrition	-.264	-.129	-.225	-.304		
	Combined	-.245	-.074	-.224	-.265		
	Total	-.248	-.095	-.232	-.264		
MFI-General Fatigue	Psychology	15.952	2.845	15.066	16.839	3.219 <sup>a</sup>	-.043 <sup>*</sup>
	Nutrition	16.977	2.601	16.186	17.768		
	Combined	17.327	2.587	16.607	18.047		
	Total	16.797	2.716	16.340	17.254		
MFI-Physical Fatigue	Psychology	15.929	3.331	14.891	16.966	3.343 <sup>a</sup>	-.038 <sup>*</sup>
	Nutrition	16.727	3.358	15.707	17.748		
	Combined	17.615	2.823	16.830	18.401		

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	Total	16.819	3.211	16.278	17.359		
MFI	Psychology	13.857	4.112	12.576	15.138	1.030 <sup>a</sup>	-.360
Reduced Activity	Nutrition	14.136	4.027	12.912	15.361		
	Combined	14.962	3.662	13.942	15.981		
	Total	14.362	3.921	13.702	15.022		
MFI	Psychology	10.357	4.287	9.021	11.693	1.324 <sup>a</sup>	-.270
Reduced Motivation	Nutrition	10.500	3.474	9.444	11.556		
	Combined	11.462	3.153	10.584	12.339		
	Total	10.819	3.639	10.206	11.431		
MFI	Psychology	13.524	4.363	12.164	14.883	.064 <sup>a</sup>	-.938
Mental Fatigue	Nutrition	13.682	4.328	12.366	14.998		
	Combined	13.846	4.345	12.637	15.056		
	Total	13.696	4.315	12.969	14.422		
CDC-CFS	Psychology	2.571	3.109	1.603	3.540	1.414 <sup>a</sup>	-.247
Sore Throat	Nutrition	3.977	3.776	2.829	5.125		
	Combined	3.202	4.494	1.951	4.454		
	Total	3.257	3.898	2.601	3.914		
CDC-CFS Swollen Lymph nodes Glands	Psychology	1.976	3.382	.922	3.030	7.161 <sup>b</sup>	-.028*
	Nutrition	5.561	6.491	3.587	7.534		
	Combined	3.462	4.881	2.103	4.820		
	Total	3.679	5.250	2.795	4.563		
CDC-CFS	Psychology	2.071	3.249	1.059	3.084	.850 <sup>a</sup>	-.430
Diarrhoea/Diarrhea	Nutrition	2.841	4.832	1.372	4.310		
	Combined	3.135	3.773	2.084	4.185		
	Total	2.717	3.998	2.044	3.390		



CDC-CFS Fatigue after exertion	Psychology	13.286	6.271	11.331	15.240	.219 <sup>a</sup>	-.803
	Nutrition	13.722	6.450	11.761	15.682		
	Combined	14.154	6.270	12.408	15.899		
	Total	13.752	6.292	12.693	14.811		
CDC-CFS Muscle Aches or Muscle Pains	Psychology	8.286	6.747	6.183	10.388	-.166 <sup>a</sup>	-.847
	Nutrition	9.091	6.383	7.151	11.031		
	Combined	8.519	6.932	6.589	10.449		
	Total	8.630	6.664	7.509	9.752		
CDC-CFS Pain In Joints	Psychology	3.476	5.334	1.814	5.138	1.373 <sup>a</sup>	-.257
	Nutrition	4.696	5.560	3.006	6.386		
	Combined	5.474	6.386	3.696	7.251		
	Total	4.618	5.837	3.635	5.600		
CDC-CFS Fever	Psychology	1.238	2.516	-.454	2.022	.027 <sup>a</sup>	-.973
	Nutrition	1.394	2.562	-.615	2.173		
	Combined	1.333	3.909	-.245	2.421		
	Total	1.324	3.106	-.801	1.846		
CDC-CFS Chills	Psychology	3.357	4.637	1.912	4.802	-.206 <sup>a</sup>	-.814
	Nutrition	3.750	3.924	2.557	4.943		
	Combined	3.192	4.343	1.983	4.402		
	Total	3.420	4.283	2.699	4.141		
CDC-CFS Unrefreshing Sleep	Psychology	12.905	6.792	10.788	15.021	.150 <sup>a</sup>	-.861
	Nutrition	12.250	7.088	10.095	14.405		
	Combined	12.154	7.147	10.164	14.144		
	Total	12.413	6.978	11.238	13.588		
CDC-CFS Sleeping	Psychology	9.286	7.658	6.899	11.672	.085 <sup>a</sup>	-.918

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Problems	Nutrition	8.614	7.317	6.389	10.838		
	Combined	8.904	7.684	6.766	11.042		
	Total	8.928	7.509	7.664	10.192		
CDC-CFS Headaches	Psychology	5.262	5.548	3.533	6.991	1.611 <sup>a</sup>	-.203
	Nutrition	7.646	7.040	5.506	9.786		
	Combined	6.346	5.857	4.715	7.977		
	Total	6.431	6.200	5.3871	7.474		
CDC-CFS Memory Problems	Psychology	6.333	4.996	4.777	7.890	3.403 <sup>b</sup>	-.182
	Nutrition	9.409	7.183	7.225	11.593		
	Combined	8.173	7.610	6.055	10.292		
	Total	8.007	6.835	6.857	9.158		
CDC-CFS Difficulty Concentrating	Psychology	8.500	6.094	6.601	10.399	.391 <sup>a</sup>	-.677
	Nutrition	9.822	7.641	7.499	12.145		
	Combined	9.135	6.942	7.202	11.067		
	Total	9.161	6.903	7.999	10.323		
CDC-CFS Nausea	Psychology	3.476	4.845	1.966	4.986	1.162 <sup>a</sup>	-.316
	Nutrition	4.769	5.135	3.208	6.330		
	Combined	3.327	4.902	1.962	4.692		
	Total	3.832	4.966	2.996	4.668		
CDC-CFS Abdominal Pain	Psychology	2.548	3.270	1.529	3.567	5.971 <sup>b</sup>	-.051
	Nutrition	5.064	5.165	3.493	6.634		
	Combined	3.750	4.635	2.460	5.041		
	Total	3.803	4.535	3.040	4.566		
CDC-CFS Sinus Nasal Symptoms	Psychology	3.524	4.702	2.059	4.989	1.192 <sup>a</sup>	-.307
	Nutrition	5.469	6.476	3.500	7.438		

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	Combined	4.789	6.304	3.034	6.544		
	Total	4.620	5.932	3.622	5.619		
CDC-CFS Shortness Of Breath	Psychology	3.000	4.191	1.694	4.306	.095 <sup>a</sup>	.909
	Nutrition	3.285	4.090	2.026	4.543		
	Combined	3.392	4.788	2.046	4.739		
	Total	3.237	4.365	2.497	3.977		
CDC-CFS Sensitivity To Light	Psychology	3.429	5.347	1.762	5.095	.794 <sup>a</sup>	.454
	Nutrition	5.031	6.097	3.177	6.884		
	Combined	4.481	6.360	2.710	6.251		
	Total	4.336	5.975	3.330	5.342		
CDC-CFS Depression	Psychology	3.952	3.938	2.725	5.180	.160 <sup>b</sup>	.923
	Nutrition	4.477	5.450	2.821	6.134		
	Combined	5.077	5.950	3.420	6.734		
	Total	4.544	5.231	3.663	5.424		
CDC-CFS Maladaptive Stress Index Scale Score	Psychology	94.381	16.836	89.134	99.628	.465 <sup>a</sup>	.629
	Nutrition	96.386	21.946	89.714	103.059		
	Combined	98.269	19.165	92.934	103.605		
	Total	96.486	19.373	93.225	99.747		

<sup>a</sup>F-statistic for one-way analysis of variance, d.f.=2,134

<sup>b</sup>H-statistic for Kruskal-Wallis test, d.f.=2

<sup>c</sup> $\chi^2$ -statistic for comparison of nominal level data, d.f.=2

<sup>d</sup>number of males

\* test is significant at the  $p < .05$  level

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Table 2. Outcome variable comparisons across time

		Baseline				3-month follow-up				Comparisons	
		Mean	SD	95% CI for Mean		Mean	SD	95% CI for Mean		z-statistic	p-value
				Lower	Upper			Lower	Upper		
SF-36	Psychology	49.339	22.698	42.266	56.413	59.267	30.346	41.745	76.788	-2.707	.007**
Physical Functioning	Nutrition	47.855	26.226	39.882	55.829	46.706	30.744	34.544	58.868	-1.136	.256
	Combined	45.299	25.479	38.206	52.393	49.288	26.403	39.604	58.973	-1.850	.064
	Total	47.344	24.791	43.171	51.517	50.260	28.818	43.488	57.032	-3.120	.002**
SF-36	Psychology	7.143	15.894	2.190	12.096	46.429	39.048	23.883	68.974	-2.379	.017*
Role limitations physical	Nutrition	7.574	17.500	2.254	12.895	19.444	20.016	11.526	27.363	-2.907	.004**
	Combined	9.774	21.051	3.914	15.635	22.742	25.161	13.513	31.971	-2.225	.026*
	Total	8.272	18.387	5.177	11.367	26.111	28.225	19.479	32.744	-4.354	.001***
SF-36	Psychology	61.548	25.614	53.566	69.530	63.929	29.786	46.731	81.127	-1.196	.232
Bodily pain	Nutrition	55.625	30.242	46.434	64.819	58.889	32.943	45.857	71.921	-1.800	.072
	Combined	53.606	27.019	46.084	61.128	58.629	27.301	48.615	68.643	-1.048	.294
	Total	56.667	27.683	52.007	61.327	59.757	29.649	52.790	66.724	-2.240	.025*
SF-36	Psychology	37.202	21.824	30.402	44.003	59.821	33.318	40.584	79.058	-2.689	.007**
Social functioning	Nutrition	32.671	25.888	24.800	40.541	43.519	33.679	30.196	56.841	-2.476	.013*
	Combined	32.452	24.786	25.551	39.352	41.936	28.604	31.443	52.428	-2.426	.015*
	Total	33.967	24.212	29.892	38.043	46.007	31.805	38.533	53.481	-4.504	.001***
SF-36	Psychology	60.286	19.584	54.183	66.389	74.571	13.276	66.906	82.237	-2.497	.013*
General mental health	Nutrition	59.727	19.355	53.843	65.612	64.741	20.548	56.612	72.869	-1.696	.090
	Combined	58.308	20.948	52.476	64.140	64.129	16.637	58.027	70.232	-.524	.600

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	Total	59.362	19.911	56.011	62.714	66.389	17.897	62.183	70.594	-2.665	.008**
SF-36	Psychology	55.554	46.368	41.105	70.004	76.191	33.150	57.051	95.331	-.842	.400
Role	Nutrition	48.482	47.390	34.074	62.890	55.594	38.130	40.510	70.678	-1.788	.074
limitations	Combined	47.780	43.924	35.551	60.008	67.742	32.756	55.727	79.757	-2.313	.021*
emotional	Total	50.370	45.590	42.695	58.044	64.829	35.335	56.526	73.133	-3.159	.002**
SF-36	Psychology	20.714	16.139	15.685	25.743	41.071	20.586	29.186	52.957	-3.066	.002**
Vitality-Energy	Nutrition	20.114	14.5670	15.685	24.542	31.111	23.588	21.780	40.442	-2.734	.006**
or-Fatigue	Combined	19.039	17.658	14.123	23.955	27.097	19.527	19.934	34.259	-1.558	.119
	Total	19.891	16.159	17.171	22.611	31.319	21.657	26.230	36.409	-4.205	.001***
SF-36	Psychology	37.024	17.945	31.432	42.616	45.714	21.109	33.526	57.903	-2.561	.010*
General health	Nutrition	28.636	15.528	23.915	33.357	36.482	18.903	29.004	43.959	-2.157	.031*
perceptions	Combined	30.962	17.575	26.069	35.854	42.097	21.632	34.162	50.032	-2.423	.015*
	Total	32.065	17.286	29.156	34.975	40.694	20.561	35.863	45.526	-3.996	.001***
MHLCS	Psychology	-.677	-.159	-.627	-.726	-.821	-.251	-.676	-.966	-2.983	.003**
Internal	Nutrition	-.622	-.177	-.568	-.675	-.193	2.969	-.019	2.368	-.687	.492
	Combined	-.662	-.174	-.613	-.710	-.779	-.318	-.662	-.896	-1.755	.079
	Total	-.653	-.171	-.624	-.682	-.942	1.822	-.514	1.371	-2.962	.003**
MHLCS	Psychology	-.368	-.156	-.320	-.417	-.351	-.152	-.263	-.439	-2.594	.009**
Chance	Nutrition	-.340	-.133	-.299	-.380	-.911	3.020	-.284	2.105	-.143	.886
	Combined	-.354	-.155	-.311	-.397	-.314	-.133	-.265	-.363	-.672	.501
	Total	-.354	-.148	-.329	-.379	-.545	1.853	-.109	.980	-1.552	.121
MHLCS	Psychology	-.404	-.134	-.362	-.446	-.441	-.315	-.259	-.624	-.000	1.000
Powerful	Nutrition	-.418	-.141	-.374	-.460	-.804	2.244	-.084	1.691	-1.843	.065
Others	Combined	-.407	-.101	-.379	-.436	-.434	-.279	-.331	-.536	-.577	.564
	Total	-.409	-.124	-.388	-.430	-.574	1.3880	-.248	.900	-1.601	.109

MHLCS	Psychology	-.169	-.082	-.143	-.194	-.131	-.093	-.077	-.185	-.122	-.262
Doctors	Nutrition	-.171	-.089	-.144	-.197	-.657	2.668	-.398	1.713	-.686	-.092
	Combined	-.191	-.147	-.150	-.232	-.153	-.070	-.128	-.179	-.1384	-.166
	Total	-.178	-.112	-.159	-.196	-.338	1.635	-.0462	-.722	-.2381	-.017*
MHLCS	Psychology	-.235	-.075	-.212	-.259	-.268	-.189	-.159	-.377	-.118	-.906
Other People	Nutrition	-.264	-.129	-.225	-.304	-.739	2.652	-.311	1.788	-.697	-.090
	Combined	-.245	-.074	-.224	-.265	-.252	-.118	-.209	-.295	-.213	-.831
	Total	-.248	-.095	-.232	-.264	-.438	1.626	-.055	-.820	-.1186	-.236
MFI	Psychology	15.952	2.845	15.066	16.839	13.786	4.441	11.222	16.350	-2.657	-.008**
General	Nutrition	16.977	2.601	16.186	17.768	14.704	4.898	12.766	16.641	-2.548	-.011*
Fatigue	Combined	17.327	2.588	16.607	18.047	16.645	2.811	15.614	17.676	-.854	-.393
	Total	16.797	2.716	16.340	17.254	15.361	4.136	14.389	16.333	-3.692	-.001***
MFI	Psychology	15.929	3.331	14.891	16.966	13.071	4.632	10.397	15.746	-2.810	-.005**
Physical	Nutrition	16.727	3.358	15.707	17.748	14.222	4.987	12.249	16.195	-2.791	-.005**
Fatigue	Combined	17.615	2.823	16.830	18.401	16.484	3.395	15.239	17.729	-2.364	-.018*
	Total	16.819	3.211	16.278	17.359	14.972	4.453	13.926	16.019	-4.591	-.001***
MFI	Psychology	13.857	4.112	12.576	15.138	10.643	5.153	7.668	13.618	-2.142	-.032*
Reduced	Nutrition	14.136	4.027	12.912	15.361	12.259	5.012	10.277	14.242	-2.164	-.030*
Activity	Combined	14.962	3.662	13.942	15.981	14.936	3.777	13.550	16.321	-.070	-.944
	Total	14.362	3.921	13.702	15.022	13.097	4.798	11.970	14.225	-2.421	-.015*
MFI	Psychology	10.357	4.287	9.021	11.693	7.286	4.214	4.853	9.719	-2.131	-.033*
Reduced	Nutrition	10.500	3.474	9.444	11.556	8.963	3.736	7.485	10.441	-1.985	-.047*
Motivation	Combined	11.462	3.153	10.584	12.339	10.774	3.095	9.639	11.910	-1.082	-.279
	Total	10.819	3.639	10.206	11.431	9.417	3.767	8.532	10.302	-2.986	-.003**
MFI	Psychology	13.524	4.363	12.164	14.883	10.500	4.468	7.920	13.080	-2.950	-.003*

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Mental-Fatigue	Nutrition	13.682	4.328	12.366	14.998	11.926	5.334	9.816	14.036	-2.082	.037*
	Combined	13.846	4.345	12.637	15.056	12.613	3.827	11.209	14.017	-1.586	.113
	Total	13.696	4.315	12.969	14.422	11.944	4.568	10.871	13.018	-3.661	.001***
CDC-CFS	Psychology	2.571	3.109	1.603	3.540	1.429	2.278	.114	2.744	-1.365	.172
Sore-Throat	Nutrition	3.977	3.776	2.829	5.125	1.741	2.087	.915	2.566	-2.211	.027*
	Combined	3.202	4.494	1.951	4.454	1.904	2.821	.870	2.939	-.804	.422
	Total	3.257	3.898	2.601	3.914	1.750	2.437	1.178	2.323	-2.387	.017*
CDC-CFS	Psychology	1.976	3.382	.922	3.030	1.786	3.378	-.165	3.736	-.341	.733
Swollen Lymph-nodes Glands	Nutrition	5.561	6.491	3.587	7.534	5.000	6.760	2.326	7.674	-2.212	.027*
	Combined	3.462	4.881	2.103	4.820	2.690	4.477	1.0458	4.332	-.725	.468
	Total	3.679	5.250	2.795	4.563	3.380	5.385	2.115	4.646	-1.684	.092
CDC-CFS	Psychology	2.071	3.249	1.059	3.084	1.643	2.818	.016	3.270	-.730	.465
DiarrhoeaDiarrhea	Nutrition	2.841	4.832	1.372	4.310	1.444	3.274	.149	2.740	-1.649	.099
	Combined	3.135	3.773	2.084	4.185	1.631	2.483	.720	2.542	-1.996	.046*
	Total	2.717	3.998	2.044	3.390	1.563	2.827	-.899	2.228	-2.481	.013*
CDC-CFS	Psychology	13.286	6.271	11.331	15.240	11.071	6.673	7.218	14.925	-1.550	.121
Fatigue after exertion	Nutrition	13.722	6.450	11.761	15.682	11.815	7.217	8.960	14.670	-2.209	.027*
	Combined	14.154	6.270	12.408	15.899	11.436	6.275	9.134	13.738	-2.392	.017*
	Total	13.752	6.292	12.693	14.811	11.507	6.629	9.949	13.065	-3.574	.001***
CDC-CFS	Psychology	8.286	6.747	6.183	10.388	7.429	6.892	3.450	11.408	-2.145	.032*
Muscle-Aches or-Muscle Pains	Nutrition	9.091	6.383	7.151	11.031	7.222	6.278	4.739	9.706	-2.901	.004**
	Combined	8.519	6.932	6.589	10.449	6.188	5.528	4.160	8.215	-1.908	.056
	Total	8.630	6.664	7.509	9.752	6.817	6.029	5.400	8.234	-3.995	.001***
CDC-CFS	Psychology	3.476	5.334	1.814	5.138	2.786	4.458	.212	5.360	-1.778	.075
Pain-In-Joints	Nutrition	4.696	5.560	3.006	6.386	3.926	5.099	1.909	5.943	-2.022	.043*

	Combined	5.474	6.386	3.696	7.251	3.010	4.140	1.492	4.528	-1.840	.066
	Total	4.618	5.837	3.635	5.600	3.310	4.543	2.242	4.377	-3.141	.002**
CDC-CFS	Psychology	1.238	2.516	.454	2.022	1.643	4.181	-.771	4.057	-.135	.892
Fever	Nutrition	1.394	2.562	-.615	2.173	-.630	2.041	-.178	1.437	-1.487	-.137
	Combined	1.333	3.909	-.245	2.421	-.378	.709	-.118	.638	-1.517	-.129
	Total	1.324	3.106	-.801	1.846	-.718	2.272	-.185	1.252	-1.876	-.061
CDC-CFS	Psychology	3.357	4.637	1.912	4.802	2.571	4.398	.032	5.111	-1.970	.049*
Chills	Nutrition	3.750	3.924	2.557	4.943	2.222	4.098	-.601	3.843	-3.401	.001***
	Combined	3.192	4.343	1.983	4.402	1.908	2.797	-.882	2.934	-2.049	.040*
	Total	3.420	4.283	2.699	4.141	2.155	3.614	-1.306	3.004	-4.206	.001***
CDC-CFS	Psychology	12.905	6.792	10.788	15.021	10.643	6.698	6.776	14.510	-.802	.422
Unrefreshing	Nutrition	12.250	7.088	10.095	14.405	9.444	7.738	6.384	12.505	-1.421	.155
Sleep	Combined	12.154	7.147	10.164	14.143	10.161	7.959	7.242	13.080	-1.513	.130
	Total	12.413	6.978	11.238	13.588	9.986	7.557	8.210	11.762	-2.295	.022*
CDC-CFS	Psychology	9.286	7.658	6.899	11.672	5.286	4.921	2.444	8.127	-1.738	.082
Sleeping	Nutrition	8.614	7.317	6.389	10.838	9.482	9.200	5.842	13.121	-.190	.849
Problems	Combined	8.904	7.681	6.766	11.042	6.529	6.749	4.053	9.004	-1.794	.073
	Total	8.928	7.509	7.664	10.192	7.394	7.585	5.612	9.177	-1.983	.047*
CDC-CFS	Psychology	5.262	5.548	3.533	6.991	4.357	3.411	2.388	6.326	-1.200	.230
Headaches	Nutrition	7.646	7.040	5.506	9.786	5.185	6.294	2.695	7.675	-2.084	.037*
	Combined	6.346	5.857	4.715	7.977	4.050	3.527	2.756	5.343	-2.807	.005**
	Total	6.431	6.200	5.387	7.474	4.535	4.708	3.429	5.642	-3.000	.003**
CDC-CFS	Psychology	6.333	4.996	4.777	7.890	3.500	3.995	1.193	5.807	-1.965	.049*
Memory	Nutrition	9.409	7.183	7.225	11.593	8.667	7.681	5.628	11.705	-.338	.735
Problems	Combined	8.173	7.610	6.055	10.292	6.148	4.905	4.349	7.947	-1.446	.148



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	Total	8.007	6.835	6.857	9.158	6.578	6.189	5.123	8.032	-2.053	.040*
CDC-CFS	Psychology	8.500	6.094	6.601	10.399	5.143	5.559	1.933	8.353	-2.809	.005**
Difficulty	Nutrition	9.822	7.641	7.499	12.145	7.778	6.941	5.032	10.524	-1.196	.232
Concentrating	Combined	9.135	6.942	7.202	11.067	6.507	4.843	4.731	8.283	-1.899	.058
	Total	9.161	6.903	7.999	10.323	6.718	5.844	5.345	8.092	-3.440	.001***
CDC-CFS	Psychology	3.476	4.845	1.966	4.986	2.286	2.946	.585	3.987	-.213	.832
Nausea	Nutrition	4.769	5.135	3.208	6.330	3.407	5.746	1.134	5.681	-1.686	.092
	Combined	3.327	4.902	1.962	4.692	3.458	3.585	2.144	4.773	-.855	.392
	Total	3.832	4.966	2.996	4.668	3.211	4.396	2.178	4.244	-.584	.559
CDC-CFS	Psychology	2.548	3.270	1.529	3.567	2.786	4.003	-.474	5.097	-.343	.732
Abdominal	Nutrition	5.064	5.165	3.493	6.634	3.593	3.905	2.048	5.137	-1.968	.049*
Pain	Combined	3.750	4.635	2.460	5.041	2.548	2.791	1.524	3.572	-.598	.550
	Total	3.803	4.535	3.040	4.566	2.986	3.470	2.171	3.801	-1.727	.084
CDC-CFS	Psychology	3.524	4.702	2.059	4.989	2.357	2.437	.950	3.764	-.724	.469
Sinus-Nasal	Nutrition	5.469	6.476	3.500	7.438	4.889	6.104	2.474	7.304	-1.400	.162
Symptoms	Combined	4.789	6.304	3.034	6.544	3.804	6.710	1.343	6.266	-2.482	.013*
	Total	4.620	5.931	3.622	5.619	3.930	5.882	2.547	5.312	-2.971	.003**
CDC-CFS	Psychology	3.000	4.191	1.694	4.306	1.571	2.209	.296	2.847	-1.556	.120
Shortness-Of	Nutrition	3.285	4.090	2.026	4.543	2.407	4.060	.801	4.013	-1.849	.064
Breath	Combined	3.392	4.788	2.046	4.739	2.526	3.631	1.194	3.858	-.976	.329
	Total	3.237	4.365	2.497	3.977	2.296	3.554	1.461	3.131	-2.538	.011*
CDC-CFS	Psychology	3.429	5.347	1.762	5.095	1.214	2.517	-.239	2.668	-1.973	.049*
Sensitivity-To	Nutrition	5.031	6.097	3.177	6.884	4.111	6.198	1.659	6.563	-2.136	.033*
Light	Combined	4.481	6.360	2.710	6.251	3.297	5.557	1.259	5.335	-.787	.431
	Total	4.336	5.975	3.330	5.342	3.197	5.419	1.924	4.471	-2.542	.011*

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CDC-CFS	Psychology	3.952	3.938	2.725	5.180	1.571	3.228	-.292	3.435	-1.614	-.106
Depression	Nutrition	4.477	5.450	2.821	6.134	3.333	4.883	1.402	5.265	-1.584	-.113
	Combined	5.077	5.950	3.420	6.734	2.766	3.324	1.547	3.985	-1.304	-.192
	Total	4.544	5.230	3.663	5.424	2.747	3.964	1.815	3.678	-2.297	.022*
CDC-CFS	Psychology	94.381	16.836	89.134	99.628	78.571	18.434	67.928	89.215	-3.111	.002**
Maladaptive	Nutrition	96.386	21.946	89.714	103.059	85.259	27.665	74.315	96.203	-3.443	.001***
Stress-Index	Combined	98.269	19.165	92.934	103.605	87.484	22.965	79.060	95.908	-2.215	.027*
Scale-Score	Total	96.486	19.373	93.225	99.747	84.917	24.004	79.276	90.557	-5.123	.001***

\*z-statistic for Wilcoxon Signed-Rank Test

Table 3. Change score comparisons between intervention groups

		% change over time for sig. results <sup>a</sup>	Mean	Std. Deviation	Std. Error	95% CI for Mean		H <sup>b</sup>	p-value
						Lower	Upper		
SF-36 Physical Functioning	Psychology	16.75	-13.629	14.990	4.006	-22.285	-4.974	3.215	.200
	Nutrition		-.407	19.967	3.843	-8.306	7.492		
	Combined		-6.813	18.242	3.276	-13.505	-.122		
	Total	5.80	-5.736	18.744	2.209	-10.141	-1.332		
SF-36	Psychology	84.61	-33.929	39.960	10.680	-57.001	-10.856	1.558	.459

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Role limitations physical	Nutrition	61.05	-14.509	21.005	4.042	-22.818	-6.199		
	Combined	57.02	-13.871	31.457	5.650	-25.409	-2.333		
	Total	63.32	-18.010	30.564	3.602	-25.192	-10.828		
SF-36	Psychology		-6.071	15.588	4.166	-15.072	2.929	.163	-.922
Bodily pain	Nutrition		-6.574	18.800	3.618	-14.011	.863		
	Combined		-3.387	25.532	4.586	-12.752	5.978		
	Total	5.17	-5.104	21.252	2.505	-10.098	-1.10		
SF-36	Psychology	37.81	-24.107	24.741	6.612	-38.392	-9.822	3.301	-.192
Social functioning	Nutrition	24.93	-10.648	20.423	3.931	-18.727	-2.569		
	Combined	22.60	-11.290	24.013	4.313	-20.098	-2.482		
	Total	26.17	-13.542	23.149	2.728	-18.981	-8.102		
SF-36	Psychology	19.15	-12.000	14.294	3.820	-20.253	-3.747	4.404	-.111
General mental health	Nutrition		-3.259	15.963	3.072	-9.574	3.056		
	Combined		-.645	16.911	3.037	-6.848	5.558		
	Total	10.58	-3.833	16.409	1.934	-7.689	-.022		
SF-36	Psychology		-9.527	49.664	13.273	-38.202	19.148	-.573	-.751
Role limitations emotional	Nutrition		-18.561	55.759	10.731	-40.618	3.497		
	Combined	29.47	-18.284	52.240	9.383	-37.446	.878		
	Total	10.58	-16.685	52.496	6.187	-29.021	-4.349		
SF-36	Psychology	49.57	-17.500	15.902	4.250	-26.682	-8.318	4.988	-.083
Vitality Energy or Fatigue	Nutrition	35.35	-11.482	19.206	3.696	-19.079	-3.884		
	Combined		-6.129	17.688	3.177	-12.617	.359		
	Total	22.30	-10.347	18.219	2.147	-14.628	-6.066		
SF-36	Psychology	19.01	-11.429	14.335	3.831	-19.705	-3.152	-.627	-.731
General health	Nutrition	29.73	-6.852	15.201	2.925	-12.865	-.839		

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perceptions	Combined	26.45	-10.161	22.154	3.97	-18.288	-2.035		
	Total	36.49	-9.167	18.251	2.151	-13.455	-4.878		
MHLCS Internal	Psychology	17.56	-.146	-.203	-.054	-.263	-.029	3.402	-.183
	Nutrition		-.573	3.028	-.583	-1.771	-.625		
	Combined		-.106	-.315	-.057	-.222	.010		
	Total	30.67	-.289	1.859	-.219	-.726	-.148		
MHLCS Chance	Psychology	4.67	.077	-.098	-.026	.021	-.134	7.674	.022*
	Nutrition		-.570	3.019	-.581	-1.765	-.624		
	Combined		-.001	-.081	-.015	-.029	.031		
	Total		-.198	1.852	-.218	-.633	-.237		
MHLCS Powerful Others	Psychology		-.054	-.284	-.076	-.218	-.109	1.571	-.456
	Nutrition		-.375	2.282	-.439	-1.277	-.528		
	Combined		-.030	-.277	-.050	-.132	.072		
	Total		-.164	1.408	-.166	-.495	-.167		
MHLCS Doctors	Psychology		.020	-.058	-.0155	-.014	-.053	0.076	-.963
	Nutrition		-.492	2.678	-.515	-1.551	-.568		
	Combined		-.057	-.199	-.036	-.016	-.130		
	Total	47.49	-.156	1.647	-.194	-.543	-.231		
MHLCS Other People	Psychology		-.032	-.166	-.044	-.128	-.064	2.479	-.290
	Nutrition		-.446	2.692	-.518	-1.510	-.619		
	Combined		-.012	-.096	-.017	-.047	.023		
	Total		-.178	1.645	-.193	-.565	-.208		

MFI	Psychology	13.58	2.571	2.766	.739	.975	4.168	6.790	.034*
General Fatigue	Nutrition	13.39	2.074	3.842	.740	.554	3.594		
	Combined		.419	2.233	.401	-.400	1.238		
	Total	8.55	1.458	3.126	.368	.724	2.193		
MFI	Psychology	17.74	2.857	2.797	.748	1.242	4.472	3.038	.219
Physical Fatigue	Nutrition	15.00	2.444	4.371	.841	.716	4.173		
	Combined	6.42	1.290	2.735	.491	.287	2.294		
	Total	10.98	2.028	3.468	.409	1.213	2.843		
MFI	Psychology	23.20	1.857	2.932	.784	.165	3.550	1.734	.420
Reduced Activity	Nutrition	13.28	1.148	2.685	.517	.086	2.210		
	Combined		.645	3.189	.572	-.525	1.815		
	Total	8.81	1.069	2.952	.348	.376	1.763		
MFI	Psychology	11.42	2.500	3.502	.936	.478	4.522	5.171	.075
Reduced Motivation	Nutrition	14.64	1.593	3.511	.676	.204	2.982		
	Combined		.129	3.471	.624	-1.144	1.402		
	Total	12.96	1.139	3.570	.421	.300	1.978		
MFI	Psychology	29.66	3.571	3.056	.817	1.807	5.336	4.551	.103
Mental Fatigue	Nutrition	12.83	1.519	3.631	.699	.082	2.955		
	Combined		1.161	4.267	.766	-.404	2.726		
	Total	12.79	1.764	3.880	.457	.852	2.676		
CDC-CFS	Psychology		1.429	3.736	.998	.728	3.586	1.298	.523
Sore Throat	Nutrition	56.23	1.185	2.661	.512	.133	2.238		
	Combined		.500	4.591	.825	-1.184	2.184		
	Total	46.26	.937	3.769	.444	.052	1.823		
CDC-CFS Swollen Lymph	Psychology		-.143	2.932	.784	-1.835	1.550	0.462	.794

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Lymph Nodes-Glands	Nutrition	10.09	1.247	2.700	-.520	-.179	2.316		
	Combined		-.794	6.549	1.176	-1.608	3.197		
	Total		-.782	4.756	-.560	-.336	1.900		
CDC-CFS Diarrhoea/Diarrhea	Psychology		-.286	1.490	-.398	-1.146	-.575	3.619	-.164
	Nutrition		-.926	2.868	-.552	-.209	2.060		
	Combined	47.97	1.272	3.789	-.681	-.118	2.662		
	Total	42.47	-.839	3.134	-.369	-.103	1.576		
CDC-CFS Fatigue after exertion	Psychology		2.286	4.811	1.286	-.492	5.063	0.379	-.827
	Nutrition	13.90	2.593	5.507	1.060	-.414	4.771		
	Combined	19.20	2.532	5.578	1.002	-.486	4.578		
	Total	16.32	2.507	5.339	-.629	1.252	3.761		
CDC-CFS Muscle Aches or Muscle Pains	Psychology	10.34	2.500	4.034	1.078	-.171	4.829	0.469	-.791
	Nutrition	20.56	2.333	3.637	-.700	-.894	3.772		
	Combined		2.070	5.335	-.958	-.113	4.027		
	Total	21.01	2.253	4.459	-.526	1.205	3.300		
CDC-CFS Pain In Joints	Psychology		1.857	4.036	1.079	-.473	4.187	0.054	-.973
	Nutrition	16.40	1.393	3.721	-.716	-.079	2.865		
	Combined		1.978	5.622	1.010	-.084	4.040		
	Total	28.32	1.735	4.634	-.546	-.646	2.824		
CDC-CFS Fever	Psychology		-.214	1.968	-.526	-1.351	-.922	0.399	-.819
	Nutrition		-.604	2.311	-.445	-.310	1.519		
	Combined		1.245	4.816	-.865	-.521	3.012		
	Total		-.721	3.573	-.421	-.118	1.561		
CDC-CFS Chills	Psychology	23.40	1.571	2.738	-.732	-.009	3.152	1.517	-.468
	Nutrition	40.74	2.148	3.097	-.596	-.923	3.373		

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	Combined	40.23	1.447	3.986	.716	-.015	2.909		
	Total	37.00	1.734	3.421	-.403	-.930	2.538		
CDC-CFS Unrefreshing Sleep	Psychology		1.857	6.803	1.818	-2.071	5.785	0.160	.948
	Nutrition		2.148	6.904	1.329	-.583	4.879		
	Combined		1.581	5.726	1.029	-.520	3.681		
	Total	19.55	1.847	6.3123	-.744	-.364	3.331		
CDC-CFS Sleeping Problems	Psychology		2.786	5.352	1.430	-.304	5.876	3.218	.200
	Nutrition		-.222	5.139	-.989	-2.255	1.811		
	Combined		1.762	4.871	-.875	-.025	3.548		
	Total	17.17	1.217	5.133	-.605	-.011	2.423		
CDC-CFS Headaches	Psychology		-.7143	2.091	-.559	-1.922	-.493	6.625	-.036*
	Nutrition	32.19	1.572	3.507	-.675	-.184	2.959		
	Combined	36.18	2.467	4.944	-.888	-.653	4.280		
	Total	29.32	1.512	4.124	-.486	-.543	2.482		
CDC-CFS Memory Problems	Psychology	44.73	2.857	4.655	1.244	-.169	5.545	2.316	-.314
	Nutrition		-.111	4.925	-.947	-2.059	1.837		
	Combined		1.949	6.011	1.080	-.256	4.154		
	Total	17.86	1.353	5.435	-.641	-.076	2.630		
CDC-CFS Difficulty Concentrating	Psychology	39.50	4.643	4.534	1.212	2.025	7.261	5.945	-.051
	Nutrition		-.815	4.359	-.839	-.910	2.539		
	Combined		2.170	5.877	1.056	-.015	4.326		
	Total	26.66	2.143	5.217	-.615	-.917	3.369		
CDC-CFS Nausea	Psychology		-.143	2.770	-.740	-1.456	1.742	4.773	-.092
	Nutrition		-.660	2.667	-.513	-.395	1.716		
	Combined		-.251	4.468	-.803	-1.388	1.890		

	Total		.384	3.535	.417	-.447	1.214		
CDC-CFS-Abdominal Pain	Psychology		-.286	1.729	-.462	-.713	1.284	1.082	-.582
	Nutrition	29.05	-.882	2.165	-.417	-.025	1.738		
	Combined		-.839	4.390	-.789	-.771	2.449		
	Total		-.747	3.234	-.381	-.013	1.507		
CDC-CFS-Sinus-Nasal Symptoms	Psychology		-.929	3.125	-.835	-.876	2.733	1.255	-.534
	Nutrition		1.060	4.193	-.807	-.599	2.719		
	Combined	20.56	1.906	5.923	1.063	-.267	4.078		
	Total	14.95	1.399	4.822	-.568	-.266	2.532		
CDC-CFS-Shortness-Of-Breath	Psychology		1.500	3.459	-.924	-.497	3.497	0.707	-.702
	Nutrition	18.28	-.779	2.057	-.403	-.052	1.609		
	Combined		-.690	3.972	-.725	-.793	2.173		
	Total	29.08	-.885	3.243	-.388	-.112	1.658		
CDC-CFS-Sensitivity-To-Light	Psychology	64.58	1.429	2.472	-.661	-.001	2.856	0.939	-.625
	Nutrition		1.568	3.764	-.725	-.079	3.057		
	Combined		-.961	5.178	-.930	-.938	2.860		
	Total	26.26	1.280	4.209	-.496	-.291	2.269		
CDC-CFS-Depression	Psychology		1.429	3.502	-.936	-.593	3.451	0.490	-.783
	Nutrition		-.704	3.268	-.629	-.589	1.996		
	Combined		1.363	5.345	-.960	-.598	3.323		
	Total	39.55	1.129	4.282	-.505	-.122	2.135		
CDC-CFS-Maladaptive Stress-Index-Scale-Score	Psychology	16.75	16.286	13.234	3.537	8.645	23.927	4.379	-.112
	Nutrition	11.54	12.815	17.802	3.426	5.772	19.857		
	Combined	10.98	9.613	26.424	4.746	-.080	19.305		
	Total	11.99	12.111	21.201	2.499	7.129	17.093		



<sup>a</sup>see table 2 for descriptive and inferential statistics

<sup>b</sup>H-statistic for Kruskal-Wallis test, d.f. = 2

\* significant at the .05 level

**Table 1. Demographics for gender, age and illness duration across the three treatment groups**

		Mean	SD	95% CI for Mean		Test statistic	p-value
				Lower	Upper		
Gender	Psychology	9 (21.4%) <sup>d</sup>				.179 <sup>c</sup>	.915
	Nutrition	8 (18.2%) <sup>d</sup>					
	Combined	11 (21.2%) <sup>d</sup>					
	Total	28 (20.3%) <sup>d</sup>					
Age	Psychology	42.881	13.986	38.523	47.239	.000 <sup>a</sup>	1.000
	Nutrition	42.864	12.504	39.062	46.665		
	Combined	42.843	11.125	39.714	45.972		
	Total	42.861	12.406	40.765	44.957		
Illness duration	Psychology	8.874	8.252	6.302	11.445	.252 <sup>a</sup>	.778
	Nutrition	10.023	7.375	7.781	12.265		
	Combined	9.625	7.291	7.595	11.655		
	Total	9.523	7.580	8.247	10.800		

**Table 2. Comparisons across time within the primary outcome measures**

		Baseline				3-month follow-up				Comparisons	
		Mean	SD	95% CI for Mean		Mean	SD	95% CI for Mean		z-statistic	p-value
				Lower	Upper			Lower	Upper		
SF-36	Psychology	49.339	22.698	42.266	56.413	59.267	30.346	41.745	76.788	-2.707	.007**
Physical	Nutrition	47.855	26.226	39.882	55.829	46.706	30.744	34.544	58.868	-1.136	.256
Functioning	Combined	45.299	25.479	38.206	52.393	49.288	26.403	39.604	58.973	-1.850	.064
	Total	47.344	24.791	43.171	51.517	50.260	28.818	43.488	57.032	-3.120	.002**
SF-36	Psychology	7.143	15.894	2.190	12.096	46.429	39.048	23.883	68.974	-2.379	.017*
Role	Nutrition	7.574	17.500	2.254	12.895	19.444	20.016	11.526	27.363	-2.907	.004**
limitations	Combined	9.774	21.051	3.914	15.635	22.742	25.161	13.513	31.971	-2.225	.026*
physical	Total	8.272	18.387	5.177	11.367	26.111	28.225	19.479	32.744	-4.354	.001***
SF-36	Psychology	61.548	25.614	53.566	69.530	63.929	29.786	46.731	81.127	-1.196	.232
Bodily pain	Nutrition	55.625	30.242	46.434	64.819	58.889	32.943	45.857	71.921	-1.800	.072
	Combined	53.606	27.019	46.084	61.128	58.629	27.301	48.615	68.643	-1.048	.294
	Total	56.667	27.683	52.007	61.327	59.757	29.649	52.790	66.724	-2.240	.025*
SF-36	Psychology	37.202	21.824	30.402	44.003	59.821	33.318	40.584	79.058	-2.689	.007**
Social	Nutrition	32.671	25.888	24.800	40.541	43.519	33.679	30.196	56.841	-2.476	.013*
functioning	Combined	32.452	24.786	25.551	39.352	41.936	28.604	31.443	52.428	-2.426	.015*
	Total	33.967	24.212	29.892	38.043	46.007	31.805	38.533	53.481	-4.504	.001***
SF-36	Psychology	60.286	19.584	54.183	66.389	74.571	13.276	66.906	82.237	-2.497	.013*
General mental	Nutrition	59.727	19.355	53.843	65.612	64.741	20.548	56.612	72.869	-1.696	.090
health	Combined	58.308	20.948	52.476	64.140	64.129	16.637	58.027	70.232	-.524	.600
	Total	59.362	19.911	56.011	62.714	66.389	17.897	62.183	70.594	-2.665	.008**
SF-36	Psychology	55.554	46.368	41.105	70.004	76.191	33.150	57.051	95.331	-.842	.400

Role	Nutrition	48.482	47.390	34.074	62.890	55.594	38.130	40.510	70.678	-1.788	.074
limitations	Combined	47.780	43.924	35.551	60.008	67.742	32.756	55.727	79.757	-2.313	.021*
emotional	Total	50.370	45.590	42.695	58.044	64.829	35.335	56.526	73.133	-3.159	.002**
SF-36	Psychology	20.714	16.139	15.685	25.743	41.071	20.586	29.186	52.957	-3.066	.002**
Vitality Energy	Nutrition	20.114	14.5670	15.685	24.542	31.111	23.588	21.780	40.442	-2.734	.006**
or Fatigue	Combined	19.039	17.658	14.123	23.955	27.097	19.527	19.934	34.259	-1.558	.119
	Total	19.891	16.159	17.171	22.611	31.319	21.657	26.230	36.409	-4.205	.001***
SF-36	Psychology	37.024	17.945	31.432	42.616	45.714	21.109	33.526	57.903	-2.561	.010*
General health	Nutrition	28.636	15.528	23.915	33.357	36.482	18.903	29.004	43.959	-2.157	.031*
perceptions	Combined	30.962	17.575	26.069	35.854	42.097	21.632	34.162	50.032	-2.423	.015*
	Total	32.065	17.286	29.156	34.975	40.694	20.561	35.863	45.526	-3.996	.001***
MFI	Psychology	15.952	2.845	15.066	16.839	13.786	4.441	11.222	16.350	-2.657	.008**
General	Nutrition	16.977	2.601	16.186	17.768	14.704	4.898	12.766	16.641	-2.548	.011*
Fatigue	Combined	17.327	2.588	16.607	18.047	16.645	2.811	15.614	17.676	-.854	.393
	Total	16.797	2.716	16.340	17.254	15.361	4.136	14.389	16.333	-3.692	.001***
MFI	Psychology	15.929	3.331	14.891	16.966	13.071	4.632	10.397	15.746	-2.810	.005**
Physical	Nutrition	16.727	3.358	15.707	17.748	14.222	4.987	12.249	16.195	-2.791	.005**
Fatigue	Combined	17.615	2.823	16.830	18.401	16.484	3.395	15.239	17.729	-2.364	.018*
	Total	16.819	3.211	16.278	17.359	14.972	4.453	13.926	16.019	-4.591	.001***
MFI	Psychology	13.857	4.112	12.576	15.138	10.643	5.153	7.668	13.618	-2.142	.032*
Reduced	Nutrition	14.136	4.027	12.912	15.361	12.259	5.012	10.277	14.242	-2.164	.030*
Activity	Combined	14.962	3.662	13.942	15.981	14.936	3.777	13.550	16.321	-.070	.944
	Total	14.362	3.921	13.702	15.022	13.097	4.798	11.970	14.225	-2.421	.015*
MFI	Psychology	10.357	4.287	9.021	11.693	7.286	4.214	4.853	9.719	-2.131	.033*
Reduced	Nutrition	10.500	3.474	9.444	11.556	8.963	3.736	7.485	10.441	-1.985	.047*

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<u>Motivation</u>	<u>Combined</u>	<u>11.462</u>	<u>3.153</u>	<u>10.584</u>	<u>12.339</u>	<u>10.774</u>	<u>3.095</u>	<u>9.639</u>	<u>11.910</u>	<u>-1.082</u>	<u>.279</u>
	<u>Total</u>	<u>10.819</u>	<u>3.639</u>	<u>10.206</u>	<u>11.431</u>	<u>9.417</u>	<u>3.767</u>	<u>8.532</u>	<u>10.302</u>	<u>-2.986</u>	<u>.003**</u>
<u>MFI</u>	<u>Psychology</u>	<u>13.524</u>	<u>4.363</u>	<u>12.164</u>	<u>14.883</u>	<u>10.500</u>	<u>4.468</u>	<u>7.920</u>	<u>13.080</u>	<u>-2.950</u>	<u>.003*</u>
<u>Mental Fatigue</u>	<u>Nutrition</u>	<u>13.682</u>	<u>4.328</u>	<u>12.366</u>	<u>14.998</u>	<u>11.926</u>	<u>5.334</u>	<u>9.816</u>	<u>14.036</u>	<u>-2.082</u>	<u>.037*</u>
	<u>Combined</u>	<u>13.846</u>	<u>4.345</u>	<u>12.637</u>	<u>15.056</u>	<u>12.613</u>	<u>3.827</u>	<u>11.209</u>	<u>14.017</u>	<u>-1.586</u>	<u>.113</u>
	<u>Total</u>	<u>13.696</u>	<u>4.315</u>	<u>12.969</u>	<u>14.422</u>	<u>11.944</u>	<u>4.568</u>	<u>10.871</u>	<u>13.018</u>	<u>-3.661</u>	<u>.001***</u>

<sup>a</sup>z-statistic for Wilcoxon Signed-Rank Test

**Table 3. Comparisons across time within the secondary outcome measures (ME/CFS-specific)**

		<u>Baseline</u>				<u>3-month follow-up</u>				<u>Comparisons</u>	
		<u>Mean</u>	<u>SD</u>	<u>95% CI for Mean</u>		<u>Mean</u>	<u>SD</u>	<u>95% CI for Mean</u>		<u>z-statistic</u>	<u>p-value</u>
				<u>Lower</u>	<u>Upper</u>			<u>Lower</u>	<u>Upper</u>		
<u>CDC CFS</u>	<u>Psychology</u>	<u>2.571</u>	<u>3.109</u>	<u>1.603</u>	<u>3.540</u>	<u>1.429</u>	<u>2.278</u>	<u>.114</u>	<u>2.744</u>	<u>-1.365</u>	<u>.172</u>
<u>Sore Throat</u>	<u>Nutrition</u>	<u>3.977</u>	<u>3.776</u>	<u>2.829</u>	<u>5.125</u>	<u>1.741</u>	<u>2.087</u>	<u>.915</u>	<u>2.566</u>	<u>-2.211</u>	<u>.027*</u>
	<u>Combined</u>	<u>3.202</u>	<u>4.494</u>	<u>1.951</u>	<u>4.454</u>	<u>1.904</u>	<u>2.821</u>	<u>.870</u>	<u>2.939</u>	<u>-.804</u>	<u>.422</u>
	<u>Total</u>	<u>3.257</u>	<u>3.898</u>	<u>2.601</u>	<u>3.914</u>	<u>1.750</u>	<u>2.437</u>	<u>1.178</u>	<u>2.323</u>	<u>-2.387</u>	<u>.017*</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>1.976</u>	<u>3.382</u>	<u>.922</u>	<u>3.030</u>	<u>1.786</u>	<u>3.378</u>	<u>-.165</u>	<u>3.736</u>	<u>-.341</u>	<u>.733</u>
<u>Swollen</u>	<u>Nutrition</u>	<u>5.561</u>	<u>6.491</u>	<u>3.587</u>	<u>7.534</u>	<u>5.000</u>	<u>6.760</u>	<u>2.326</u>	<u>7.674</u>	<u>-2.212</u>	<u>.027*</u>
<u>Lymph nodes</u>	<u>Combined</u>	<u>3.462</u>	<u>4.881</u>	<u>2.103</u>	<u>4.820</u>	<u>2.690</u>	<u>4.477</u>	<u>1.0458</u>	<u>4.332</u>	<u>-.725</u>	<u>.468</u>
<u>Glands</u>	<u>Total</u>	<u>3.679</u>	<u>5.250</u>	<u>2.795</u>	<u>4.563</u>	<u>3.380</u>	<u>5.385</u>	<u>2.115</u>	<u>4.646</u>	<u>-1.684</u>	<u>.092</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>2.071</u>	<u>3.249</u>	<u>1.059</u>	<u>3.084</u>	<u>1.643</u>	<u>2.818</u>	<u>.016</u>	<u>3.270</u>	<u>-.730</u>	<u>.465</u>

<u>Diarrhea</u>	<u>Nutrition</u>	<u>2.841</u>	<u>4.832</u>	<u>1.372</u>	<u>4.310</u>	<u>1.444</u>	<u>3.274</u>	<u>.149</u>	<u>2.740</u>	<u>-1.649</u>	<u>.099</u>
	<u>Combined</u>	<u>3.135</u>	<u>3.773</u>	<u>2.084</u>	<u>4.185</u>	<u>1.631</u>	<u>2.483</u>	<u>.720</u>	<u>2.542</u>	<u>-1.996</u>	<u>.046*</u>
	<u>Total</u>	<u>2.717</u>	<u>3.998</u>	<u>2.044</u>	<u>3.390</u>	<u>1.563</u>	<u>2.827</u>	<u>.899</u>	<u>2.228</u>	<u>-2.481</u>	<u>.013*</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>13.286</u>	<u>6.271</u>	<u>11.331</u>	<u>15.240</u>	<u>11.071</u>	<u>6.673</u>	<u>7.218</u>	<u>14.925</u>	<u>-1.550</u>	<u>.121</u>
<u>Fatigue after exertion</u>	<u>Nutrition</u>	<u>13.722</u>	<u>6.450</u>	<u>11.761</u>	<u>15.682</u>	<u>11.815</u>	<u>7.217</u>	<u>8.960</u>	<u>14.670</u>	<u>-2.209</u>	<u>.027*</u>
	<u>Combined</u>	<u>14.154</u>	<u>6.270</u>	<u>12.408</u>	<u>15.899</u>	<u>11.436</u>	<u>6.275</u>	<u>9.134</u>	<u>13.738</u>	<u>-2.392</u>	<u>.017*</u>
	<u>Total</u>	<u>13.752</u>	<u>6.292</u>	<u>12.693</u>	<u>14.811</u>	<u>11.507</u>	<u>6.629</u>	<u>9.949</u>	<u>13.065</u>	<u>-3.574</u>	<u>.001***</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>8.286</u>	<u>6.747</u>	<u>6.183</u>	<u>10.388</u>	<u>7.429</u>	<u>6.892</u>	<u>3.450</u>	<u>11.408</u>	<u>-2.145</u>	<u>.032*</u>
<u>Muscle Aches or Muscle Pains</u>	<u>Nutrition</u>	<u>9.091</u>	<u>6.383</u>	<u>7.151</u>	<u>11.031</u>	<u>7.222</u>	<u>6.278</u>	<u>4.739</u>	<u>9.706</u>	<u>-2.901</u>	<u>.004**</u>
	<u>Combined</u>	<u>8.519</u>	<u>6.932</u>	<u>6.589</u>	<u>10.449</u>	<u>6.188</u>	<u>5.528</u>	<u>4.160</u>	<u>8.215</u>	<u>-1.908</u>	<u>.056</u>
	<u>Total</u>	<u>8.630</u>	<u>6.664</u>	<u>7.509</u>	<u>9.752</u>	<u>6.817</u>	<u>6.029</u>	<u>5.400</u>	<u>8.234</u>	<u>-3.995</u>	<u>.001***</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>3.476</u>	<u>5.334</u>	<u>1.814</u>	<u>5.138</u>	<u>2.786</u>	<u>4.458</u>	<u>.212</u>	<u>5.360</u>	<u>-1.778</u>	<u>.075</u>
<u>Pain In Joints</u>	<u>Nutrition</u>	<u>4.696</u>	<u>5.560</u>	<u>3.006</u>	<u>6.386</u>	<u>3.926</u>	<u>5.099</u>	<u>1.909</u>	<u>5.943</u>	<u>-2.022</u>	<u>.043*</u>
	<u>Combined</u>	<u>5.474</u>	<u>6.386</u>	<u>3.696</u>	<u>7.251</u>	<u>3.010</u>	<u>4.140</u>	<u>1.492</u>	<u>4.528</u>	<u>-1.840</u>	<u>.066</u>
	<u>Total</u>	<u>4.618</u>	<u>5.837</u>	<u>3.635</u>	<u>5.600</u>	<u>3.310</u>	<u>4.543</u>	<u>2.242</u>	<u>4.377</u>	<u>-3.141</u>	<u>.002**</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>1.238</u>	<u>2.516</u>	<u>.454</u>	<u>2.022</u>	<u>1.643</u>	<u>4.181</u>	<u>-.771</u>	<u>4.057</u>	<u>-.135</u>	<u>.892</u>
<u>Fever</u>	<u>Nutrition</u>	<u>1.394</u>	<u>2.562</u>	<u>.615</u>	<u>2.173</u>	<u>.630</u>	<u>2.041</u>	<u>-.178</u>	<u>1.437</u>	<u>-1.487</u>	<u>.137</u>
	<u>Combined</u>	<u>1.333</u>	<u>3.909</u>	<u>.245</u>	<u>2.421</u>	<u>.378</u>	<u>.709</u>	<u>.118</u>	<u>.638</u>	<u>-1.517</u>	<u>.129</u>
	<u>Total</u>	<u>1.324</u>	<u>3.106</u>	<u>.801</u>	<u>1.846</u>	<u>.718</u>	<u>2.272</u>	<u>.185</u>	<u>1.252</u>	<u>-1.876</u>	<u>.061</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>3.357</u>	<u>4.637</u>	<u>1.912</u>	<u>4.802</u>	<u>2.571</u>	<u>4.398</u>	<u>.032</u>	<u>5.111</u>	<u>-1.970</u>	<u>.049*</u>
<u>Chills</u>	<u>Nutrition</u>	<u>3.750</u>	<u>3.924</u>	<u>2.557</u>	<u>4.943</u>	<u>2.222</u>	<u>4.098</u>	<u>.601</u>	<u>3.843</u>	<u>-3.401</u>	<u>.001***</u>
	<u>Combined</u>	<u>3.192</u>	<u>4.343</u>	<u>1.983</u>	<u>4.402</u>	<u>1.908</u>	<u>2.797</u>	<u>.882</u>	<u>2.934</u>	<u>-2.049</u>	<u>.040*</u>
	<u>Total</u>	<u>3.420</u>	<u>4.283</u>	<u>2.699</u>	<u>4.141</u>	<u>2.155</u>	<u>3.614</u>	<u>1.306</u>	<u>3.004</u>	<u>-4.206</u>	<u>.001***</u>
<u>CDC CFS</u>	<u>Psychology</u>	<u>12.905</u>	<u>6.792</u>	<u>10.788</u>	<u>15.021</u>	<u>10.643</u>	<u>6.698</u>	<u>6.776</u>	<u>14.510</u>	<u>-.802</u>	<u>.422</u>
<u>UnrefreshingSl</u>	<u>Nutrition</u>	<u>12.250</u>	<u>7.088</u>	<u>10.095</u>	<u>14.405</u>	<u>9.444</u>	<u>7.738</u>	<u>6.384</u>	<u>12.505</u>	<u>-1.421</u>	<u>.155</u>

8	<u>cep</u>	<u>Combined</u>	<u>12.154</u>	<u>7.147</u>	<u>10.164</u>	<u>14.143</u>	<u>10.161</u>	<u>7.959</u>	<u>7.242</u>	<u>13.080</u>	<u>-1.513</u>	<u>.130</u>
9		<u>Total</u>	<u>12.413</u>	<u>6.978</u>	<u>11.238</u>	<u>13.588</u>	<u>9.986</u>	<u>7.557</u>	<u>8.210</u>	<u>11.762</u>	<u>-2.295</u>	<u>.022*</u>
10	<u>CDC CFS</u>	<u>Psychology</u>	<u>9.286</u>	<u>7.658</u>	<u>6.899</u>	<u>11.672</u>	<u>5.286</u>	<u>4.921</u>	<u>2.444</u>	<u>8.127</u>	<u>-1.738</u>	<u>.082</u>
11	<u>Sleeping</u>	<u>Nutrition</u>	<u>8.614</u>	<u>7.317</u>	<u>6.389</u>	<u>10.838</u>	<u>9.482</u>	<u>9.200</u>	<u>5.842</u>	<u>13.121</u>	<u>-.190</u>	<u>.849</u>
12	<u>Problems</u>	<u>Combined</u>	<u>8.904</u>	<u>7.681</u>	<u>6.766</u>	<u>11.042</u>	<u>6.529</u>	<u>6.749</u>	<u>4.053</u>	<u>9.004</u>	<u>-1.794</u>	<u>.073</u>
13		<u>Total</u>	<u>8.928</u>	<u>7.509</u>	<u>7.664</u>	<u>10.192</u>	<u>7.394</u>	<u>7.585</u>	<u>5.612</u>	<u>9.177</u>	<u>-1.983</u>	<u>.047*</u>
14	<u>CDC CFS</u>	<u>Psychology</u>	<u>5.262</u>	<u>5.548</u>	<u>3.533</u>	<u>6.991</u>	<u>4.357</u>	<u>3.411</u>	<u>2.388</u>	<u>6.326</u>	<u>-1.200</u>	<u>.230</u>
15	<u>Headaches</u>	<u>Nutrition</u>	<u>7.646</u>	<u>7.040</u>	<u>5.506</u>	<u>9.786</u>	<u>5.185</u>	<u>6.294</u>	<u>2.695</u>	<u>7.675</u>	<u>-2.084</u>	<u>.037*</u>
16		<u>Combined</u>	<u>6.346</u>	<u>5.857</u>	<u>4.715</u>	<u>7.977</u>	<u>4.050</u>	<u>3.527</u>	<u>2.756</u>	<u>5.343</u>	<u>-2.807</u>	<u>.005**</u>
17		<u>Total</u>	<u>6.431</u>	<u>6.200</u>	<u>5.387</u>	<u>7.474</u>	<u>4.535</u>	<u>4.708</u>	<u>3.429</u>	<u>5.642</u>	<u>-3.000</u>	<u>.003**</u>
18	<u>CDC CFS</u>	<u>Psychology</u>	<u>6.333</u>	<u>4.996</u>	<u>4.777</u>	<u>7.890</u>	<u>3.500</u>	<u>3.995</u>	<u>1.193</u>	<u>5.807</u>	<u>-1.965</u>	<u>.049*</u>
19	<u>Memory</u>	<u>Nutrition</u>	<u>9.409</u>	<u>7.183</u>	<u>7.225</u>	<u>11.593</u>	<u>8.667</u>	<u>7.681</u>	<u>5.628</u>	<u>11.705</u>	<u>-.338</u>	<u>.735</u>
20	<u>Problems</u>	<u>Combined</u>	<u>8.173</u>	<u>7.610</u>	<u>6.055</u>	<u>10.292</u>	<u>6.148</u>	<u>4.905</u>	<u>4.349</u>	<u>7.947</u>	<u>-1.446</u>	<u>.148</u>
21		<u>Total</u>	<u>8.007</u>	<u>6.835</u>	<u>6.857</u>	<u>9.158</u>	<u>6.578</u>	<u>6.189</u>	<u>5.123</u>	<u>8.032</u>	<u>-2.053</u>	<u>.040*</u>
22	<u>CDC CFS</u>	<u>Psychology</u>	<u>8.500</u>	<u>6.094</u>	<u>6.601</u>	<u>10.399</u>	<u>5.143</u>	<u>5.559</u>	<u>1.933</u>	<u>8.353</u>	<u>-2.809</u>	<u>.005**</u>
23	<u>Difficulty</u>	<u>Nutrition</u>	<u>9.822</u>	<u>7.641</u>	<u>7.499</u>	<u>12.145</u>	<u>7.778</u>	<u>6.941</u>	<u>5.032</u>	<u>10.524</u>	<u>-1.196</u>	<u>.232</u>
24	<u>Concentrating</u>	<u>Combined</u>	<u>9.135</u>	<u>6.942</u>	<u>7.202</u>	<u>11.067</u>	<u>6.507</u>	<u>4.843</u>	<u>4.731</u>	<u>8.283</u>	<u>-1.899</u>	<u>.058</u>
25		<u>Total</u>	<u>9.161</u>	<u>6.903</u>	<u>7.999</u>	<u>10.323</u>	<u>6.718</u>	<u>5.844</u>	<u>5.345</u>	<u>8.092</u>	<u>-3.440</u>	<u>.001***</u>
26	<u>CDC CFS</u>	<u>Psychology</u>	<u>3.476</u>	<u>4.845</u>	<u>1.966</u>	<u>4.986</u>	<u>2.286</u>	<u>2.946</u>	<u>.585</u>	<u>3.987</u>	<u>-.213</u>	<u>.832</u>
27	<u>Nausea</u>	<u>Nutrition</u>	<u>4.769</u>	<u>5.135</u>	<u>3.208</u>	<u>6.330</u>	<u>3.407</u>	<u>5.746</u>	<u>1.134</u>	<u>5.681</u>	<u>-1.686</u>	<u>.092</u>
28		<u>Combined</u>	<u>3.327</u>	<u>4.902</u>	<u>1.962</u>	<u>4.692</u>	<u>3.458</u>	<u>3.585</u>	<u>2.144</u>	<u>4.773</u>	<u>-.855</u>	<u>.392</u>
29		<u>Total</u>	<u>3.832</u>	<u>4.966</u>	<u>2.996</u>	<u>4.668</u>	<u>3.211</u>	<u>4.396</u>	<u>2.178</u>	<u>4.244</u>	<u>-.584</u>	<u>.559</u>
30	<u>CDC CFS</u>	<u>Psychology</u>	<u>2.548</u>	<u>3.270</u>	<u>1.529</u>	<u>3.567</u>	<u>2.786</u>	<u>4.003</u>	<u>.474</u>	<u>5.097</u>	<u>-.343</u>	<u>.732</u>
31	<u>Abdominal</u>	<u>Nutrition</u>	<u>5.064</u>	<u>5.165</u>	<u>3.493</u>	<u>6.634</u>	<u>3.593</u>	<u>3.905</u>	<u>2.048</u>	<u>5.137</u>	<u>-1.968</u>	<u>.049*</u>
32	<u>Pain</u>	<u>Combined</u>	<u>3.750</u>	<u>4.635</u>	<u>2.460</u>	<u>5.041</u>	<u>2.548</u>	<u>2.791</u>	<u>1.524</u>	<u>3.572</u>	<u>-.598</u>	<u>.550</u>

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	<u>Total</u>	<u>3.803</u>	<u>4.535</u>	<u>3.040</u>	<u>4.566</u>	<u>2.986</u>	<u>3.470</u>	<u>2.171</u>	<u>3.801</u>	<u>-1.727</u>	<u>.084</u>
CDC CFS	Psychology	3.524	4.702	2.059	4.989	2.357	2.437	.950	3.764	-.724	.469
Sinus Nasal	Nutrition	5.469	6.476	3.500	7.438	4.889	6.104	2.474	7.304	-1.400	.162
Symptoms	Combined	4.789	6.304	3.034	6.544	3.804	6.710	1.343	6.266	-2.482	.013*
	<u>Total</u>	<u>4.620</u>	<u>5.931</u>	<u>3.622</u>	<u>5.619</u>	<u>3.930</u>	<u>5.882</u>	<u>2.547</u>	<u>5.312</u>	<u>-2.971</u>	<u>.003**</u>
CDC CFS	Psychology	3.000	4.191	1.694	4.306	1.571	2.209	.296	2.847	-1.556	.120
Shortness Of	Nutrition	3.285	4.090	2.026	4.543	2.407	4.060	.801	4.013	-1.849	.064
Breath	Combined	3.392	4.788	2.046	4.739	2.526	3.631	1.194	3.858	-.976	.329
	<u>Total</u>	<u>3.237</u>	<u>4.365</u>	<u>2.497</u>	<u>3.977</u>	<u>2.296</u>	<u>3.554</u>	<u>1.461</u>	<u>3.131</u>	<u>-2.538</u>	<u>.011*</u>
CDC CFS	Psychology	3.429	5.347	1.762	5.095	1.214	2.517	-.239	2.668	-1.973	.049*
Sensitivity To	Nutrition	5.031	6.097	3.177	6.884	4.111	6.198	1.659	6.563	-2.136	.033*
Light	Combined	4.481	6.360	2.710	6.251	3.297	5.557	1.259	5.335	-.787	.431
	<u>Total</u>	<u>4.336</u>	<u>5.975</u>	<u>3.330</u>	<u>5.342</u>	<u>3.197</u>	<u>5.419</u>	<u>1.924</u>	<u>4.471</u>	<u>-2.542</u>	<u>.011*</u>
CDC CFS	Psychology	3.952	3.938	2.725	5.180	1.571	3.228	-.292	3.435	-1.614	.106
Depression	Nutrition	4.477	5.450	2.821	6.134	3.333	4.883	1.402	5.265	-1.584	.113
	Combined	5.077	5.950	3.420	6.734	2.766	3.324	1.547	3.985	-1.304	.192
	<u>Total</u>	<u>4.544</u>	<u>5.230</u>	<u>3.663</u>	<u>5.424</u>	<u>2.747</u>	<u>3.964</u>	<u>1.815</u>	<u>3.678</u>	<u>-2.297</u>	<u>.022*</u>

<sup>a</sup>z-statistic for Wilcoxon Signed-Rank Test

**Table 4. Comparisons across time within the secondary outcome measures (psychological)**

	<u>Baseline</u>				<u>3-month follow-up</u>				<u>Comparisons</u>	
	<u>Mean</u>	<u>SD</u>	<u>95% CI for Mean</u>		<u>Mean</u>	<u>SD</u>	<u>95% CI for Mean</u>		<u>z-statistic</u>	<u>p-value</u>
			<u>Lower</u>	<u>Upper</u>			<u>Lower</u>	<u>Upper</u>		

MHLCS	Psychology	.677	.159	.627	.726	.821	.251	.676	.966	-2.983	.003**
Internal	Nutrition	.622	.177	.568	.675	1.193	2.969	.019	2.368	-.687	.492
	Combined	.662	.174	.613	.710	.779	.318	.662	.896	-1.755	.079
	Total	.653	.171	.624	.682	.942	1.822	.514	1.371	-2.962	.003**
MHLCS	Psychology	.368	.156	.320	.417	.351	.152	.263	.439	-2.594	.009**
Chance	Nutrition	.340	.133	.299	.380	.911	3.020	-.284	2.105	-.143	.886
	Combined	.354	.155	.311	.397	.314	.133	.265	.363	-.672	.501
	Total	.354	.148	.329	.379	.545	1.853	.109	.980	-1.552	.121
MHLCS	Psychology	.404	.134	.362	.446	.441	.315	.259	.624	.000	1.000
Powerful	Nutrition	.418	.141	.374	.460	.804	2.244	-.084	1.691	-1.843	.065
Others	Combined	.407	.101	.379	.436	.434	.279	.331	.536	-.577	.564
	Total	.409	.124	.388	.430	.574	1.3880	.248	.900	-1.601	.109
MHLCS	Psychology	.169	.082	.143	.194	.131	.093	.077	.185	-1.122	.262
Doctors	Nutrition	.171	.089	.144	.197	.657	2.668	-.398	1.713	-1.686	.092
	Combined	.191	.147	.150	.232	.153	.070	.128	.179	-1.384	.166
	Total	.178	.112	.159	.196	.338	1.635	-.0462	.722	-2.381	.017*
MHLCS	Psychology	.235	.075	.212	.259	.268	.189	.159	.377	-.118	.906
Other People	Nutrition	.264	.129	.225	.304	.739	2.652	-.311	1.788	-1.697	.090
	Combined	.245	.074	.224	.265	.252	.118	.209	.295	-.213	.831
	Total	.248	.095	.232	.264	.438	1.626	.055	.820	-1.186	.236
CDC CFS	Psychology	94.381	16.836	89.134	99.628	78.571	18.434	67.928	89.215	-3.111	.002**
Maladaptive	Nutrition	96.386	21.946	89.714	103.059	85.259	27.665	74.315	96.203	-3.443	.001***
Stress Index	Combined	98.269	19.165	92.934	103.605	87.484	22.965	79.060	95.908	-2.215	.027*
Scale Score	Total	96.486	19.373	93.225	99.747	84.917	24.004	79.276	90.557	-5.123	.001***

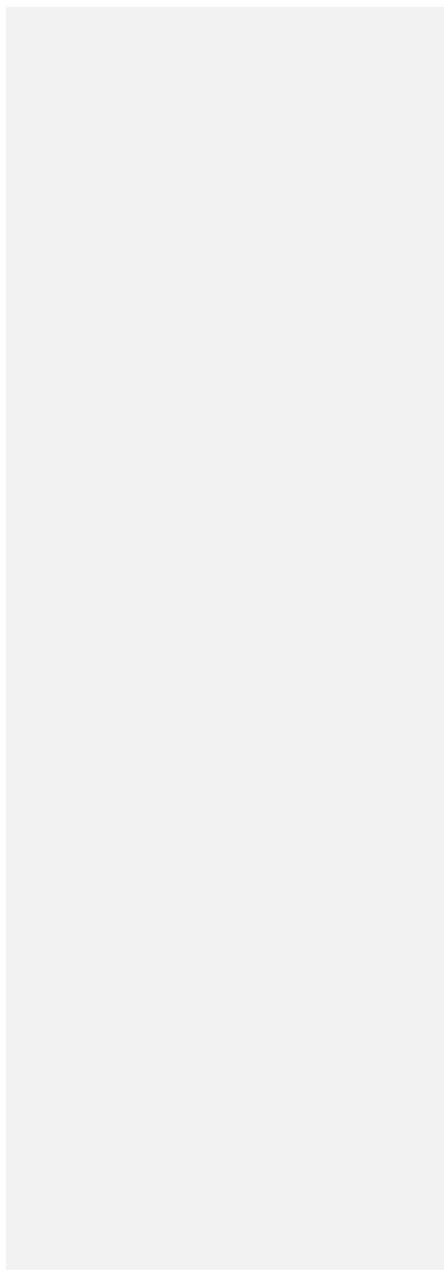
<sup>a</sup>z-statistic for Wilcoxon Signed-Rank Test



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**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\***  
**Checklist for cohort, case-control, and cross-sectional studies (combined)**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Title and Abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Title and Abstract
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1-4
Objectives	3	State specific objectives, including any pre-specified hypotheses	3-4
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	4
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	14
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	9-10

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	8-9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	8-9 9
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	6-7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	12-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

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**A preliminary prospective study of nutritional, psychological and combined therapies for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) in a private care setting.**

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2012-001079.R3
Article Type:	Research
Date Submitted by the Author:	13-Sep-2012
Complete List of Authors:	Arroll, Megan; The Optimum Health Clinic, Howard, Alex; The Optimum Health Clinic,
<b>Primary Subject Heading</b>:	Complementary medicine
Secondary Subject Heading:	Rehabilitation medicine, Nutrition and metabolism, Pharmacology and therapeutics
Keywords:	COMPLEMENTARY MEDICINE, SOCIAL MEDICINE, REHABILITATION MEDICINE

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## **Abstract**

Background: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a condition characterized by severe and persistent fatigue, neurological disturbances, autonomic and endocrine dysfunctions and sleep difficulties that have a pronounced and significant impact on individuals' lives. Current NICE guidelines within the United Kingdom suggest that this condition should be treated with cognitive behavioral therapy and/or graded exercise therapy where appropriate. There is currently a lack of evidence base concerning - alternative techniques that may be beneficial to those with ME/CFS. Objectives: This study aimed to investigate whether three modalities of psychology, nutrition and combined treatment, influenced symptom report measures in those with ME/CFS over a 3-month time period and whether there were significant differences in these changes between groups.

Design and setting: This is a preliminary prospective study with one follow-up point conducted at a private secondary health care facility in London, UK.

Participants: One-hundred and thirty-eight individuals (110 females, 79.7%; 42 participants in psychology, 44 in nutrition and 52 in combined) participated at baseline and 72 participants completed the battery of measures at follow-up (52.17% response rate; 14, 27, 31 participants in each group, respectively).

Outcome measures: Self-report measures of ME/CFS symptoms, functional ability, multidimensional fatigue and perceived control.

Results: Baseline comparisons showed those in the combined group had higher levels of fatigue. At follow-up, all groups saw improvements in fatigue, functional physical and symptomatology; those within the psychology group also experienced a shift in perceived control over time.

Conclusions: This study provides early evidence that psychological, nutritional and combined techniques for the treatment of ME/CFS may influence symptomatology, fatigue, function and perceived control. However, these results must be viewed with caution as the allocation

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3 to groups was not randomized, there was no control group and the study suffered from high  
4 drop-out rates.  
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## 8 **Summary**

### 9 **Article focus**

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- 13 • This preliminary prospective study investigated three (psychological, nutritional and  
14 combined) tailored interventions for ME/CFS over time.  
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  - 17 • Differences between the reported changes over time between groups were also  
18 assessed.  
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### 21 **Key messages**

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- 24 • Psychological, nutritional and combined approaches for the management of ME/CFS  
25 influence symptomatology over time in some individuals with this disorder.  
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  - 28 • Self-reported functional ability (physical and social) are influenced following tailored  
29 interventions lasting 3 months.  
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  - 32 • This study provides preliminary evidence that tailored psychological, nutritional and  
33 combined interventions may influence self-reported symptomatology in some people with  
34 ME/CFS; however due to the study's methodological limitations, it is important that these  
35 findings are investigated further in high quality randomized controlled studies.  
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### 42 **Strengths and limitations of this study**

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- 45 • The findings here are an initial step to fill the gap in the extant literature regarding the  
46 utility of tailored and multidisciplinary (psychological, nutritional and combined) treatments  
47 for ME/CFS.  
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  - 50 • There is bias in this study as the participants were self-selected in the sense that they  
51 chose to attend the clinic and which treatment option they preferred (with advice), i.e. the  
52 study was not randomized.  
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3 • There were low retention rates in this study which may constitute a bias in that those  
4 who remained in the study may have experienced benefits and those who experienced little or  
5 no benefits may have dropped out.  
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### 19 **Introduction**

20 Chronic Fatigue Syndrome or myalgic encephalomyelitis (ME/CFS) is a condition  
21 characterized by prolonged and debilitating fatigue, although the exact cause of this disorder  
22 is still under debate. Due to the lack of a definitive biological marker, diagnosis is made on  
23 the basis of the exclusion of other explanatory conditions. The most widely used case  
24 definition by the Centers for Disease Control <sup>1</sup> states that there must be at least six months  
25 severe fatigue of new and definite onset, not the result of ongoing exertion, not alleviated by  
26 rest and resulting in reduced levels of physical activity. The CDC definition also sets out a  
27 series of minor complaints that must accompany the fatigue (cognitive impairment, sore  
28 throat, tender cervical or axillary lymph nodes, muscle pain, multi-joint pain, headaches of a  
29 new type, pattern or severity at onset, unrefreshing sleep and post-exertion malaise), with  
30 individuals needing to have the occurrence of four or more symptoms to be diagnosed with  
31 ME/CFS. Estimates of the prevalence of ME/CFS have been made as low as 3 and as high as  
32 2,800 per 100,000 <sup>2</sup>.  
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52 The most widely researched strategies for alleviating the symptoms of ME/CFS are Cognitive  
53 Behavior Therapy (CBT) and Graded Exercise Therapy (GET). Two reviews of studies on  
54 CBT <sup>3,4</sup> found that it significantly improved physical functioning in adult out-patients as  
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3 compared with medical management, counseling, guided support, education and support or  
4 relaxation. Regarding GET, a systematic review illustrated that this form of therapy was  
5 potentially beneficial for people with ME/CFS, especially when combined with a patient  
6 education programme<sup>5</sup>. However, drop-out rates were higher in the GET groups than control  
7 groups suggesting that individuals with ME/CFS are averse to this type of therapy. Recently,  
8 a large scale, longitudinal study investigating CBT, GET, Adaptive Pacing Therapy (APT)  
9 and specialist medical care (SMC) which had very low drop-out rates, found that CBT and  
10 GET (when added to SMC) were moderately effective outpatient treatments for this patient  
11 group as opposed to APT or SMC alone<sup>6</sup>.  
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25 Although CBT and GET studies have shown some promising outcomes, there is no known  
26 cure for ME/CFS. Therefore the National Institute for Health and Clinical Excellence (NICE)  
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<sup>7</sup> recommends a number of symptom management strategies and interventions aimed at  
helping individuals to cope with their condition and reduce physical deconditioning brought  
about by the illness. Pharmacological interventions are, at times, suggested for patients with  
poor sleep or pain, for instance, low-dose antidepressants, as these have been shown to be  
effective<sup>8-14</sup>. However, patient expectations must be realistic as the drugs may help elevate  
mood and psychological outlook but not reduce fatigue and other symptomatology associated  
with ME/CFS<sup>15</sup>. Numerous drugs such as thyroxine, hydrocortisone and antiviral agents are  
not advised by NICE due to contradictory findings<sup>16;17</sup>.

In terms of function and quality of life management, NICE offers general advice concerning  
sleep management, appropriate rest periods, and pacing. Sleep hygiene instruction, together  
with pharmacological treatment tailored to the individual patient can be beneficial in  
combating fatigue<sup>18</sup>. Dietary management may also reduce symptomatology for those with

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3 concurrent irritable bowel syndrome (IBS) <sup>19</sup>, although this is not currently recommended by  
4 NICE. Dietary supplementation has been investigated in relation to ME/CFS. Fatty acids <sup>20</sup>,  
5 folic acid <sup>21</sup>, vitamin C <sup>22</sup>, co-enzyme Q10 <sup>23</sup>, magnesium <sup>24</sup>, multivitamins <sup>25</sup> and minerals <sup>26</sup>  
6  
7 have all been shown to reduce symptomatology in ME/CFS patients. However other studies  
8  
9 have shown conflicting findings with regard to nutritional supplementation, therefore it is  
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11 perhaps wise to treat with supplements on a case-by-case basis <sup>27;28</sup>.  
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19 Due to the lack of clear and definitive treatment strategies, individuals often seek out  
20 Complementary and Alternative Medicines (CAM). Although NICE does not recommend the  
21 use of CAM they do acknowledge that many people with ME/CFS use such therapies and  
22 find them beneficial for symptom management. This view is due to the lack of published  
23 evidence for the effectiveness of these treatments. Examples of CAM treatments used by  
24 individuals with ME/CFS include religious healing, massage therapy, relaxation, meditation,  
25 homeopathy, acupuncture, naturopathy and herbal therapies <sup>29;30</sup>; patient satisfaction with  
26 such approaches as CAM has been high, over 80% in some instances <sup>29</sup>. A recent systematic  
27 review of such interventions identified 70 controlled clinical trials (randomized and non-  
28 randomized) and found that 86% of these studies illustrated at least one positive effect, with  
29 74% showing a decrease of illness-related symptomatology <sup>31</sup>. Meditative or mindfulness  
30 approaches warranted further investigation based on these results as did supplement programs  
31 of magnesium, l-carnitine, and S-adenosylmethionine. A subsequent review based solely on  
32 randomized controlled trials (RCTs) of CAM techniques identified 26 such studies and  
33 observed that qigong, massage and tuina (approaches based within Chinese Traditional  
34 Medicine and based upon relaxation and connection with the body) illustrated positive effects  
35 as did supplementation studies utilizing nicotinamide adenine dinucleotide (NADH) and  
36 magnesium <sup>32</sup>. However, within both reviews it was noted that the methodological quality of  
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3 reporting was poor and the sample sizes in these studies were small; hence ability to draw  
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5 strong conclusions on the efficacy of CAM methods is limited. Porter et al. (2010)<sup>31</sup> did note  
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7 that individualized treatment protocols which include a range of tailored strategies are a  
8  
9 promising area for further investigation for this complex, multi-system illness.  
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## 12 13 14 15 16 17 18 **Objectives**

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20 There is still much debate and uncertainty regarding alternative interventions for those with  
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22 ME/CFS. A recent review of CAM techniques<sup>31</sup> highlight the need for further exploration of  
23  
24 individually tailored interventions for the alleviation of the condition's often debilitating and  
25  
26 intrusive symptomatology. This study therefore aims to provide preliminary evidence for the  
27  
28 utility of three types of approaches (psychological, nutritional and combined) to the  
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30 management of ME/CFS over time (baseline and follow-up) offered at a private health-care  
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32 center in the UK.  
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## 38 **Methods**

### 39 **Study design and setting**

40  
41 This preliminary prospective study aimed to investigate whether psychological, nutritional  
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43 and combined approaches to the treatment of ME/CFS influenced symptom report measures  
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45 over a 3-month time period and whether there were significant differences in these changes  
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47 between groups. The research was conducted at one private secondary health care facility. All  
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49 potential patients of the clinic are first asked to complete a comprehensive symptom profile  
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51 and medical history, including questions relating to triggering factors, psychology sub-types  
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53 and structural/biological sub-types (this is distinct from the research data collected).  
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3 Subsequent to this, every individual receives a 15-minute screening with one of the  
4 practitioners (please note, this was not either of the authors of the current study) who  
5 recommends the best course of action for his/her needs; this will be the psychology-related  
6 interventions, nutritional advice and support or a combination of the two.  
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14 All individuals requesting treatment at the private care setting were offered the opportunity to  
15 participate in the study. Those that expressed an interest (N = 145) were emailed a  
16 spreadsheet that contained the questionnaires and asked to complete it at their convenience.  
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18 Informed consent was obtained prior to the completion of the questionnaires and the study  
19 was approved by the University of East London Ethics Committee. Participants were told that  
20 they could withdraw from the study at any time and that withdrawal would not affect their  
21 care at the clinic. Participants were able to ask questions at any point in the study and no  
22 deception was used as the participants were informed of the nature of the research program  
23 before they agreed to participate. Subsequently, participants were requested to complete the  
24 questionnaire pack on a second occasion, three months from the baseline measures.  
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### 38 *Psychology*

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40 The clinic offers a 3-month intervention which consists of a combination of Neuro-linguistic  
41 Programming (NLP), Emotional Freedom Technique (EFT), life coaching and  
42 hypnotherapy/self-hypnosis constructed in a manner specific to the needs of those with  
43 ME/CFS. The primary aim of this approach is to reduce the anxiety that is associated with  
44 having a debilitating and unpredictable condition, improve emotional well-being and help  
45 individuals slowly manage and increase their activity within their own limits (i.e. pacing).  
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47 The program is offered as a series of group sessions and the peer support is seen as an  
48 important component of the intervention, which is solidified via the use of moderated online  
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3 support forums, narratives of previous clients' experiences and online materials that can be  
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5 accessed as often as necessary. In addition to, or as an alternative to this course, individuals  
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7 receive a series of one-to-one sessions and for the most severely affected ME/CFS patients,  
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9 telephone sessions are arranged and support materials can be accessed in their own homes.  
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11 Over the three-month period of this preliminary study, the participants experienced one of  
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13 three treatment options. The first option included 13 hours of practitioner contact time in a  
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15 mix of group training in person, group telephone conference calls and one-to-one telephone  
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17 sessions, the second option was four hours of one-to-one telephone sessions and the final  
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19 option was three hours of in person sessions. Participants all had access to various support  
20  
21 materials which included CDs and online resources. The amount of time spent on these was  
22  
23 patient-led, but was in the region of a further six hours. All the practitioners offering this  
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25 option are qualified in hypnotherapy, NLP, life coaching and EFT and undergo an intensive  
26  
27 period of training in the clinic's own integrative approach (please see Howard and Arroll <sup>33</sup>  
28  
29 for more details of this approach) and ongoing supervision (individual and group supervision  
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31 on a biweekly basis) from the department director, who is the only senior practitioner in the  
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33 team.  
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#### 40 *Nutrition*

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42 Tailored nutritional therapy is achieved via one-to-one consultations with individuals. To  
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44 begin, a very detailed history is taken based upon the information given in the  
45  
46 aforementioned symptom profile. Qualified nutritional therapists (who have been given  
47  
48 specialist training regarding ME/CFS from the clinic) then suggest tests consistent with  
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50 symptomatology, for instance the Adrenal Stress Index Test, comprehensive stool  
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52 analysis/gastro-intestinal function, vitamin & mineral status, etc. Results from these tests are  
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54 then used to compose an evidence-driven diet and supplement program. As most cases of  
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3 ME/CFS are complex involving multiple body systems, this process is often iterative and  
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5 follow-up consultations are necessary to check progress and make alterations to the protocol.  
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7 The nutritional therapy program consists of an initial one-hour evaluation (which includes the  
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9 tailored advice) and follow-up approximately every six weeks; therefore, during the course  
10  
11 of the present study, the participants received a minimum of two one-hour sessions with  
12  
13 email support for any queries and detailed nutritional guidance. All the nutritional therapists  
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15 are qualified to diploma level and members of (voluntary) regulatory bodies such as the  
16  
17 British Association for Applied Nutrition and Nutritional Therapy (BANT) and the  
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19 Complementary and Natural Healthcare Council (CNHC). Similar to the psychology  
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21 department, the nutrition department is led by one senior practitioner who supervises the team  
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23 with individual and group supervisory arrangements.  
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### 29 *Combined*

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31 Within the combined program, a multidisciplinary approach is taken with practitioners  
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33 discussing the patients in case meetings to ensure that the psychological and nutritional  
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35 aspects complement each other in order to achieve the best outcome. It should be noted that  
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37 the interventions in the combined program are phased-in as it was found that asking  
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39 individuals to engage in numerous therapeutic activities at the same time resulted in high  
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41 drop-out rates.  
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### 47 **Primary Outcome Measures**

#### 48 *Medical Outcomes Survey Short-Form 36 (SF-36)*

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50 This 36-item measure is the short form of the original Medical Outcomes Survey <sup>34</sup> to  
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52 measure functional impairment and contains eight sub-sections: 1) physical activity  
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54 limitations due to health problems; 2) social activity limitations due to physical or emotional  
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3 problems; 3) usual role activity limitations due to physical health problems; 4) bodily pain; 5)  
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5 general mental health; 6) role activity limitations due to emotional problems; 7) vitality  
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7 (energy and fatigue); and 8) general health perceptions<sup>34</sup>. The items are scored so that higher  
8  
9 scores indicate greater functional ability. In terms of the psychometric properties of this  
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11 measure, reliability estimates for all sub-scales are good, exceeding a Cronbach's alpha  
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13 coefficient value of 0.70<sup>35</sup>. In terms of validity, the SF-36 correlates amply,  $r \geq 0.40$ , with the  
14  
15 frequency and severity of numerous symptoms and general health conditions<sup>36,37</sup>.

### 20 21 *Multidimensional Fatigue Inventory (MFI)*

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23 This 20-item measure contains five fatigue dimensions: general fatigue, physical fatigue,  
24  
25 mental fatigue, reduced motivation and reduced activity<sup>38</sup>. Items such as 'I tire easily' are  
26  
27 rated on a 5-point scale (1 = yes, that is true; 5 = no, that is not true) with lower scores  
28  
29 reflecting higher levels of fatigue. The MFI has good internal consistency with average  
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31 Cronbach's alpha coefficient equaling 0.84 across the sub-scales. Convergent validity based  
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33 on a sample of radiotherapy patients found correlations between the sub-scales and a visual  
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35 analog fatigue scale to be 0.77 for general fatigue, 0.70 for physical fatigue, 0.61 for reduced  
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37 activity, 0.56 for reduced motivation ( $p < 0.001$ ) to 0.23 for mental fatigue ( $p < 0.01$ )<sup>38</sup>.

### 42 43 **Secondary Outcome Measures**

#### 44 45 *CDC CFS Symptom Inventory*

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47 CDC CFS Symptom Inventory<sup>39</sup> was used to measure specific ME/CFS symptoms and  
48  
49 confirm diagnosis. This instrument is based upon the CDC case definition<sup>1</sup> and includes a  
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51 fatigue item and the eight distinct symptoms are also included in the CDC guidelines with an  
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53 additional ten associated symptoms. The format of this self-report measure is a six-point scale  
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55 of perceived frequency (0 = absent, 5 = all the time) and severity (0 = none, 5 = very severe).



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3 The psychometric properties of this instrument are good: Cronbach's alpha coefficient = 0.88;  
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5  $r = .74$  convergent validity with the Chalder Fatigue Scale <sup>40</sup>;  $r = -.68$  and  $-.87$  convergent  
6  
7 validity with the SF-36 'vitality' and 'bodily pain' sub-scales, respectively.  
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### 10 11 *Multidimensional Health Locus of Control Scale (MHLCS)*

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14 Multidimensional Health Locus of Control <sup>41-43</sup> measures perceived control via three distinct  
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16 sub-scales: 'internal', 'chance' and 'powerful others' which has two dimensions, that of  
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18 'doctors' and 'other people'. The instrument contains 18 items in total (six items each for the  
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20 'internal' and 'chance' scales and three items for both the 'powerful others' scales) and is  
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22 scored on a 6-point Likert scale from 'strongly agree' to 'strongly disagree'. Internal  
23  
24 reliability of the instrument is good with Cronbach's alpha coefficients ranging from 0.67 for  
25  
26 'powerful others' to 0.77 for 'internal'. The measure correlates positively and significantly  
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28 with associated scales from Levenson's <sup>44</sup> locus of control measure from which the MHLOC  
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30 was based, which demonstrates good convergent validity <sup>41</sup>.  
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### 40 **Statistical methods**

41 The data was initially screened for missing data. Four cases contained substantial amounts of  
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43 missing data; therefore these were excluded from the analysis (one individual from the  
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45 nutrition group and three from the combined group). Subsequent analyses were conducted on  
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47 complete data only. . The baseline data was subsequently of the quality for parametric tests,  
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49 except for the variables CDC CFS swollen lymph nodes and glands, memory problems,  
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51 abdominal pain and depression. However, the follow-up data suffered from high levels of  
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53 skew and kurtosis which was not substantially alleviated by data transformation. This  
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55 violated a key criterion for parametric testing, that of normality of distribution, so non-  
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3 parametric tests were selected. In addition, as the sample sizes in each individual treatment  
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5 group were small, the more conservative non-parametric tests were the preferred choice as  
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7 even though tests such as analysis of variance are generally robust against non-normality, this  
8  
9 does not hold true with small sample sizes. One-way analysis of variance tests and Kruskal-  
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11 Wallis tests (the former for those variables that met the criteria for parametric tests, and the  
12  
13 latter that did not) were used to investigate baseline variation and analysis of covariance  
14  
15 (ANCOVA) tests were used to account for this variation and test to for differences between  
16  
17 the three groups. Wilcoxon sign-rank tests were employed to look for differences over time  
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19 (baseline and 3-month follow-up) and if differences were significant, percentage change was  
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21 calculated. Please note, as this is an exploratory study with only one time-point and no  
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23 control group, any significant findings do not infer clinical significance, rather statistical  
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25 significance, and as such exact p-values are presented.  
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## 32 **Results**

### 33 **Participants**

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35 Of the 145 individuals who expressed an interest in the study, 142 time-one questionnaires  
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37 were returned, equating to a 97.9% response rate at baseline (two participants from the  
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39 psychology group and one from the combined group dropped out at this stage). Therefore,  
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41 excluding the four cases deleted due to insufficient data, 138 cases were used for baseline  
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43 analysis; 42 participants in the psychology group, 44 in the nutrition group and 52 in the  
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45 combined group. There was no significant association between gender and group ( $\chi^2 (2) =$   
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47  $0.179, p = .915$ ), all groups consisting of approximately one-fifth males (Table 1). There was  
48  
49 not a significant difference in age ( $F(2,135) = 0.001, p = 1.000$ ); in fact group means for age  
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51 were near identical at 42.881, 42.864 and 42.843 for psychology, nutrition and combined  
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53 groups, respectively. There was also a non-significant result for illness duration ( $F(2, 135) =$   
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0.252,  $p = .778$ ). Therefore, in terms of demographics, the groups were comparable. With regard to the outcome measures, there were significant differences between the groups in terms of the MFI sub-scale 'general fatigue' ( $F(2, 135) = 3.219, p = .043$ ), MFI 'physical fatigue' ( $F(2, 135) = 3.343, p = .038$ ) and the CDC CFS symptom 'swollen lymph nodes and glands' ( $H(2) = 7.161, p = .028$ ). To investigate the source of these differences, post-hoc tests were conducted (unrelated t-tests for the fatigue variables and Mann-Whitney tests for swollen lymph glands as the former did not meet criteria for parametric tests, all with Bonferroni correction for multiple comparisons). A significant difference was observed between the psychology and combined groups with regards to general fatigue ( $t(92) = -2.449, p = .016$ ) and physical fatigue ( $t(92) = -2.658, p = .009$ ) and also between the nutrition and psychology group in terms of the degree of lymph node and gland swelling ( $U = 635.00, p = .009$ ). Within the fatigue measures, the combined group reported significantly higher levels of both general and physical fatigued than the psychology group whereas those undertaking nutritional support stated a higher occurrence of swollen lymph nodes and glands.

### *Retention analysis*

Seventy-two of the original 138 participants (14 participants in the psychology group, 27 in the nutrition group and 31 in the combined group) completed the battery of measures at the 3-month follow-up, resulting in retention rates of 52.17% in the study overall, 33.33% in the psychology group, 61.36% in the nutrition group and 59.62% in the combined group. To investigate whether the individuals who did not complete the time-two measures were significantly different from those at baseline on demographic and outcome measures, a series of t-tests and Mann-Whitney tests were performed. Those that dropped out of the research (although still receiving treatment at the clinic) differed significantly in terms of age ( $t(136) = -2.227, p = .028$ ) and illness duration ( $t(136) = -2.549, p = .012$ ). Those who remained in the

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3 study were of significantly older age (mean age of those that remained in the study = 45.056,  
4 SD = 11.535; mean age of drop-outs = 40.400, SD =12.932) and longer illness duration than  
5 those who dropped out (mean age of those that remained in the study = 10.836, SD = 7.383;  
6 mean illness duration of drop-outs =7.571, SD = 7.472). Individuals who did not remain in  
7 the study did not differ significantly in terms of gender ( $\chi^2 (2) = 1.222, p = .269$ ) or any of the  
8 outcome measures.  
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### 19 **Comparisons within-groups across time**

#### 20 **Overall sample**

##### 21 *Primary outcomes*

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23 The following percentage change scores represent statistically significant changes, rather than  
24 clinically significant shifts, as this was an exploratory study. In the sample as a whole, there  
25 were improvements in all areas of the SF-36 (Table 2), with a 5.80% improvement in  
26 physical functioning, a 68.98% improvement in role limitations due to physical difficulties, a  
27 5.17% improvement in bodily pain, a 26.17% improvement in social functioning, a 5.77%  
28 improvement in general mental health, a 10.58% improvement in role limitations due to  
29 emotional difficulties, a 22.30% improvement in vitality, energy or fatigue and a 36.49%  
30 improvement in general health perception. When looking at the fatigue sub-scales of the MFI,  
31 all five sub-scales showed significant reductions in fatigue; 8.55% in general fatigue, 10.98%  
32 in physical fatigue, 8.81% in reduced activity, 12.96% in reduced motivation and 12.79% in  
33 mental fatigue.  
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##### 51 *Secondary outcomes*

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53 Within the CFS Symptom Inventory (Table 3), there were improvements in occurrence of  
54 sore throats (34.48%), diarrhea (42.47%), fatigue after exertion (16.32%), muscle aches or  
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3 muscle pains (21.01%), pain in joints (34.55%) chills (37.00%), unrefreshing sleep (19.55%),  
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5 sleeping problems (17.17%), headaches (24.94%), memory problems (17.86%), difficulty  
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7 concentrating (26.66%), sinus and nasal symptoms (26.38%), shortness of breath (29.28%),  
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9 sensitivity to light (28.62%) and depression (39.55%). There were no significant differences  
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11 from time-one to time-two in the MHLCS sub-scale of 'chance', 'powerful others' and 'other  
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13 people' (Table 3), however the MHLCS did illustrate significant increases in internal locus of  
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15 control (30.67%) and that of doctors (47.49%).  
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## 20 21 **Psychology group**

### 22 *Primary outcomes*

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24 Within the group of individuals who opted for a purely psychological intervention,  
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26 improvements were seen in physical functioning (16.75%), role limitations due to physical  
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28 problems (84.61%), social functioning (37.81%), general mental health (19.15%), vitality,  
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30 energy or fatigue (49.57%) and general health perceptions (19.01%). Also, all the MFI  
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32 fatigue scales decreased over a 3-month period, 13.58% in general fatigue, 17.74% in  
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34 physical fatigue, 23.20% in reduced activity, 11.42% in reduced motivation and 29.66% in  
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36 mental fatigue (Table 4).  
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### 40 *Secondary outcomes*

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42 Within those taking part in the psychology intervention, ratings of muscle aches or muscle  
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44 pains (10.34%), chills (23.40%), memory problems (44.73%), difficulty concentrating  
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46 (39.50%) and sensitivity to light (64.58%) decreased (Table 5). A significant increase of  
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48 17.56% was observed in internal locus of control, a decrease of 4.67% in the perception that  
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50 chance played an influential part in the individuals' lives (Table 5).  
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## 55 56 **Nutrition group**

### *Primary outcomes*

The nutrition group saw improvements in role limitations due to physical problems (75.28%), social functioning (24.93%), vitality, energy or fatigue (35.35%), and general health perceptions (29.73%). Once again, all the MFI fatigue scales decreased over a 3-month period, 13.39% in general fatigue, 15.00% in physical fatigue, 13.28% in reduced activity, 14.64% in reduced motivation and 12.83% in mental fatigue (Table 6).

### *Secondary outcomes*

In the nutrition group, numerous symptom-related indices also showed improvements (Table 7); sore throat (56.23%), swollen lymph glands (21.21%), fatigue after exertion (13.90%), muscle aches or muscle pains (20.56%), chills (40.74%), nausea (16.42%) and abdominal pain (20.16%). No significant differences were found from baseline to follow-up in perceived control (Table 7).

## **Combined group**

### *Primary outcomes*

In terms of general health as gauged by the SF-36 measure, the group who received both psychological and nutritional intervention reported reductions in role limitations due to physical difficulties (57.02%), social functioning (22.61%), role limitations due to emotional difficulties (29.47%) and general health perceptions (26.45%). Only one measure of fatigue, that of physical fatigue, saw significant improvements over time (6.42%) in the combined group (Table 8).

### *Secondary outcomes*

Those in the combined group saw significant reductions over the 3-month interval in diarrhea (47.97%), fatigue after exertion (19.20%), chills (40.23%), headaches (36.18%) and sinus and nasal symptoms (20.56%) (Table 9). No significant differences were found from baseline to

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3 follow-up in perceived control as measured by the MHLCS in the combined treatment group  
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5 (Table 9).  
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### 19 **Comparisons across groups**

20 With correction for baseline variation, there were no significant differences between the three  
21 groups in terms of change scores.  
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## 27 **Discussion**

### 28 **Key results**

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31 There was statistically significant (rather than known clinically significant) change over time  
32 of numerous measures in all groups investigated. However, this is not to say that these  
33 changes were due to the interventions as the design of this study was exploratory, rather than  
34 experimental (please see below for a further critique of the design). The psychology group  
35 contained the most significant findings, including those concerned with daily functioning,  
36 fatigue, locus of control and cognitive CDC CFS specific symptoms. These findings appear  
37 consistent with outcomes from other psychological interventions<sup>3;4;6</sup>. As expected, changes in  
38 perceived control were not observed in the nutrition group as this is not an area that is  
39 targeted in this program. However, the more immune-type symptoms such as sore throat and  
40 swollen lymph nodes or glands did see significant reductions over time as would be  
41 envisaged in treatment protocols based upon nutritional expertise. The group that exhibited  
42 the least significant findings was the combined group and, as noted below, this may be due to  
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3 the greater general severity of symptoms in this group and the need for a more lengthy  
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5 intervention. Nevertheless, considering the small sample sizes in the groups at follow-up,  
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7 these results are very promising and warrant further attention.  
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### 10 11 **Interpretation**

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13 As noted previously<sup>31</sup> individualized treatment protocols which include a range of tailored  
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15 strategies is a favorable direction for dealing with a complex and multi-system disorder such  
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17 as ME/CFS. The present study has demonstrated that such interventions may be useful in  
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19 lowering symptomatology, improving functioning and helping individuals gain a greater  
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21 sense of control over their health status.  
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### 25 26 27 **Limitations and Generalisability**

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29 This study was a preliminary study in a naturalistic setting and as such did not have a robust  
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31 design. There was not a control group and the participants were not randomly assigned to  
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33 groups, therefore the results should be treated with caution. In order to ascertain whether the  
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35 changes in symptom and functional reports were due to the interventions, a randomized  
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37 control trial should be conducted (RCT). Also, there was a high drop-out rate from time-one  
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39 to time-two and this rate differed across groups. The highest drop-out rate was in the  
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41 psychology group; whilst we cannot be sure why this occurred, it is postulated that the  
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43 retention was poor in the group as the individuals in the psychology program had more  
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45 activities to engage in and may have felt overburdened with the research questionnaires in  
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47 addition to their session and homework (this would not be the case in the combined group as  
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49 the therapeutic activities are phased-in as mentioned above).  
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3 In this study, each individual was guided to appropriate treatment within an initial screening  
4 with clinic staff; therefore the group was dependent on the nature of the individual's  
5 symptoms and their personal choice as the programs on offer were privately funded. Notably,  
6 the groups did differ in general and physical fatigue with participants in the combined groups  
7 reporting greater fatigue than those in the psychology group which suggests that this group's  
8 general symptomatology was more severe. The combined group illustrated less change over  
9 time compared to the psychology and nutrition groups and it is feasible to infer that  
10 individuals with a greater number and degree of complaints are referred to the combined  
11 group within the clinic. Also, those in the combined group will not experience the intensity of  
12 each intervention as this has been demonstrated to result in non-compliance; therefore,  
13 changes in outcome measures in this group may not be noted at an interval of three months.  
14 Further studies underway presently will investigate follow-ups at 6- and 12-months to  
15 identify whether the findings here are maintained over time and also whether those with  
16 greater symptom severity benefit with a longer intervention. The results from this study will  
17 then inform plans for an RCT of the clinic's practices. As the participants were self-selected  
18 onto these programs, the findings lack generalizability; future work should sample from the  
19 overall ME/CFS population and be randomly-assigned to groups in order to make valid  
20 assumptions regarding the illness-group as a whole.  
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### 45 **Funding**

46 No external funding was obtained for this research; the work was accomplished in-house at  
47 the clinic in question.  
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### **Data Sharing**

Dataset available from the corresponding author at drarroll@theoptimumhealthclinic.com.

Consent was not obtained for data sharing but the presented data are anonymised and risk of identification is low.

### **Contributorship**

Alex Howard made substantial contributions to the conception and design and acquisition of data, whilst Megan Arroll made a substantial contribution to the analysis and interpretation of data. Both authors made a substantial contribution to the drafting of the article and revisions for the critical review of important intellectual content. Final approval of the version to be published was also granted by both authors.

### **Acknowledgements**

We would like to thank Dr Tomas Ros for preparing the questionnaire spreadsheet, Niki Gratrix for helping in setting-up the study and Dr Andy McLellan and Val Duschinsky for proof-reading and editing.

### **Competing Interests**

Alex Howard is the founder and CEO of The Optimum Health Clinic and Megan Arroll is the Director of Research at the Optimum Health Clinic, where this study was conducted.

1  
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3 List of abbreviations

4  
5 ME: myalgic encephalomyelitis

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7 CFS: Chronic Fatigue Syndrome

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9 NICE: National Institute for Health and Clinical Excellence

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11 CBT: Cognitive Behavioral Therapy

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13 GET: Graded Exercise Therapy

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15 APT: Adaptive Pacing Therapy

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17 SMC: specialist medical care

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19 CAM: Complementary and Alternative Medicine

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21 NLP: Neuro-linguistic Programming

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23 EFT: Emotional Freedom Technique

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25 SF-36: Medical Outcomes Survey Short-Form 36

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27 MHLCS: Multidimensional Health Locus of Control Scale

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29 MFI: Multidimensional Fatigue Inventory

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31 RCT: randomized controlled trial

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**Table 1. Demographics for gender, age and illness duration across the three treatment groups**

		Mean	SD	95% CI for Mean		Test statistic	p-value
				Lower	Upper		
Gender	Psychology	9 (21.4%) <sup>d</sup>				.179 <sup>c</sup>	.915
	Nutrition	8 (18.2%) <sup>d</sup>					
	Combined	11 (21.2%) <sup>d</sup>					
	Total	28 (20.3%) <sup>d</sup>					
Age	Psychology	42.881	13.986	38.523	47.239	.000 <sup>a</sup>	1.000
	Nutrition	42.864	12.504	39.062	46.665		
	Combined	42.843	11.125	39.714	45.972		
	Total	42.861	12.406	40.765	44.957		
Illness duration	Psychology	8.874	8.252	6.302	11.445	.252 <sup>a</sup>	.778
	Nutrition	10.023	7.375	7.781	12.265		
	Combined	9.625	7.291	7.595	11.655		
	Total	9.523	7.580	8.247	10.800		

Table 2. Comparisons across time within the primary outcome measures within the overall sample

	<i>N</i>	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	<i>p</i> -value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
SF-36 Physical Functioning	72	18.075	41.644	66.667	25.694	47.222	77.583	-3.120	.002**
SF-36 Role limitations physical	71	0	0	0	0	25	50	-4.321	.001***
SF-36 Bodily pain	72	32.5	56.25	79.375	32.500	67.500	90	-2.240	.025*
SF-36 Social functioning	72	12.5	25	50	12.500	50	75	-4.504	.001***
SF-36 General mental health	72	53	60	75	57	68	80	-2.665	.008**
SF-36 Role limitations emotional	72	0	33.317	100	41.667	66.670	100	-3.159	.002**
SF-36 Vitality Energy or Fatigue	72	10	15	35	11.250	30	45	-4.205	.001***
SF-36 General health perceptions	72	20	30	40	25	40	50	-3.996	.001***
MFI General Fatigue	72	15	18	19	12	16	19	-3.692	.001***
MFI Physical Fatigue	72	15	18	20	12	16	19	-4.591	.001***
MFI Reduced Activity	72	11	15	18	9	14	17	-2.421	.015*
MFI Reduced Motivation	72	8	10	13.750	7	9	12	-2.986	.003**
MFI Mental Fatigue	72	11	14	18	8.250	12.500	15	-3.661	.001***



Table 3. Comparisons across time within the secondary outcome measures within the overall sample

	<i>N</i>	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			<i>z</i> -statistic	<i>p</i> -value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
CDC CFS Sore throat	70	0	1.5	4	0	1	2	-2.257	.024*
CDC CFS Swollen lymph nodes/glands	71	0	2	6	0	1	4	-1.567	.115
CDC CFS Diarrhea	72	0	1	4	0	0	2	-2.481	.013*
CDC CFS Fatigue after exertion	72	9	15	20	6.500	12	16	-3.574	.001***
CDC CFS Muscle aches/pains	72	4	9	12	1.250	6	12	-3.995	.001***
CDC CFS Pain in joints	70	0	4	9	0	1	6	-2.908	.004**
CDC CFS Fever	70	0	0	1	0	0	0	-1.667	.095
CDC CFS Chills	72	0	2	6	0	0	2.113	-4.206	.001***
CDC CFS Unrefreshing sleep	72	6	12	16	4	6	16	-2.295	.022*
CDC CFS Sleeping problems	72	2	8	12	2	4	12	-1.983	.047*
CDC CFS Headaches	71	1	6	9	1	6	11.250	-2.850	.004**

CDC CFS Memory Problems	72	2	6	12	1	6	11.250	-2.053	.040*
CDC CFS Difficulty Concentrating	72	2.500	8.500	12	1	6	12	-3.440	.001***
CDC CFS Nausea	71	0	1	4	0	2	6	-0.898	.369
CDC CFS Abdominal Pain	71	0	2	6	0	2	6	-1.932	.053
CDC CFS Sinus nasal symptoms	71	1	4	6	0	1	6	-2.862	.004**
CDC CFS Shortness of breath	69	0	2	4	0	1	4	-2.402	.016*
CDC CFS Sensitivity to light	71	0	2	6	0	1	4	-2.388	.017*
CDC CFS Depression	72	0	2	6	0	1	4	-2.297	.022*
MHLCS Internal	72	0.528	0.681	0.799	0.611	0.722	0.889	-2.962	.003**
MHLCS Chance	72	0.222	0.344	0.417	0.201	0.320	0.444	-1.552	.121
MHLCS Powerful Others	72	0.333	0.389	0.500	0.306	0.361	0.500	-1.601	.109
MHLCS Doctors	72	0.0833	0.139	0.222	0.083	0.111	0.194	-2.381	.017*
MHLCS Other People	72	0.194	0.250	0.3056	0.174	0.250	0.278	-1.186	.236

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Table 4. Comparisons across time within the primary outcome measures within the psychology group

	N	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	p-value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
SF-36 Physical Functioning	14	25.008	44.444	58.367	27.083	69.450	84.700	-2.707	.007**
SF-36 Role limitations physical	14	0	0	25	0	50	81.250	-2.379	.017*
SF-36 Bodily pain	14	39.375	57.500	80.625	32.500	72.500	90	-1.195	.232
SF-36 Social functioning	14	25	37.500	50	34.375	56.250	90.625	-2.689	.007**
SF-36 General mental health	14	47	62	80	67	76	88	-2.497	.013*
SF-36 Role limitations emotional	14	24.974	100	100	58.336	100	100	-.842	.400
SF-36 Vitality Energy or Fatigue	14	10	20	40	28.750	45	52.500	-3.066	.002**
SF-36 General health perceptions	14	23.750	30	41.250	31.250	40	63.750	-2.561	.010*
MFI General Fatigue	14	14	16.500	18.500	9.750	13.500	18.500	-2.657	.008**
MFI Physical Fatigue	14	13.750	16	19.250	8.750	13	16.750	-2.810	.005**
MFI Reduced Activity	14	9.750	12.500	18.250	7	9	14.500	-2.142	.032*

MFI Reduced Motivation	14	5.750	8	11.750	4.750	5.500	8.250	-2.131	.033*
MFI Mental Fatigue	14	11.750	15.500	18	6.500	9.500	15	-2.950	.003*

**Table 5. Comparisons across time within the secondary outcome measures within the psychology group**

	<i>N</i>	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	<i>p</i> -value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
CDC CFS Sore throat	14	0	2	6	0	0	2.500	-1.365	.172
CDC CFS Swollen lymph nodes/glands	14	0	0.5	2.5	0	0	4	-.341	.733
CDC CFS Diarrhea	14	0	0	2	0	0	2.500	-.730	.465
CDC CFS Fatigue after exertion	14	9	12	20	7.750	9	14	-1.550	.121
CDC CFS Muscle aches/pains	14	4	9	15.25	1.750	9	14	-2.145	.032*
CDC CFS Pain in joints	14	0	2.5	9	0	0.500	4.500	-1.778	.075
CDC CFS Fever	14	0	0	1.5	0	0	0.500	-.135	.892
CDC CFS Chills	14	0	1	6.75	0	0	4.500	-1.970	.049*
CDC CFS Unrefreshing sleep	14	9	12	15.25	5.500	9	16	-.802	.422

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CDC CFS Sleeping problems	14	2.75	7	12	1	3	9.750	-1.738	.082
CDC CFS Headaches	14	1	2.5	6	0.750	1	6.750	-1.200	.230
CDC CFS Memory Problems	14	1	6	9	0.750	1	6.750	-1.965	.049*
CDC CFS Difficulty Concentrating	14	3.5	9	17	1	5	6.750	-2.809	.005**
CDC CFS Nausea	14	0	0	4.25	0	1	4.500	-.213	.832
CDC CFS Abdominal Pain	14	0	2	5.25	0	0	6	-.343	.732
CDC CFS Sinus nasal symptoms	14	1	3.5	4.5	0	1.500	4.500	-.724	.469
CDC CFS Shortness of breath	14	0	1.5	4.5	0	0.500	2.50	-1.556	.120
CDC CFS Sensitivity to light	14	0	1	4.5	0	0	1.250	-1.973	.049*
CDC CFS Depression	14	0	1.5	6	0	0	2	-1.614	.106
MHLCS Internal	14	0.556	0.653	0.840	0.611	0.872	0.923	-2.983	.003**
MHLCS Chance	14	0.326	0.417	0.535	0.167	0.361	0.451	-2.594	.009**
MHLCS Powerful Others	14	0.319	0.375	0.451	0.299	0.356	0.431	.000	1.000
MHLCS Doctors	14	0.083	0.125	0.194	0.083	0.083	0.174	-1.122	.262
MHLCS Other People	14	0.194	0.236	0.285	0.194	0.222	0.257	-.118	.906

Table 6. Comparisons across time within the primary outcome measures within the nutrition group

	<i>N</i>	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	<i>p</i> -value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
SF-36 Physical Functioning	27	16.7	44.444	77.778	16.700	38.889	77.778	-1.136	.256
SF-36 Role limitations physical	26	0	0	0	0	25	25	-2.878	.004**
SF-36 Bodily pain	27	32.5	45	67.5	35.200	67.500	90	-1.800	.072
SF-36 Social functioning	27	0	25	50	12.500	37.500	75	-2.476	.013*
SF-36 General mental health	27	52	60	72	52	64	80	-1.696	.090
SF-36 Role limitations emotional	27	0	0	100	0	66.670	100	-1.788	.074
SF-36 Vitality Energy or Fatigue	27	5	15	35	15	25	45	-2.734	.006**
SF-36 General health perceptions	27	20	25	35	25	35	45	-2.157	.031*
MFI General Fatigue	27	15	18	19	12	15	19	-2.548	.011*
MFI Physical Fatigue	27	14	18	19	11	16	19	-2.791	.005**
MFI Reduced Activity	27	10	14	18	8	13	16	-2.164	.030*
MFI Reduced Motivation	27	8	10	12	6	8	12	-1.985	.047*

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MFI Mental Fatigue	27	11	13	16	8	13	15	-2.082	.037*
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Table 7. Comparisons across time within the secondary outcome measures within the nutrition group

	<i>N</i>	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	p-value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
CDC CFS Sore throat	27	8	1	2	0	1	2	-2.211	.027*
CDC CFS Swollen lymph nodes/glands	26	20	0	5	0	1	12	-2.051	.040*
CDC CFS Diarrhea	27	16	0	1	0	0	1	-1.649	.099
CDC CFS Fatigue after exertion	27	25	9	16	4	12	20	-2.209	.027*
CDC CFS Muscle aches/pains	27	20	4	9	2	6	12	-2.901	.004**
CDC CFS Pain in joints	26	20	0.750	4	0	1	6	-1.827	.068
CDC CFS Fever	26	9	0	0	0	0	0	-1.254	.210
CDC CFS Chills	27	12	1	3	0	0	1	-3.401	.001***
CDC CFS Unrefreshing sleep	27	25	6	12	4	6	16	-1.421	.155
CDC CFS Sleeping problems	27	25	1	9	2	4	16	-0.190	.849

CDC CFS Headaches	26	25	0.750	6	1	3	6	-1.895	.058
CDC CFS Memory Problems	27	25	2	6	2	6	12	-0.338	.735
CDC CFS Difficulty Concentrating	27	25	2	6	4	6	12	-1.196	.232
CDC CFS Nausea	26	25	0	2	0	1	6	-2.407	.016*
CDC CFS Abdominal Pain	26	16	0.750	3	0	3	6	-2.322	.020*
CDC CFS Sinus nasal symptoms	26	20	1	3.500	0	1	9	-1.244	.213
CDC CFS Shortness of breath	25	20	0	2	0	1	3	-1.651	.099
CDC CFS Sensitivity to light	26	25	0	4	0	2	6	-1.890	.059
CDC CFS Depression	27	20	0	4	0	2	4	-1.584	.113
MHLCS Internal	27	0.944	0.528	0.667	0.528	0.639	0.778	-.687	.492
MHLCS Chance	27	0.694	0.222	0.333	0.222	0.333	0.472	-.143	.886
MHLCS Powerful Others	27	0.694	0.333	0.389	0.278	0.361	0.528	-1.843	.065
MHLCS Doctors	27	0.417	0.0833	0.139	0.083	0.139	0.222	-1.686	.092
MHLCS Other People	27	0.833	0.222	0.278	0.167	0.250	0.306	-1.697	.090



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**Table 8. Comparisons across time within the primary outcome measures within the combined group**

	<i>N</i>	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	<i>p</i> -value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
SF-36 Physical Functioning	31	22.200	33.333	61.111	27.778	55.556	72.222	-1.850	.064
SF-36 Role limitations physical	31	0	0	0	0	25	25	-2.225	.026*
SF-36 Bodily pain	31	32.500	45	80	32.500	57.500	80	-1.048	.294
SF-36 Social functioning	31	12.500	25	37.500	12.500	37.500	62.500	-2.426	.015*
SF-36 General mental health	31	56	60	72	56	68	76	-0.524	.600
SF-36 Role limitations emotional	31	0	33.333	100	66.667	66.670	100	-2.313	.021*
SF-36 Vitality Energy or Fatigue	31	10	15	30	10	25	40	-1.558	.119
SF-36 General health perceptions	31	20	30	40	25	40	55	-2.423	.015*
MFI General Fatigue	31	16	18	19	14	17	19	-0.854	.393
MFI Physical Fatigue	31	15	19	20	13	17	20	-2.364	.018*

MFI Reduced Activity	31	12	16	18	11	16	18	-0.070	.944
MFI Reduced Motivation	31	9	11	14	8	10	13	-1.082	.279
MFI Mental Fatigue	31	10	14	18	11	13	16	-1.586	.113

**Table 9. Comparisons across time within the secondary outcome measures within the combined group**

	<i>N</i>	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	<i>p</i> -value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
CDC CFS Sore throat	29	0	0	3.500	0	1	2.030	-0.567	.571
CDC CFS Swollen lymph nodes/glands	31	0	2	4	0	1	3	-0.725	.468
CDC CFS Diarrhea	31	0	2	4	0	0	2	-1.996	.046*
CDC CFS Fatigue after exertion	31	8	15	20	6	12	16	-2.392	.017*
CDC CFS Muscle aches/pains	31	2	6	12	1	6	9	-1.908	.056
CDC CFS Pain in joints	30	0	1.500	8	0	1	4	-1.680	.093
CDC CFS Fever	30	0	0	1	0	0	0.720	-1.383	.167
CDC CFS Chills	31	0	2	6	0	1	2.150	-2.049	.040*

CDC CFS Unrefreshing sleep	31	6	12	16	4	9	16	-1.513	.130
CDC CFS Sleeping problems	31	1	6	12	2	4	9	-1.794	.073
CDC CFS Headaches	31	2	6	9	1	3	6	-2.807	.005**
CDC CFS Memory Problems	31	2	6	12	1	3	9	-1.446	.148
CDC CFS Difficulty Concentrating	31	2	8	12	1	6	12	-1.899	.058
CDC CFS Nausea	31	0	1	6	0	2	6	-0.855	.392
CDC CFS Abdominal Pain	31	0	1	6	0	2	4	-0.598	.550
CDC CFS Sinus nasal symptoms	31	0	5	8	0	1	4	-2.482	.013*
CDC CFS Shortness of breath	30	0	2	6	0	1	4	-0.976	.329
CDC CFS Sensitivity to light	31	0	1	6	0	1	4	-0.787	.431
CDC CFS Depression	31	0	2	6	0	1	6	-1.304	.192
MHLCS Internal	31	0.556	0.694	0.861	0.639	0.750	0.889	-1.755	.079
MHLCS Chance	31	0.222	0.333	0.361	0.167	0.306	0.417	-0.672	.501
MHLCS Powerful Others	31	0.333	0.389	0.500	0.333	0.389	0.500	-0.577	.564
MHLCS Doctors	31	0.111	0.167	0.222	0.083	0.139	0.500	-1.384	.166
MHLCS Other People	31	0.167	0.250	0.278	0.194	0.250	0.306	-0.213	.831

\* significant at .05 level

\*\* significant at .01 level

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For peer review only

## Abstract

Background: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a condition characterized by severe and persistent fatigue, neurological disturbances, autonomic and endocrine dysfunctions and sleep difficulties that have a pronounced and significant impact on individuals' lives. Current NICE guidelines within the United Kingdom suggest that this condition should be treated with cognitive behavioral therapy and/or graded exercise therapy where appropriate. There is currently a lack of evidence base concerning ~~other, more integrative interventions~~ [alternative techniques](#) that may be beneficial to those with ME/CFS.

Objectives: This study aimed to ~~investigate evaluate~~ whether three ~~patient-centered treatment~~ modalities of psychology, nutrition and combined treatment, influenced symptom report measures in those with ME/CFS over a 3-month time period and whether there were significant differences in these changes between groups.

Design and setting: This is a preliminary prospective study with one follow-up point conducted at a private secondary health care facility in London, UK.

Participants: One-hundred and thirty-eight individuals (110 females, 79.7%; 42 participants in psychology, 44 in nutrition and 52 in combined) participated at baseline and 72 participants completed the battery of measures at follow-up (52.17% response rate; 14, 27, 31 participants in each group, respectively).

Outcome measures: Self-report measures of ME/CFS symptoms, functional ability, multidimensional fatigue, [and](#) perceived control ~~and maladaptive stress~~.

Results: Baseline comparisons showed those in the combined group had higher levels of fatigue. At follow-up, all groups saw improvements in fatigue, functional physical [and](#) symptomatology ~~and maladaptive stress~~; those within the psychology group also experienced a shift in perceived control over time.

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Conclusions: This study provides early evidence that [psychological, nutritional and combined patient centered](#) techniques for the treatment of ME/CFS may influence symptomatology, fatigue, function, [and](#) perceived control ~~and inappropriate responses to stressors~~. However, these results must be viewed with caution as the allocation to groups was not randomized, there was no control group and the study suffered from high drop-out rates.

### **Summary**

#### **Article focus**

- This preliminary prospective study investigated three (psychological, nutritional and combined) tailored [patient centered](#) interventions for ME/CFS over time.
- Differences between the reported changes over time between groups were also assessed.

#### **Key messages**

- [Psychological, nutritional and combined Patient centered](#) approaches for the management of ME/CFS influence symptomatology over time in some individuals with this disorder.
- Self-reported functional ability (physical and social) are influenced following tailored interventions lasting 3 months.
- This study provides preliminary evidence that tailored psychological, nutritional and combined interventions ~~may be effective treatments for~~ [may influence self-reported symptomatology in](#) some people with ME/CFS; however due to the study's methodological limitations, it is important that ~~these findings is potential treatment effect is are~~ -investigated further in high quality randomized controlled studies.

#### **Strengths and limitations of this study**

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7 • The findings here are an initial step to fill the gap in the extant literature regarding the  
8 utility of tailored ~~and~~ multidisciplinary ([psychological, nutritional and combined](#)) ~~and~~  
9 ~~patient-centered~~ treatments for ME/CFS.  
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12 • There is bias in this study as the participants were self-selected in the sense that they  
13 chose to attend the clinic and which treatment option they preferred (with advice), i.e. the  
14 study was not randomized.  
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17 • There were low retention rates in this study which may constitute a bias in that those  
18 who remained in the study may have experienced benefits and those who experienced little or  
19 no benefits may have dropped out.  
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### **Introduction**

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33 Chronic Fatigue Syndrome or myalgic encephalomyelitis (ME/CFS) is a condition  
34 characterized by prolonged and debilitating fatigue, although the exact cause of this disorder  
35 is still under debate. Due to the lack of a definitive biological marker, diagnosis is made on  
36 the basis of the exclusion of other explanatory conditions. The most widely used case  
37 definition by the Centers for Disease Control <sup>1</sup> states that there must be at least six months  
38 severe fatigue of new and definite onset, not the result of ongoing exertion, not alleviated by  
39 rest and resulting in reduced levels of physical activity. The CDC definition also sets out a  
40 series of minor complaints that must accompany the fatigue (cognitive impairment, sore  
41 throat, tender cervical or axillary lymph nodes, muscle pain, multi-joint pain, headaches of a  
42 new type, pattern or severity at onset, unrefreshing sleep and post-exertion malaise), with  
43 individuals needing to have the occurrence of four or more symptoms to be diagnosed with  
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7 ME/CFS. Estimates of the prevalence of ME/CFS have been made as low as 3 and as high as  
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9 2,800 per 100,000 <sup>2</sup>.

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12 The most widely researched strategies for alleviating the symptoms of ME/CFS are Cognitive  
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14 Behavior Therapy (CBT) and Graded Exercise Therapy (GET). Two reviews of studies on  
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16 CBT <sup>3,4</sup> found that it significantly improved physical functioning in adult out-patients as  
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18 compared with medical management, counseling, guided support, education and support or  
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20 relaxation. Regarding GET, a systematic review illustrated that this form of therapy was  
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22 potentially beneficial for people with ME/CFS, especially when combined with a patient  
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24 education programme <sup>5</sup>. However, drop-out rates were higher in the GET groups [than control](#)  
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26 [groups](#) suggesting that individuals with ME/CFS are averse to this type of therapy. Recently,  
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28 a large scale, longitudinal study investigating CBT, GET, Adaptive Pacing Therapy (APT)  
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30 and specialist medical care (SMC) [which had very low drop-out rates](#), found that CBT and  
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32 GET (when added to SMC) were moderately effective outpatient treatments for this patient  
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34 group as opposed to APT or SMC alone <sup>6</sup>.

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37 Although CBT and GET studies have shown some promising outcomes, there is no known  
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39 cure for ME/CFS. Therefore the National Institute for Health and Clinical Excellence (NICE)  
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41 <sup>7</sup> recommends a number of symptom management strategies and interventions aimed at  
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43 helping individuals to cope with their condition and reduce physical deconditioning brought  
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45 about by the illness. Pharmacological interventions are, at times, suggested for patients with  
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47 poor sleep or pain, for instance, low-dose antidepressants, as these have been shown to be  
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49 effective <sup>8-14</sup>. However, patient expectations must be realistic as the drugs may help elevate  
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51 mood and psychological outlook but not reduce fatigue and other symptomatology associated  
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7 with ME/CFS<sup>15</sup>. Numerous drugs such as thyroxin, hydrocortisone and antiviral agents are  
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9 not advised by NICE due to contradictory findings<sup>16,17</sup>.

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12 In terms of function and quality of life management, NICE offers general advice concerning  
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14 sleep management, appropriate rest periods, and pacing. Sleep hygiene instruction, together  
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16 with pharmacological treatment tailored to the individual patient can be beneficial in  
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18 combating fatigue<sup>18</sup>. Dietary management may also reduce symptomatology for those with  
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20 concurrent irritable bowel syndrome (IBS). ~~Management approaches recommended for IBS,~~  
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22 ~~such as diet restriction, are thus also recommended for those with ME/CFS<sup>19</sup>, although this is~~  
23  
24 ~~not currently recommended by NICE.~~ Dietary supplementation has been investigated in  
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26 relation to ME/CFS. Fatty acids<sup>20</sup>, folic acid<sup>21</sup>, vitamin C<sup>22</sup>, co-enzyme Q10<sup>23</sup>, magnesium  
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28<sup>24</sup>, multivitamins<sup>25</sup> and minerals<sup>26</sup> have all been shown to reduce symptomatology in  
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30 ME/CFS patients. However other studies have shown conflicting findings with regard to  
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32 nutritional supplementation, therefore it is perhaps wise to treat with supplements on a case-  
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34 by-case basis<sup>27,28</sup>.

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37 Due to the lack of clear and definitive treatment strategies, individuals often seek out  
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39 Complementary and Alternative Medicines (CAM). Although NICE does not recommend the  
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41 use of CAM they do acknowledge that many people with ME/CFS use such therapies and  
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43 find them beneficial for symptom management. This view is due to the lack of published  
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45 evidence for the effectiveness of these treatments. Examples of CAM treatments used by  
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47 individuals with ME/CFS include religious healing, massage therapy, relaxation, meditation,  
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49 homeopathy, acupuncture, naturopathy and herbal therapies<sup>29,30</sup>; patient satisfaction with  
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51 such approaches as CAM has been high, over 80% in some instances<sup>29</sup>. A recent systematic  
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53 review of such interventions identified 70 controlled clinical trials (randomized and non-  
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7 randomized) and found that 86% of these studies illustrated at least one positive effect, with  
8 74% showing a decrease of illness-related symptomatology <sup>31</sup>. Meditative or mindfulness  
9 approaches warranted further investigation based on these results as did supplement programs  
10 of magnesium, l-carnitine, and S-adenosylmethionine. A subsequent review based solely on  
11 randomized controlled trials (RCTs) of CAM techniques identified 26 such studies and  
12 observed that qigong, massage and tuina (approaches based within Chinese Traditional  
13 Medicine and based upon relaxation and connection with the body) illustrated positive effects  
14 as did supplementation studies utilizing nicotinamide adenine dinucleotide (NADH) and  
15 magnesium <sup>32</sup>. However, within both reviews it was noted that the methodological quality of  
16 reporting was poor and the sample sizes in these studies were small; hence ability to draw  
17 strong conclusions on the efficacy of CAM methods is limited. Porter et al. (2010) <sup>31</sup> did note  
18 that ~~patient centered~~, individualized treatment protocols which include a range of tailored  
19 strategies are a promising area for further investigation for this complex, multi-system illness.  
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### 37 Objectives

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39 There is still much debate and uncertainty regarding ~~alternative interventions the most~~  
40 ~~effective treatment for for those with~~ -ME/CFS. ~~A r~~Recent reviews of CAM techniques <sup>31</sup>  
41 highlight the need for further exploration of ~~patient centered and~~ individually tailored  
42 interventions for the alleviation of the condition's often debilitating and intrusive  
43 symptomatology. This study therefore aims to provide preliminary evidence for the utility of  
44 three types of ~~patient centered~~ approaches (~~psychological, nutritional and combined~~) to the  
45 management of ME/CFS over time (baseline and follow-up) offered at a private health-care  
46 center in the UK.  
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## **Methods**

### **Study design and setting**

This preliminary prospective study aimed to [investigate whether psychological, nutritional and combined approaches to the ~~explore the effectiveness of three~~ treatment ~~of options offered to individuals with~~ ME/CFS \[influenced symptom report measures over a 3-month time period and whether there were significant differences in these changes between groups.\]\(#\)](#)

The research was conducted at one private secondary health care facility. All potential patients of the clinic are first asked to complete a comprehensive symptom profile and medical history, including questions relating to triggering factors, psychology sub-types and structural/biological sub-types (this is distinct from the research data collected). Subsequent to this, every individual receives a 15-minute screening with one of the practitioners (please note, this was not either of the authors of the current study) who recommends the best course of action for his/her needs; this will be the psychology-related interventions, nutritional advice and support or a combination of the two.

All individuals requesting treatment at the private care setting were offered the opportunity to participate in the study. Those that expressed an interest (N = 145) were emailed a spreadsheet that contained the questionnaires and asked to complete it at their convenience. Informed consent was obtained prior to the completion of the questionnaires and the study was approved by the University of East London Ethics Committee. Participants were told that they could withdraw from the study at any time and that withdrawal would not affect their care at the clinic. Participants were able to ask questions at any point in the study and no deception was used as the participants were informed of the nature of the research program

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7 before they agreed to participate. Subsequently, participants were requested to complete the  
8 questionnaire pack on a second occasion, three months from the baseline measures.  
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### 10 11 12 *Psychology*

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14 The clinic offers a 3-month intervention which consists of a combination of Neuro-linguistic  
15 Programming (NLP), Emotional Freedom Technique (EFT), life coaching and  
16 hypnotherapy/self-hypnosis constructed in a manner specific to the needs of those with  
17 ME/CFS. The primary aim of this approach is to reduce the anxiety that is associated with  
18 having a debilitating and unpredictable condition, improve emotional well-being and help  
19 individuals slowly manage and increase their activity within their own limits (i.e. pacing).  
20

21 The program is offered as a series of group sessions and the peer support is seen as an  
22 important component of the intervention, which is solidified via the use of moderated online  
23 support forums, narratives of previous clients' experiences and online materials that can be  
24 accessed as often as necessary. In addition to, or as an alternative to this course, individuals  
25 receive a series of one-to-one sessions and for the most severely affected ME/CFS patients,  
26 telephone sessions are arranged and support materials can be accessed in their own homes.  
27

28 Over the three-month period of this preliminary study, the participants experienced one of  
29 three treatment options. The first option included 13 hours of practitioner contact time in a  
30 mix of group training in person, group telephone conference calls and one-to-one telephone  
31 sessions, the second option was four hours of one-to-one telephone sessions and the final  
32 option was three hours of in person sessions. Participants all had access to various support  
33 materials which included CDs and online resources. The amount of time spent on these was  
34 patient-led, but was in the region of a further six hours. All the practitioners offering this  
35 option are qualified in hypnotherapy, NLP, life coaching and EFT and undergo an intensive  
36 period of training in the clinic's own integrative approach (please see Howard and Arroll <sup>33</sup>  
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7 for more details of this approach) and ongoing supervision (individual and group supervision  
8 on a biweekly basis) from the department director, who is the only senior practitioner in the  
9 team.  
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### 12 13 14 *Nutrition*

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16 Tailored nutritional therapy is achieved via one-to-one consultations with individuals. To  
17 begin, a very detailed history is taken based upon the information given in the  
18 aforementioned symptom profile. Qualified nutritional therapists (who have been given  
19 specialist training regarding ME/CFS from the clinic) then suggest tests consistent with  
20 symptomatology, for instance the Adrenal Stress Index Test, comprehensive stool  
21 analysis/gastro-intestinal function, vitamin & mineral status, etc. Results from these tests are  
22 then used to compose an evidence-driven diet and supplement program. As most cases of  
23 ME/CFS are complex involving multiple body systems, this process is often iterative and  
24 follow-up consultations are necessary to check progress and make alterations to the protocol.  
25  
26 The nutritional therapy program consists of an initial one-hour evaluation (which includes the  
27 tailored advice) and follow-up approximately every six weeks; therefore, during the course  
28 of the present study, the participants received a minimum of two one-hour sessions with  
29 email support for any queries and detailed nutritional guidance. All the nutritional therapists  
30 are qualified to diploma level and members of (voluntary) regulatory bodies such as the  
31 British Association for Applied Nutrition and Nutritional Therapy (BANT) and the  
32 Complementary and Natural Healthcare Council (CNHC). Similar to the psychology  
33 department, the nutrition department is led by one senior practitioner who supervises the team  
34 with individual and group supervisory arrangements.  
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### 53 *Combined*

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7 Within the combined program, a multidisciplinary approach is taken with practitioners  
8 discussing the patients in case meetings to ensure that the psychological and nutritional  
9 aspects complement each other in order to achieve the best outcome. It should be noted that  
10 the interventions in the combined program are phased-in as it was found that asking  
11 individuals to engage in numerous therapeutic activities at the same time resulted in high  
12 drop-out rates.  
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### 20 **Primary Outcome Measures**

#### 21 *Medical Outcomes Survey Short-Form 36 (SF-36)*

22 This 36-item measure is the short form of the original Medical Outcomes Survey <sup>34</sup> to  
23 measure functional impairment and contains eight sub-sections: 1) physical activity  
24 limitations due to health problems; 2) social activity limitations due to physical or emotional  
25 problems; 3) usual role activity limitations due to physical health problems; 4) bodily pain; 5)  
26 general mental health; 6) role activity limitations due to emotional problems; 7) vitality  
27 (energy and fatigue); and 8) general health perceptions <sup>34</sup>. The items are scored so that higher  
28 scores indicate greater functional ability. In terms of the psychometric properties of this  
29 measure, reliability estimates for all sub-scales are good, exceeding a Cronbach's alpha  
30 coefficient value of 0.70 <sup>35</sup>. In terms of validity, the SF-36 correlates amply,  $r \geq 0.40$ , with the  
31 frequency and severity of numerous symptoms and general health conditions <sup>36,37</sup>.  
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#### 45 *Multidimensional Fatigue Inventory (MFI)*

46 This 20-item measure contains five fatigue dimensions: general fatigue, physical fatigue,  
47 mental fatigue, reduced motivation and reduced activity <sup>38</sup>. Items such as 'I tire easily' are  
48 rated on a 5-point scale (1 = yes, that is true; 5 = no, that is not true) with lower scores  
49 reflecting higher levels of fatigue. The MFI has good internal consistency with average  
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7 Cronbach's alpha coefficient equaling 0.84 across the sub-scales. Convergent validity based  
8 on a sample of radiotherapy patients found correlations between the sub-scales and a visual  
9 analog fatigue scale to be 0.77 for general fatigue, 0.70 for physical fatigue, 0.61 for reduced  
10 activity, 0.56 for reduced motivation ( $p < 0.001$ ) to 0.23 for mental fatigue ( $p < 0.01$ )<sup>38</sup>.

### 16 **Secondary Outcome Measures (ME/CFS-specific)**

#### 17 *CDC CFS Symptom Inventory*

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20 CDC CFS Symptom Inventory<sup>39</sup> was used to measure specific ME/CFS symptoms and  
21 confirm diagnosis. This instrument is based upon the CDC case definition<sup>1</sup> and includes a  
22 fatigue item and the eight distinct symptoms are also included in the CDC guidelines with an  
23 additional ten associated symptoms. The format of this self-report measure is a six-point scale  
24 of perceived frequency (0 = absent, 5 = all the time) and severity (0 = none, 5 = very severe).  
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26 The psychometric properties of this instrument are good: Cronbach's alpha coefficient = 0.88;  
27  $r = .74$  convergent validity with the Chalder Fatigue Scale<sup>40</sup>;  $r = -.68$  and  $-.87$  convergent  
28 validity with the SF-36 'vitality' and 'bodily pain' sub-scales, respectively.  
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### 37 **Secondary Outcome Measures (psychological)**

#### 38 *Multidimensional Health Locus of Control Scale (MHLCS)*

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41 Multidimensional Health Locus of Control<sup>41-43</sup> measures perceived control via three distinct  
42 sub-scales: 'internal', 'chance' and 'powerful others' which has two dimensions, that of  
43 'doctors' and 'other people'. The instrument contains 18 items in total (six items each for the  
44 'internal' and 'chance' scales and three items for both the 'powerful others' scales) and is  
45 scored on a 6-point Likert scale from 'strongly agree' to 'strongly disagree'. Internal  
46 reliability of the instrument is good with Cronbach's alpha coefficients ranging from 0.67 for  
47 'powerful others' to 0.77 for 'internal'. The measure correlates positively and significantly  
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7 with associated scales from Levenson's<sup>44</sup> locus of control measure from which the MHLOC  
8 was based, which demonstrates good convergent validity<sup>41</sup>.  
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### 10 11 12 *Maladaptive Stress Index*

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14 ~~This 32 item measure contains three sub scales (cognitive/mood, sleep and ME/CFS~~  
15 ~~symptoms) and was designed specifically for this population<sup>45</sup>. Items such as 'I constantly~~  
16 ~~replay or pre-empt situations and conversations' are scored on a 5 point scale where 1 =~~  
17 ~~never true and 5 = always true; higher scores illustrate a greater degree of disturbance.~~  
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### 22 23 24 **Statistical methods**

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26 The data was initially screened for missing data. Four cases contained substantial amounts of  
27 missing data; therefore these were excluded from the analysis (one individual from the  
28 nutrition group and three from the combined group). Subsequent analyses were conducted on  
29 complete data only. Once this was done, all the variables had less than 5% missing data,  
30 hence mean substitution was carried out in line with guidance<sup>46</sup>. The baseline data was  
31 subsequently of the quality for parametric tests, except for the variables CDC CFS swollen  
32 lymph nodes and glands, memory problems, abdominal pain and depression. However, the  
33 follow-up data suffered from high levels of skew and kurtosis which was not substantially  
34 alleviated by data transformation. This violated a key criterion for parametric testing, that of  
35 normality of distribution, so non-parametric tests were selected. In addition, as the sample  
36 sizes in each individual treatment group were small, the more conservative non-parametric  
37 tests were the preferred choice as even though tests such as analysis of variance are generally  
38 robust against non-normality, this does not hold true with small sample sizes. One-way  
39 analysis of variance tests and Kruskal-Wallis tests (the former for those variables that met the  
40 criteria for parametric tests, and the latter that did not) were used to investigate baseline  
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7 variation and analysis of covariance (ANCOVA) tests were used to account for this variation  
8 and test to for differences between the three groups. Wilcoxon sign-rank tests were  
9 employed to look for differences over time (baseline and 3-month follow-up) and if  
10 differences were significant, percentage change was calculated. Please note, as this is an  
11 exploratory study with only one time-point and no control group, any significant findings do  
12 not infer clinical significance, rather statistical significance, and as such exact p-values are  
13 presented.  
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## 22 **Results**

### 23 **Participants**

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25 Of the 145 individuals who expressed an interest in the study, 142 time-one questionnaires  
26 were returned, equating to a 97.9% response rate at baseline (two participants from the  
27 psychology group and one from the combined group dropped out at this stage). Therefore,  
28 excluding the four cases deleted due to insufficient data, 138 cases were used for baseline  
29 analysis; 42 participants in the psychology group, 44 in the nutrition group and 52 in the  
30 combined group. There was no significant association between gender and group ( $\chi^2 (2) =$   
31  $0.179, p = .915$ ), all groups consisting of approximately one-fifth males (Table 1). There was  
32 not a significant difference in age ( $F(2,135) = 0.001, p = 1.000$ ); in fact group means for age  
33 were near identical at 42.881, 42.864 and 42.843 for psychology, nutrition and combined  
34 groups, respectively. There was also a non-significant result for illness duration ( $F(2, 135) =$   
35  $0.252, p = .778$ ). Therefore, in terms of demographics, the groups were comparable. With  
36 regard to the outcome measures, there were significant differences between the groups in  
37 terms of the MFI sub-scale 'general fatigue' ( $F(2, 135) = 3.219, p = .043$ ), MFI 'physical  
38 fatigue' ( $F(2, 135) = 3.343, p = .038$ ) and the CDC CFS symptom 'swollen lymph nodes and  
39 glands' ( $H(2) = 7.161, p = .028$ ). To investigate the source of these differences, post-hoc tests  
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7 were conducted (unrelated t-tests for the fatigue variables and Mann-Whitney tests for  
8 swollen lymph glands as the former did not meet criteria for parametric tests, all with  
9 Bonferroni correction for multiple comparisons). A significant difference was observed  
10 between the psychology and combined groups with regards to general fatigue ( $t(92) = -2.449$ ,  
11  $p = .016$ ) and physical fatigue ( $t(92) = -2.658$ ,  $p = .009$ ) and also between the nutrition and  
12 psychology group in terms of the degree of lymph node and gland swelling ( $U = 635.00$ ,  $p =$   
13  $.009$ ). Within the fatigue measures, the combined group reported significantly higher levels  
14 of both general and physical fatigued than the psychology group whereas those undertaking  
15 nutritional support stated a higher occurrence of swollen lymph nodes and glands.  
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#### 24 25 26 *Retention analysis*

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28 Seventy-two of the original 138 participants (14 participants in the psychology group, 27 in  
29 the nutrition group and 31 in the combined group) completed the battery of measures at the 3-  
30 month follow-up, resulting in retention rates of 52.17% in the study overall, 33.33% in the  
31 psychology group, 61.36% in the nutrition group and 59.62% in the combined group. To  
32 investigate whether the individuals who did not complete the time-two measures were  
33 significantly different from those at baseline on demographic and outcome measures, a series  
34 of t-tests and Mann-Whitney tests were performed. Those that dropped out of the research  
35 (although still receiving treatment at the clinic) differed significantly in terms of age ( $t(136) =$   
36  $-2.227$ ,  $p = .028$ ) and illness duration ( $t(136) = -2.549$ ,  $p = .012$ ). Those who remained in the  
37 study were of significantly older age (mean age of those that remained in the study = 45.056,  
38 SD = 11.535; mean age of drop-outs = 40.400, SD = 12.932) and longer illness duration than  
39 those who dropped out (mean age of those that remained in the study = 10.836, SD = 7.383;  
40 mean illness duration of drop-outs = 7.571, SD = 7.472). Individuals who did not remain in  
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7 the study did not differ significantly in terms of gender ( $\chi^2 (2) = 1.222, p = .269$ ) or any of the  
8  
9 outcome measures.

### 10 11 12 **Comparisons within-groups across time**

#### 13 14 Overall sample

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##### 15 16 *Primary outcomes*

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18 The following percentage change scores represent statistically significant changes, rather than  
19  
20 clinically significant shifts, as this was an exploratory study. (Please see Table 2 for the exact  
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22 ~~p value for each repeated measures comparison.~~ In the sample as a whole, there were  
23  
24 improvements in all areas of the SF-36 (Table 2), with a 5.80% improvement in physical  
25  
26 functioning, a ~~68.9863.32%~~ improvement in role limitations due to physical difficulties, a  
27  
28 5.17% improvement in bodily pain, a 26.17% improvement in social functioning, a 5.77%  
29  
30 improvement in general mental health, a 10.58% improvement in role limitations due to  
31  
32 emotional difficulties, a 22.30% improvement in vitality, energy or fatigue and a 36.49%  
33  
34 improvement in general health perception. When looking at the fatigue sub-scales of the MFI,  
35  
36 all five sub-scales showed significant reductions in fatigue; 8.55% in general fatigue, 10.98%  
37  
38 in physical fatigue, 8.81% in reduced activity, 12.96% in reduced motivation and 12.79% in  
39  
40 mental fatigue.

##### 41 42 43 Secondary outcomes

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45 Within the CFS Symptom Inventory (Table 3), there were improvements in occurrence of  
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47 sore throats (34.48%), diarrhea (42.47%), fatigue after exertion (16.32%), muscle aches or  
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49 muscle pains (21.01%), pain in joints (34.55%) chills (37.00%), unrefreshing sleep (19.55%),  
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51 sleeping problems (17.17%), headaches (24.94%), memory problems (17.86%), difficulty  
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53 concentrating (26.66%), sinus and nasal symptoms (26.38%), shortness of breath (29.28%),  
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7 [sensitivity to light \(28.62%\) and depression \(39.55%\). There were no significant differences](#)  
8 [from time-one to time-two in the MHLCS sub-scale of ‘chance’, ‘powerful others’ and ‘other](#)  
9 [people’ \(Table 3\), however the MHLCS did illustrate significant increases in internal locus of](#)  
10 [control \(30.67%\) and that of doctors \(47.49%\).](#)

### 14 **Psychology group**

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#### 15 *Primary outcomes*

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20 Within the group of individuals who opted for a purely psychological intervention,  
21 improvements were seen in physical functioning (16.75%), role limitations due to physical  
22 problems (84.61%), social functioning (37.81%), general mental health (19.15%), vitality,  
23 energy or fatigue (49.57%) and general health perceptions (19.01%). Also, all the MFI  
24 fatigue scales decreased over a 3-month period, 13.58% in general fatigue, 17.74% in  
25 physical fatigue, 23.20% in reduced activity, 11.42% in reduced motivation and 29.66% in  
26 mental fatigue (Table 4).

#### 27 *Secondary outcomes*

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32 [Within those taking part in the psychology intervention, ratings of muscle aches or muscle](#)  
33 [pains \(10.34%\), chills \(23.40%\), memory problems \(44.73%\), difficulty concentrating](#)  
34 [\(39.50%\) and sensitivity to light \(64.58%\) decreased \(Table 5\). A significant increase of](#)  
35 [17.56% was observed in internal locus of control, a decrease of 4.67% in the perception that](#)  
36 [chance played an influential part in the individuals’ lives \(Table 5\).](#)

### 37 **Nutrition group**

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#### 38 *Primary outcomes*

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51 The nutrition group saw improvements in role limitations due to physical problems  
52 [\(75.2861.05%\)](#), social functioning (24.93%), vitality, energy or fatigue (35.35%), and general  
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7 health perceptions (29.73%). Once again, all the MFI fatigue scales decreased over a 3-month  
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9 period, 13.39% in general fatigue, 15.00% in physical fatigue, 13.28% in reduced activity,  
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11 14.64% in reduced motivation and 12.83% in mental fatigue (Table 6).

#### Secondary outcomes

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14 In the nutrition group, numerous symptom-related indices also showed improvements (Table  
15  
16 7); sore throat (56.23%), swollen lymph glands (21.21%), fatigue after exertion (13.90%),  
17  
18 muscle aches or muscle pains (20.56%), chills (40.74%), nausea (16.42%) and abdominal  
19  
20 pain (20.16%). No significant differences were found from baseline to follow-up in perceived  
21  
22 control (Table 7).

#### **Combined group**

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#### Primary outcomes

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30 In terms of general health as ~~evaluated-gauged~~ by the SF-36 measure, the group who received  
31  
32 both psychological and nutritional intervention reported reductions in role limitations due to  
33  
34 physical difficulties (57.02%), social functioning (22.61%), role limitations due to emotional  
35  
36 difficulties (29.47%) and general health perceptions (26.45%). ~~In the combined group, Only~~  
37  
38 one measure of fatigue, that of physical fatigue, saw significant improvements over time  
39  
40 (6.42%) ~~in the combined group~~ (Table 8).

#### Secondary outcomes

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43 Those in the combined group saw significant reductions over the 3-month interval in diarrhea  
44  
45 (47.97%), fatigue after exertion (19.20%), chills (40.23%), headaches (36.18%) and sinus and  
46  
47 nasal symptoms (20.56%) (Table 9). No significant differences were found from baseline to  
48  
49 follow-up in perceived control as measured by the MHLCS in the combined treatment group  
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51 (Table 9).

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*Secondary outcomes (ME/CFS specific)*

Within the CFS Symptom Inventory, there were improvements in occurrence of sore throats (46.26%), diarrhea (42.47%), fatigue after exertion (16.32%), muscle aches or muscle pains (21.01%), pain in joints (28.32%), chills (37.00%), unrefreshing sleep (19.55%), sleeping problems (17.17%), headaches (29.47%), memory problems (17.86%), difficulty concentrating (26.66%), sinus and nasal symptoms (14.95%), shortness of breath (29.08%), sensitivity to light (26.26%) and depression (39.55%) in the merged sample. Within those taking part in the psychology intervention, ratings of muscle aches or muscle pains (10.34%), chills (23.40%), memory problems (44.73%), difficulty concentrating (39.50%) and sensitivity to light (64.58%) decreased. In the nutrition group, numerous symptom-related indices also showed improvements; sore throat (56.23%), swollen lymph glands (10.09%), fatigue after exertion (13.90%), muscle aches or muscle pains (20.56%), pain in joints (16.40%), chills (40.74%), headaches (32.19%), abdominal pain (29.05%), and sensitivity to light (18.28%). Those in the combined group saw significant reductions over the 3 month interval in diarrhea (47.97%), fatigue after exertion (19.20%), chills (40.23%), headaches (36.18%) and sinus and nasal symptoms (20.56%). (Please see Table 3 for the descriptive and inferential statistics associated with these findings and the exact p value for each repeated measures comparison.)

*Secondary outcomes (psychological)*

There were no significant differences from time one to time two in the MHLCS sub-scale of 'chance', 'powerful others' and 'other people', however the MHLCS did illustrate significant increases in internal locus of control (30.67%) and that of doctors (47.49%) in the sample as a whole. Reductions were also observed in the Maladaptive Stress Response (11.99%) in the entire group. In the psychology group, a significant increase of 17.56% was observed in

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7 internal locus of control, a decrease of 4.67% in the perception that chance played an  
8 influential part in the individuals' lives and a significant reduction in the Maladaptive Stress  
9 Response of 16.75%. No significant differences were found from baseline to follow up in  
10 perceived control in the nutrition group, however the way in which the individuals in this  
11 group responded to stress also decreased, by 11.54%. No significant differences were found  
12 from baseline to follow up in perceived control as measured by the MHLCS in the combined  
13 treatment group although there was a statistically significant difference in the Maladaptive  
14 Stress Response (10.98%). (Please see Table 4 for the descriptive and inferential statistics  
15 associated with these findings and the exact p value for each repeated measures comparison.)  
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### 26 Comparisons across groups

27 With correction for baseline variation, there were no significant differences between the three  
28 groups in terms of change scores.  
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## 32 Discussion

### 33 Key results

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37 There was statistically significant (rather than known clinically significant) change over time  
38 of numerous measures in all groups investigated. However, this is not to say that these  
39 changes were due to the interventions as the design of this study was exploratory, rather than  
40 experimental (please see below for a further critique of the design). The psychology group  
41 contained the most significant findings, including those concerned with daily functioning,  
42 fatigue, locus of control, ~~and the~~ cognitive CDC CFS specific symptoms ~~and the Maladaptive~~  
43 ~~Stress Response~~. These findings appear consistent with outcomes from other psychological  
44 interventions<sup>3;4;6</sup>. As expected, changes in perceived control were not observed in the  
45 nutrition group as this is not an area that is targeted in this program. However, the more  
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7 immune-type symptoms such as sore throat ~~and~~, swollen lymph nodes or glands ~~and pain in~~  
8 ~~joints~~ did see significant reductions over time as would be envisaged in treatment protocols  
9 based upon nutritional expertise. The group that exhibited the least significant findings was  
10 the combined group and, as noted below, this may be due to the greater general severity of  
11 symptoms in this group and the need for a more lengthy intervention. Nevertheless,  
12 considering the small sample sizes in the groups at follow-up, these results are very  
13 promising and warrant further attention.  
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### 20 21 22 **Interpretation**

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24 As noted previously <sup>31</sup> ~~patient centered~~, individualized treatment protocols which include a  
25 range of tailored strategies is a favorable direction for dealing with a complex and multi-  
26 system disorder such as ME/CFS. The present study has demonstrated that such interventions  
27 may be useful in lowering symptomatology, improving functioning and helping individuals  
28 gain a greater sense of control over their health status.  
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### 34 35 36 **Limitations and Generalisability**

37 This study was a preliminary study in a naturalistic setting and as such did not have a robust  
38 design. There was not a control group and the participants were not randomly assigned to  
39 groups, therefore the results should be treated with caution. In order to ascertain whether the  
40 changes in symptom and functional reports were due to the interventions, a randomized  
41 control trial should be conducted (RCT). Also, there was a high drop-out rate from time-one  
42 to time-two and this rate differed across groups. The highest drop-out rate was in the  
43 psychology group; whilst we cannot be sure why this occurred, it is postulated that the  
44 retention was poor in the group as the individuals in the psychology program had more  
45 activities to engage in and may have felt overburdened with the research questionnaires in  
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7 addition to their session and homework (this would not be the case in the combined group as  
8 the therapeutic activities are phased-in as mentioned above).  
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12 In this study, each individual was guided to appropriate treatment within an initial screening  
13 with clinic staff; therefore the group was dependent on the nature of the individual's  
14 symptoms and their personal choice as the programs on offer were privately funded. Notably,  
15 the groups did differ in general and physical fatigue with participants in the combined groups  
16 reporting greater fatigue than those in the psychology group which suggests that this group's  
17 general symptomatology was more severe. The combined group illustrated less change over  
18 time compared to the psychology and nutrition groups and it is feasible to infer that  
19 individuals with a greater number and degree of complaints are referred to the combined  
20 group within the clinic. Also, those in the combined group will not experience the intensity of  
21 each intervention as this has been demonstrated to result in non-compliance; therefore,  
22 changes in outcome measures in this group may not be noted at an interval of three months.  
23  
24 Further studies underway presently will investigate follow-ups at 6- and 12-months to  
25 identify whether the findings here are maintained over time and also whether those with  
26 greater symptom severity benefit with a longer intervention. The results from this study will  
27 then inform plans for an RCT of the clinic's practices. As the participants were self-selected  
28 onto these programs, the findings lack generalizability; future work should sample from the  
29 overall ME/CFS population and be randomly-assigned to groups in order to make valid  
30 assumptions regarding the illness-group as a whole.  
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#### 48 49 **Funding**

50  
51 No external funding was obtained for this research; the work was accomplished in-house at  
52 the clinic in question.  
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### Data Sharing

Dataset available from the corresponding author at drarroll@theoptimumhealthclinic.com.

Consent was not obtained for data sharing but the presented data are anonymised and risk of identification is low.

### Contributorship

Alex Howard made substantial contributions to the conception and design and acquisition of data, whilst Megan Arroll made a substantial contribution to the analysis and interpretation of data. Both authors made a substantial contribution to the drafting of the article and revisions for the critical review of important intellectual content. Final approval of the version to be published was also granted by both authors.

### Acknowledgements

We would like to thank Dr Tomas Ros for preparing the questionnaire spreadsheet, Niki Gratrix for helping in setting-up the study and Dr Andy McLellan and Val Duschinsky for proof-reading and editing.

### Competing Interests

Alex Howard is the founder and CEO of The Optimum Health Clinic and Megan Arroll is the Director of Research at the Optimum Health Clinic, where this study was conducted.

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7 List of abbreviations

8 ME: myalgic encephalomyelitis

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10 CFS: Chronic Fatigue Syndrome

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12 NICE: National Institute for Health and Clinical Excellence

13  
14 CBT: Cognitive Behavioral Therapy

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16 GET: Graded Exercise Therapy

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18 APT: Adaptive Pacing Therapy

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20 SMC: specialist medical care

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22 CAM: Complementary and Alternative Medicine

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24 NLP: Neuro-linguistic Programming

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26 EFT: Emotional Freedom Technique

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28 SF-36: Medical Outcomes Survey Short-Form 36

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30 MHLCS: Multidimensional Health Locus of Control Scale

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32 MFI: Multidimensional Fatigue Inventory

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34 RCT: randomized controlled trial

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Table 1. Demographics for gender, age and illness duration across the three treatment groups

		Mean	SD	95% CI for Mean		Test statistic	p-value
				Lower	Upper		
Gender	Psychology	9 (21.4%) <sup>d</sup>				.179 <sup>c</sup>	.915
	Nutrition	8 (18.2%) <sup>d</sup>					
	Combined	11 (21.2%) <sup>d</sup>					
	Total	28 (20.3%) <sup>d</sup>					
Age	Psychology	42.881	13.986	38.523	47.239	.000 <sup>a</sup>	1.000
	Nutrition	42.864	12.504	39.062	46.665		
	Combined	42.843	11.125	39.714	45.972		
	Total	42.861	12.406	40.765	44.957		
Illness duration	Psychology	8.874	8.252	6.302	11.445	.252 <sup>a</sup>	.778
	Nutrition	10.023	7.375	7.781	12.265		
	Combined	9.625	7.291	7.595	11.655		
	Total	9.523	7.580	8.247	10.800		

only

Table 2. Comparisons across time within the primary outcome measures within the overall sample

	N	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	p-value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
<a href="#">SF-36 Physical Functioning</a>	72	18.075	41.644	66.667	25.694	47.222	77.583	-3.120	.002**
<a href="#">SF-36 Role limitations physical</a>	71	0	0	0	0	25	50	-4.321	.001***
<a href="#">SF-36 Bodily pain</a>	72	32.5	56.25	79.375	32.500	67.500	90	-2.240	.025*
<a href="#">SF-36 Social functioning</a>	72	12.5	25	50	12.500	50	75	-4.504	.001***
<a href="#">SF-36 General mental health</a>	72	53	60	75	57	68	80	-2.665	.008**
<a href="#">SF-36 Role limitations emotional</a>	72	0	33.317	100	41.667	66.670	100	-3.159	.002**
<a href="#">SF-36 Vitality Energy or Fatigue</a>	72	10	15	35	11.250	30	45	-4.205	.001***
<a href="#">SF-36 General health perceptions</a>	72	20	30	40	25	40	50	-3.996	.001***
<a href="#">MFI General Fatigue</a>	72	15	18	19	12	16	19	-3.692	.001***
<a href="#">MFI Physical Fatigue</a>	72	15	18	20	12	16	19	-4.591	.001***
<a href="#">MFI Reduced Activity</a>	72	11	15	18	9	14	17	-2.421	.015*
<a href="#">MFI Reduced Motivation</a>	72	8	10	13.750	7	9	12	-2.986	.003**
<a href="#">MFI Mental Fatigue</a>	72	11	14	18	8.250	12.500	15	-3.661	.001***



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Table 3. Comparisons across time within the secondary outcome measures within the overall sample

	N	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	p-value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
<a href="#">CDC CFS Sore throat</a>	70	0	1.5	4	0	1	2	-2.257	.024*
<a href="#">CDC CFS Swollen lymph nodes/glands</a>	71	0	2	6	0	1	4	-1.567	.115
<a href="#">CDC CFS Diarrhea</a>	72	0	1	4	0	0	2	-2.481	.013*
<a href="#">CDC CFS Fatigue after exertion</a>	72	9	15	20	6.500	12	16	-3.574	.001***
<a href="#">CDC CFS Muscle aches/pains</a>	72	4	9	12	1.250	6	12	-3.995	.001***
<a href="#">CDC CFS Pain in joints</a>	70	0	4	9	0	1	6	-2.908	.004**
<a href="#">CDC CFS Fever</a>	70	0	0	1	0	0	0	-1.667	.095
<a href="#">CDC CFS Chills</a>	72	0	2	6	0	0	2.113	-4.206	.001***
<a href="#">CDC CFS Unrefreshing sleep</a>	72	6	12	16	4	6	16	-2.295	.022*
<a href="#">CDC CFS Sleeping problems</a>	72	2	8	12	2	4	12	-1.983	.047*
<a href="#">CDC CFS Headaches</a>	71	1	6	9	1	6	11.250	-2.850	.004**

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<a href="#">CDC CFS Memory Problems</a>	<a href="#">72</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">11.250</a>	<a href="#">-2.053</a>	<a href="#">.040*</a>
<a href="#">CDC CFS Difficulty Concentrating</a>	<a href="#">72</a>	<a href="#">2.500</a>	<a href="#">8.500</a>	<a href="#">12</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">-3.440</a>	<a href="#">.001***</a>
<a href="#">CDC CFS Nausea</a>	<a href="#">71</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">-0.898</a>	<a href="#">.369</a>
<a href="#">CDC CFS Abdominal Pain</a>	<a href="#">71</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">-1.932</a>	<a href="#">.053</a>
<a href="#">CDC CFS Sinus nasal symptoms</a>	<a href="#">71</a>	<a href="#">1</a>	<a href="#">4</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">-2.862</a>	<a href="#">.004**</a>
<a href="#">CDC CFS Shortness of breath</a>	<a href="#">69</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">4</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4</a>	<a href="#">-2.402</a>	<a href="#">.016*</a>
<a href="#">CDC CFS Sensitivity to light</a>	<a href="#">71</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4</a>	<a href="#">-2.388</a>	<a href="#">.017*</a>
<a href="#">CDC CFS Depression</a>	<a href="#">72</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4</a>	<a href="#">-2.297</a>	<a href="#">.022*</a>
<a href="#">MHLCS Internal</a>	<a href="#">72</a>	<a href="#">0.528</a>	<a href="#">0.681</a>	<a href="#">0.799</a>	<a href="#">0.611</a>	<a href="#">0.722</a>	<a href="#">0.889</a>	<a href="#">-2.962</a>	<a href="#">.003**</a>
<a href="#">MHLCS Chance</a>	<a href="#">72</a>	<a href="#">0.222</a>	<a href="#">0.344</a>	<a href="#">0.417</a>	<a href="#">0.201</a>	<a href="#">0.320</a>	<a href="#">0.444</a>	<a href="#">-1.552</a>	<a href="#">.121</a>
<a href="#">MHLCS Powerful Others</a>	<a href="#">72</a>	<a href="#">0.333</a>	<a href="#">0.389</a>	<a href="#">0.500</a>	<a href="#">0.306</a>	<a href="#">0.361</a>	<a href="#">0.500</a>	<a href="#">-1.601</a>	<a href="#">.109</a>
<a href="#">MHLCS Doctors</a>	<a href="#">72</a>	<a href="#">0.0833</a>	<a href="#">0.139</a>	<a href="#">0.222</a>	<a href="#">0.083</a>	<a href="#">0.111</a>	<a href="#">0.194</a>	<a href="#">-2.381</a>	<a href="#">.017*</a>
<a href="#">MHLCS Other People</a>	<a href="#">72</a>	<a href="#">0.194</a>	<a href="#">0.250</a>	<a href="#">0.3056</a>	<a href="#">0.174</a>	<a href="#">0.250</a>	<a href="#">0.278</a>	<a href="#">-1.186</a>	<a href="#">.236</a>

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Table 4. Comparisons across time within the primary outcome measures within the psychology group

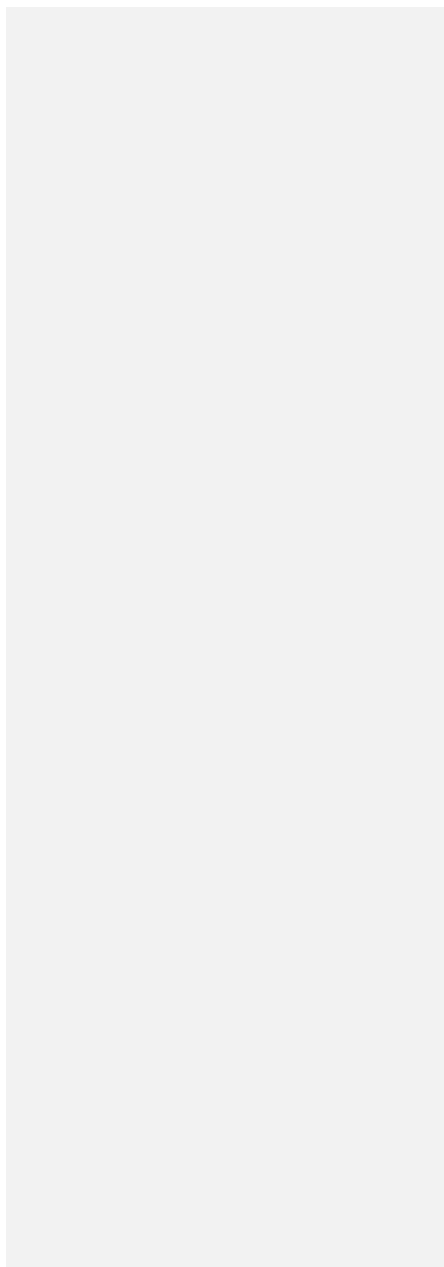
	N	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	p-value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
SF-36 Physical Functioning	14	25.008	44.444	58.367	27.083	69.450	84.700	-2.707	.007**
SF-36 Role limitations physical	14	0	0	25	0	50	81.250	-2.379	.017*
SF-36 Bodily pain	14	39.375	57.500	80.625	32.500	72.500	90	-1.195	.232
SF-36 Social functioning	14	25	37.500	50	34.375	56.250	90.625	-2.689	.007**
SF-36 General mental health	14	47	62	80	67	76	88	-2.497	.013*
SF-36 Role limitations emotional	14	24.974	100	100	58.336	100	100	-.842	.400
SF-36 Vitality Energy or Fatigue	14	10	20	40	28.750	45	52.500	-3.066	.002**
SF-36 General health perceptions	14	23.750	30	41.250	31.250	40	63.750	-2.561	.010*
MFI General Fatigue	14	14	16.500	18.500	9.750	13.500	18.500	-2.657	.008**
MFI Physical Fatigue	14	13.750	16	19.250	8.750	13	16.750	-2.810	.005**
MFI Reduced Activity	14	9.750	12.500	18.250	7	9	14.500	-2.142	.032*

<a href="#">MFI Reduced Motivation</a>	14	5.750	8	11.750	4.750	5.500	8.250	-2.131	.033*
<a href="#">MFI Mental Fatigue</a>	14	11.750	15.500	18	6.500	9.500	15	-2.950	.003*

**Table 5. Comparisons across time within the secondary outcome measures within the psychology group**

	N	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	p-value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
<a href="#">CDC CFS Sore throat</a>	14	0	2	6	0	0	2.500	-1.365	.172
<a href="#">CDC CFS Swollen lymph nodes/glands</a>	14	0	0.5	2.5	0	0	4	-.341	.733
<a href="#">CDC CFS Diarrhea</a>	14	0	0	2	0	0	2.500	-.730	.465
<a href="#">CDC CFS Fatigue after exertion</a>	14	9	12	20	7.750	9	14	-1.550	.121
<a href="#">CDC CFS Muscle aches/pains</a>	14	4	9	15.25	1.750	9	14	-2.145	.032*
<a href="#">CDC CFS Pain in joints</a>	14	0	2.5	9	0	0.500	4.500	-1.778	.075
<a href="#">CDC CFS Fever</a>	14	0	0	1.5	0	0	0.500	-.135	.892
<a href="#">CDC CFS Chills</a>	14	0	1	6.75	0	0	4.500	-1.970	.049*
<a href="#">CDC CFS Unrefreshing sleep</a>	14	9	12	15.25	5.500	9	16	-.802	.422

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<a href="#">CDC CFS Sleeping problems</a>	<a href="#">14</a>	<a href="#">2.75</a>	<a href="#">7</a>	<a href="#">12</a>	<a href="#">1</a>	<a href="#">3</a>	<a href="#">9.750</a>	<a href="#">-1.738</a>	<a href="#">.082</a>
<a href="#">CDC CFS Headaches</a>	<a href="#">14</a>	<a href="#">1</a>	<a href="#">2.5</a>	<a href="#">6</a>	<a href="#">0.750</a>	<a href="#">1</a>	<a href="#">6.750</a>	<a href="#">-1.200</a>	<a href="#">.230</a>
<a href="#">CDC CFS Memory Problems</a>	<a href="#">14</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">9</a>	<a href="#">0.750</a>	<a href="#">1</a>	<a href="#">6.750</a>	<a href="#">-1.965</a>	<a href="#">.049*</a>
<a href="#">CDC CFS Difficulty Concentrating</a>	<a href="#">14</a>	<a href="#">3.5</a>	<a href="#">9</a>	<a href="#">17</a>	<a href="#">1</a>	<a href="#">5</a>	<a href="#">6.750</a>	<a href="#">-2.809</a>	<a href="#">.005**</a>
<a href="#">CDC CFS Nausea</a>	<a href="#">14</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">4.25</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4.500</a>	<a href="#">-.213</a>	<a href="#">.832</a>
<a href="#">CDC CFS Abdominal Pain</a>	<a href="#">14</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">5.25</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">6</a>	<a href="#">-.343</a>	<a href="#">.732</a>
<a href="#">CDC CFS Sinus nasal symptoms</a>	<a href="#">14</a>	<a href="#">1</a>	<a href="#">3.5</a>	<a href="#">4.5</a>	<a href="#">0</a>	<a href="#">1.500</a>	<a href="#">4.500</a>	<a href="#">-.724</a>	<a href="#">.469</a>
<a href="#">CDC CFS Shortness of breath</a>	<a href="#">14</a>	<a href="#">0</a>	<a href="#">1.5</a>	<a href="#">4.5</a>	<a href="#">0</a>	<a href="#">0.500</a>	<a href="#">2.50</a>	<a href="#">-1.556</a>	<a href="#">.120</a>
<a href="#">CDC CFS Sensitivity to light</a>	<a href="#">14</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4.5</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">1.250</a>	<a href="#">-1.973</a>	<a href="#">.049*</a>
<a href="#">CDC CFS Depression</a>	<a href="#">14</a>	<a href="#">0</a>	<a href="#">1.5</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">-1.614</a>	<a href="#">.106</a>
<a href="#">MHLCS Internal</a>	<a href="#">14</a>	<a href="#">0.556</a>	<a href="#">0.653</a>	<a href="#">0.840</a>	<a href="#">0.611</a>	<a href="#">0.872</a>	<a href="#">0.923</a>	<a href="#">-2.983</a>	<a href="#">.003**</a>
<a href="#">MHLCS Chance</a>	<a href="#">14</a>	<a href="#">0.326</a>	<a href="#">0.417</a>	<a href="#">0.535</a>	<a href="#">0.167</a>	<a href="#">0.361</a>	<a href="#">0.451</a>	<a href="#">-2.594</a>	<a href="#">.009**</a>
<a href="#">MHLCS Powerful Others</a>	<a href="#">14</a>	<a href="#">0.319</a>	<a href="#">0.375</a>	<a href="#">0.451</a>	<a href="#">0.299</a>	<a href="#">0.356</a>	<a href="#">0.431</a>	<a href="#">.000</a>	<a href="#">1.000</a>
<a href="#">MHLCS Doctors</a>	<a href="#">14</a>	<a href="#">0.083</a>	<a href="#">0.125</a>	<a href="#">0.194</a>	<a href="#">0.083</a>	<a href="#">0.083</a>	<a href="#">0.174</a>	<a href="#">-1.122</a>	<a href="#">.262</a>
<a href="#">MHLCS Other People</a>	<a href="#">14</a>	<a href="#">0.194</a>	<a href="#">0.236</a>	<a href="#">0.285</a>	<a href="#">0.194</a>	<a href="#">0.222</a>	<a href="#">0.257</a>	<a href="#">-.118</a>	<a href="#">.906</a>

**Table 6. Comparisons across time within the primary outcome measures within the nutrition group**

	N	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	p-value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
SF-36 Physical Functioning	27	16.7	44.444	77.778	16.700	38.889	77.778	-1.136	.256
SF-36 Role limitations physical	26	0	0	0	0	25	25	-2.878	.004**
SF-36 Bodily pain	27	32.5	45	67.5	35.200	67.500	90	-1.800	.072
SF-36 Social functioning	27	0	25	50	12.500	37.500	75	-2.476	.013*
SF-36 General mental health	27	52	60	72	52	64	80	-1.696	.090
SF-36 Role limitations emotional	27	0	0	100	0	66.670	100	-1.788	.074
SF-36 Vitality Energy or Fatigue	27	5	15	35	15	25	45	-2.734	.006**
SF-36 General health perceptions	27	20	25	35	25	35	45	-2.157	.031*
MFI General Fatigue	27	15	18	19	12	15	19	-2.548	.011*
MFI Physical Fatigue	27	14	18	19	11	16	19	-2.791	.005**
MFI Reduced Activity	27	10	14	18	8	13	16	-2.164	.030*
MFI Reduced Motivation	27	8	10	12	6	8	12	-1.985	.047*

<a href="#">MFI Mental Fatigue</a>	<a href="#">27</a>	<a href="#">11</a>	<a href="#">13</a>	<a href="#">16</a>	<a href="#">8</a>	<a href="#">13</a>	<a href="#">15</a>	<a href="#">-2.082</a>	<a href="#">.037*</a>
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**Table 7. Comparisons across time within the secondary outcome measures within the nutrition group**

	N	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	p-value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
<a href="#">CDC CFS Sore throat</a>	<a href="#">27</a>	<a href="#">8</a>	<a href="#">1</a>	<a href="#">2</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">2</a>	<a href="#">-2.211</a>	<a href="#">.027*</a>
<a href="#">CDC CFS Swollen lymph nodes/glands</a>	<a href="#">26</a>	<a href="#">20</a>	<a href="#">0</a>	<a href="#">5</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">12</a>	<a href="#">-2.051</a>	<a href="#">.040*</a>
<a href="#">CDC CFS Diarrhea</a>	<a href="#">27</a>	<a href="#">16</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">-1.649</a>	<a href="#">.099</a>
<a href="#">CDC CFS Fatigue after exertion</a>	<a href="#">27</a>	<a href="#">25</a>	<a href="#">9</a>	<a href="#">16</a>	<a href="#">4</a>	<a href="#">12</a>	<a href="#">20</a>	<a href="#">-2.209</a>	<a href="#">.027*</a>
<a href="#">CDC CFS Muscle aches/pains</a>	<a href="#">27</a>	<a href="#">20</a>	<a href="#">4</a>	<a href="#">9</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">-2.901</a>	<a href="#">.004**</a>
<a href="#">CDC CFS Pain in joints</a>	<a href="#">26</a>	<a href="#">20</a>	<a href="#">0.750</a>	<a href="#">4</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">-1.827</a>	<a href="#">.068</a>
<a href="#">CDC CFS Fever</a>	<a href="#">26</a>	<a href="#">9</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">-1.254</a>	<a href="#">.210</a>
<a href="#">CDC CFS Chills</a>	<a href="#">27</a>	<a href="#">12</a>	<a href="#">1</a>	<a href="#">3</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">-3.401</a>	<a href="#">.001***</a>
<a href="#">CDC CFS Unrefreshing sleep</a>	<a href="#">27</a>	<a href="#">25</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">4</a>	<a href="#">6</a>	<a href="#">16</a>	<a href="#">-1.421</a>	<a href="#">.155</a>
<a href="#">CDC CFS Sleeping problems</a>	<a href="#">27</a>	<a href="#">25</a>	<a href="#">1</a>	<a href="#">9</a>	<a href="#">2</a>	<a href="#">4</a>	<a href="#">16</a>	<a href="#">-0.190</a>	<a href="#">.849</a>

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<a href="#">CDC CFS Headaches</a>	<a href="#">26</a>	<a href="#">25</a>	<a href="#">0.750</a>	<a href="#">6</a>	<a href="#">1</a>	<a href="#">3</a>	<a href="#">6</a>	<a href="#">-1.895</a>	<a href="#">.058</a>
<a href="#">CDC CFS Memory Problems</a>	<a href="#">27</a>	<a href="#">25</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">-0.338</a>	<a href="#">.735</a>
<a href="#">CDC CFS Difficulty Concentrating</a>	<a href="#">27</a>	<a href="#">25</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">4</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">-1.196</a>	<a href="#">.232</a>
<a href="#">CDC CFS Nausea</a>	<a href="#">26</a>	<a href="#">25</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">-2.407</a>	<a href="#">.016*</a>
<a href="#">CDC CFS Abdominal Pain</a>	<a href="#">26</a>	<a href="#">16</a>	<a href="#">0.750</a>	<a href="#">3</a>	<a href="#">0</a>	<a href="#">3</a>	<a href="#">6</a>	<a href="#">-2.322</a>	<a href="#">.020*</a>
<a href="#">CDC CFS Sinus nasal symptoms</a>	<a href="#">26</a>	<a href="#">20</a>	<a href="#">1</a>	<a href="#">3.500</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">9</a>	<a href="#">-1.244</a>	<a href="#">.213</a>
<a href="#">CDC CFS Shortness of breath</a>	<a href="#">25</a>	<a href="#">20</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">3</a>	<a href="#">-1.651</a>	<a href="#">.099</a>
<a href="#">CDC CFS Sensitivity to light</a>	<a href="#">26</a>	<a href="#">25</a>	<a href="#">0</a>	<a href="#">4</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">-1.890</a>	<a href="#">.059</a>
<a href="#">CDC CFS Depression</a>	<a href="#">27</a>	<a href="#">20</a>	<a href="#">0</a>	<a href="#">4</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">4</a>	<a href="#">-1.584</a>	<a href="#">.113</a>
<a href="#">MHLCS Internal</a>	<a href="#">27</a>	<a href="#">0.944</a>	<a href="#">0.528</a>	<a href="#">0.667</a>	<a href="#">0.528</a>	<a href="#">0.639</a>	<a href="#">0.778</a>	<a href="#">-.687</a>	<a href="#">.492</a>
<a href="#">MHLCS Chance</a>	<a href="#">27</a>	<a href="#">0.694</a>	<a href="#">0.222</a>	<a href="#">0.333</a>	<a href="#">0.222</a>	<a href="#">0.333</a>	<a href="#">0.472</a>	<a href="#">-.143</a>	<a href="#">.886</a>
<a href="#">MHLCS Powerful Others</a>	<a href="#">27</a>	<a href="#">0.694</a>	<a href="#">0.333</a>	<a href="#">0.389</a>	<a href="#">0.278</a>	<a href="#">0.361</a>	<a href="#">0.528</a>	<a href="#">-1.843</a>	<a href="#">.065</a>
<a href="#">MHLCS Doctors</a>	<a href="#">27</a>	<a href="#">0.417</a>	<a href="#">0.0833</a>	<a href="#">0.139</a>	<a href="#">0.083</a>	<a href="#">0.139</a>	<a href="#">0.222</a>	<a href="#">-1.686</a>	<a href="#">.092</a>
<a href="#">MHLCS Other People</a>	<a href="#">27</a>	<a href="#">0.833</a>	<a href="#">0.222</a>	<a href="#">0.278</a>	<a href="#">0.167</a>	<a href="#">0.250</a>	<a href="#">0.306</a>	<a href="#">-1.697</a>	<a href="#">.090</a>

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Table 8. Comparisons across time within the primary outcome measures within the combined group

	N	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			z-statistic	p-value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
<a href="#">SF-36 Physical Functioning</a>	31	22.200	33.333	61.111	27.778	55.556	72.222	-1.850	.064
<a href="#">SF-36 Role limitations physical</a>	31	0	0	0	0	25	25	-2.225	.026*
<a href="#">SF-36 Bodily pain</a>	31	32.500	45	80	32.500	57.500	80	-1.048	.294
<a href="#">SF-36 Social functioning</a>	31	12.500	25	37.500	12.500	37.500	62.500	-2.426	.015*
<a href="#">SF-36 General mental health</a>	31	56	60	72	56	68	76	-0.524	.600
<a href="#">SF-36 Role limitations emotional</a>	31	0	33.333	100	66.667	66.670	100	-2.313	.021*
<a href="#">SF-36 Vitality Energy or Fatigue</a>	31	10	15	30	10	25	40	-1.558	.119
<a href="#">SF-36 General health perceptions</a>	31	20	30	40	25	40	55	-2.423	.015*
<a href="#">MFI General Fatigue</a>	31	16	18	19	14	17	19	-0.854	.393
<a href="#">MFI Physical Fatigue</a>	31	15	19	20	13	17	20	-2.364	.018*

<a href="#">MFI Reduced Activity</a>	<a href="#">31</a>	<a href="#">12</a>	<a href="#">16</a>	<a href="#">18</a>	<a href="#">11</a>	<a href="#">16</a>	<a href="#">18</a>	<a href="#">-0.070</a>	<a href="#">.944</a>
<a href="#">MFI Reduced Motivation</a>	<a href="#">31</a>	<a href="#">9</a>	<a href="#">11</a>	<a href="#">14</a>	<a href="#">8</a>	<a href="#">10</a>	<a href="#">13</a>	<a href="#">-1.082</a>	<a href="#">.279</a>
<a href="#">MFI Mental Fatigue</a>	<a href="#">31</a>	<a href="#">10</a>	<a href="#">14</a>	<a href="#">18</a>	<a href="#">11</a>	<a href="#">13</a>	<a href="#">16</a>	<a href="#">-1.586</a>	<a href="#">.113</a>

**Table 9. Comparisons across time within the secondary outcome measures within the combined group**

	<i>N</i>	Baseline			3-month follow-up			Comparisons	
		Percentiles			Percentiles			<i>z</i> -statistic	<i>p</i> -value
		Lower	Mdn	Upper	Lower	Mdn	Upper		
<a href="#">CDC CFS Sore throat</a>	<a href="#">29</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">3.500</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">2.030</a>	<a href="#">-0.567</a>	<a href="#">.571</a>
<a href="#">CDC CFS Swollen lymph nodes/glands</a>	<a href="#">31</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">4</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">3</a>	<a href="#">-0.725</a>	<a href="#">.468</a>
<a href="#">CDC CFS Diarrhea</a>	<a href="#">31</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">4</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">-1.996</a>	<a href="#">.046*</a>
<a href="#">CDC CFS Fatigue after exertion</a>	<a href="#">31</a>	<a href="#">8</a>	<a href="#">15</a>	<a href="#">20</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">16</a>	<a href="#">-2.392</a>	<a href="#">.017*</a>
<a href="#">CDC CFS Muscle aches/pains</a>	<a href="#">31</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">9</a>	<a href="#">-1.908</a>	<a href="#">.056</a>
<a href="#">CDC CFS Pain in joints</a>	<a href="#">30</a>	<a href="#">0</a>	<a href="#">1.500</a>	<a href="#">8</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4</a>	<a href="#">-1.680</a>	<a href="#">.093</a>
<a href="#">CDC CFS Fever</a>	<a href="#">30</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">0</a>	<a href="#">0</a>	<a href="#">0.720</a>	<a href="#">-1.383</a>	<a href="#">.167</a>
<a href="#">CDC CFS Chills</a>	<a href="#">31</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">2.150</a>	<a href="#">-2.049</a>	<a href="#">.040*</a>

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<a href="#">CDC CFS Unrefreshing sleep</a>	<a href="#">31</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">16</a>	<a href="#">4</a>	<a href="#">9</a>	<a href="#">16</a>	<a href="#">-1.513</a>	<a href="#">.130</a>
<a href="#">CDC CFS Sleeping problems</a>	<a href="#">31</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">2</a>	<a href="#">4</a>	<a href="#">9</a>	<a href="#">-1.794</a>	<a href="#">.073</a>
<a href="#">CDC CFS Headaches</a>	<a href="#">31</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">9</a>	<a href="#">1</a>	<a href="#">3</a>	<a href="#">6</a>	<a href="#">-2.807</a>	<a href="#">.005**</a>
<a href="#">CDC CFS Memory Problems</a>	<a href="#">31</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">1</a>	<a href="#">3</a>	<a href="#">9</a>	<a href="#">-1.446</a>	<a href="#">.148</a>
<a href="#">CDC CFS Difficulty Concentrating</a>	<a href="#">31</a>	<a href="#">2</a>	<a href="#">8</a>	<a href="#">12</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">12</a>	<a href="#">-1.899</a>	<a href="#">.058</a>
<a href="#">CDC CFS Nausea</a>	<a href="#">31</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">-0.855</a>	<a href="#">.392</a>
<a href="#">CDC CFS Abdominal Pain</a>	<a href="#">31</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">4</a>	<a href="#">-0.598</a>	<a href="#">.550</a>
<a href="#">CDC CFS Sinus nasal symptoms</a>	<a href="#">31</a>	<a href="#">0</a>	<a href="#">5</a>	<a href="#">8</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4</a>	<a href="#">-2.482</a>	<a href="#">.013*</a>
<a href="#">CDC CFS Shortness of breath</a>	<a href="#">30</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4</a>	<a href="#">-0.976</a>	<a href="#">.329</a>
<a href="#">CDC CFS Sensitivity to light</a>	<a href="#">31</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">4</a>	<a href="#">-0.787</a>	<a href="#">.431</a>
<a href="#">CDC CFS Depression</a>	<a href="#">31</a>	<a href="#">0</a>	<a href="#">2</a>	<a href="#">6</a>	<a href="#">0</a>	<a href="#">1</a>	<a href="#">6</a>	<a href="#">-1.304</a>	<a href="#">.192</a>
<a href="#">MHLCS Internal</a>	<a href="#">31</a>	<a href="#">0.556</a>	<a href="#">0.694</a>	<a href="#">0.861</a>	<a href="#">0.639</a>	<a href="#">0.750</a>	<a href="#">0.889</a>	<a href="#">-1.755</a>	<a href="#">.079</a>
<a href="#">MHLCS Chance</a>	<a href="#">31</a>	<a href="#">0.222</a>	<a href="#">0.333</a>	<a href="#">0.361</a>	<a href="#">0.167</a>	<a href="#">0.306</a>	<a href="#">0.417</a>	<a href="#">-0.672</a>	<a href="#">.501</a>
<a href="#">MHLCS Powerful Others</a>	<a href="#">31</a>	<a href="#">0.333</a>	<a href="#">0.389</a>	<a href="#">0.500</a>	<a href="#">0.333</a>	<a href="#">0.389</a>	<a href="#">0.500</a>	<a href="#">-0.577</a>	<a href="#">.564</a>
<a href="#">MHLCS Doctors</a>	<a href="#">31</a>	<a href="#">0.111</a>	<a href="#">0.167</a>	<a href="#">0.222</a>	<a href="#">0.083</a>	<a href="#">0.139</a>	<a href="#">0.500</a>	<a href="#">-1.384</a>	<a href="#">.166</a>
<a href="#">MHLCS Other People</a>	<a href="#">31</a>	<a href="#">0.167</a>	<a href="#">0.250</a>	<a href="#">0.278</a>	<a href="#">0.194</a>	<a href="#">0.250</a>	<a href="#">0.306</a>	<a href="#">-0.213</a>	<a href="#">.831</a>

[\\* significant at .05 level](#)  
[\\*\\* significant at .01 level](#)

\*\*\* significant at .001 level

Table 2. Comparisons across time within the primary outcome measures

		Baseline				3-month follow-up				Comparisons	
		Mean	SD	95% CI for Mean		Mean	SD	95% CI for Mean		z-statistic	p-value
				Lower	Upper			Lower	Upper		
SF-36	Psychology	49.339	22.698	42.266	56.413	59.267	30.346	41.745	76.788	-2.707	.007**
Physical Functioning	Nutrition	47.855	26.226	39.882	55.829	46.706	30.744	34.544	58.868	-1.136	.256
	Combined	45.299	25.479	38.206	52.393	49.288	26.403	39.604	58.973	-1.850	.064
	Total	47.344	24.791	43.171	51.517	50.260	28.818	43.488	57.032	-3.120	.002**
SF-36	Psychology	7.143	15.894	2.190	12.096	46.429	39.048	23.883	68.974	-2.379	.017*
Role limitations physical	Nutrition	7.574	17.500	2.254	12.895	19.444	20.016	11.526	27.363	-2.907	.004**
	Combined	9.774	21.051	3.914	15.635	22.742	25.161	13.513	31.971	-2.225	.026*
	Total	8.272	18.387	5.177	11.367	26.111	28.225	19.479	32.744	-4.354	.001***
SF-36	Psychology	61.548	25.614	53.566	69.530	63.929	29.786	46.731	81.127	-1.196	.232
Bodily pain	Nutrition	55.625	30.242	46.434	64.819	58.889	32.943	45.857	71.921	-1.800	.072
	Combined	53.606	27.019	46.084	61.128	58.629	27.301	48.615	68.643	-1.048	.294
	Total	56.667	27.683	52.007	61.327	59.757	29.649	52.790	66.724	-2.240	.025*
SF-36	Psychology	37.202	21.824	30.402	44.003	59.821	33.318	40.584	79.058	-2.689	.007**
Social functioning	Nutrition	32.671	25.888	24.800	40.541	43.519	33.679	30.196	56.841	-2.476	.013*
	Combined	32.452	24.786	25.551	39.352	41.936	28.604	31.443	52.428	-2.426	.015*
	Total	33.967	24.212	29.892	38.043	46.007	31.805	38.533	53.481	-4.504	.001***
SF-36	Psychology	60.286	19.584	54.183	66.389	74.571	13.276	66.906	82.237	-2.497	.013*

General mental health	Nutrition	59.727	19.355	53.843	65.612	64.741	20.548	56.612	72.869	-1.696	.090
	Combined	58.308	20.948	52.476	64.140	64.129	16.637	58.027	70.232	-.524	-.600
	Total	59.362	19.911	56.011	62.714	66.389	17.897	62.183	70.594	-2.665	.008**
SF-36 Role limitations emotional	Psychology	55.554	46.368	41.105	70.004	76.191	33.150	57.051	95.331	-.842	-.400
	Nutrition	48.482	47.390	34.074	62.890	55.594	38.130	40.510	70.678	-1.788	-.074
	Combined	47.780	43.924	35.551	60.008	67.742	32.756	55.727	79.757	-2.313	.021*
	Total	50.370	45.590	42.695	58.044	64.829	35.335	56.526	73.133	-3.159	.002**
SF-36 Vitality Energy or Fatigue	Psychology	20.714	16.139	15.685	25.743	41.071	20.586	29.186	52.957	-3.066	.002**
	Nutrition	20.114	14.5670	15.685	24.542	31.111	23.588	21.780	40.442	-2.734	.006**
	Combined	19.039	17.658	14.123	23.955	27.097	19.527	19.934	34.259	-1.558	-.119
	Total	19.891	16.159	17.171	22.611	31.319	21.657	26.230	36.409	-4.205	.001***
SF-36 General health perceptions	Psychology	37.024	17.945	31.432	42.616	45.714	21.109	33.526	57.903	-2.561	.010*
	Nutrition	28.636	15.528	23.915	33.357	36.482	18.903	29.004	43.959	-2.157	.031*
	Combined	30.962	17.575	26.069	35.854	42.097	21.632	34.162	50.032	-2.423	.015*
	Total	32.065	17.286	29.156	34.975	40.694	20.561	35.863	45.526	-3.996	.001***
MFI General Fatigue	Psychology	15.952	2.845	15.066	16.839	13.786	4.441	11.222	16.350	-2.657	.008**
	Nutrition	16.977	2.601	16.186	17.768	14.704	4.898	12.766	16.641	-2.548	.011*
	Combined	17.327	2.588	16.607	18.047	16.645	2.811	15.614	17.676	-.854	.393
	Total	16.797	2.716	16.340	17.254	15.361	4.136	14.389	16.333	-3.692	.001***
MFI Physical Fatigue	Psychology	15.929	3.331	14.891	16.966	13.071	4.632	10.397	15.746	-2.810	.005**
	Nutrition	16.727	3.358	15.707	17.748	14.222	4.987	12.249	16.195	-2.791	.005**
	Combined	17.615	2.823	16.830	18.401	16.484	3.395	15.239	17.729	-2.364	.018*
	Total	16.819	3.211	16.278	17.359	14.972	4.453	13.926	16.019	-4.591	.001***
MFI Reduced	Psychology	13.857	4.112	12.576	15.138	10.643	5.153	7.668	13.618	-2.142	.032*
	Nutrition	14.136	4.027	12.912	15.361	12.259	5.012	10.277	14.242	-2.164	.030*

Activity	Combined	14.962	3.662	13.942	15.981	14.936	3.777	13.550	16.321	-.070	.944
	Total	14.362	3.921	13.702	15.022	13.097	4.798	11.970	14.225	-2.421	.015*
MFI	Psychology	10.357	4.287	9.021	11.693	7.286	4.214	4.853	9.719	-2.131	.033*
Reduced	Nutrition	10.500	3.474	9.444	11.556	8.963	3.736	7.485	10.441	-1.985	.047*
Motivation	Combined	11.462	3.153	10.584	12.339	10.774	3.095	9.639	11.910	-1.082	.279
	Total	10.819	3.639	10.206	11.431	9.417	3.767	8.532	10.302	-2.986	.003**
MFI	Psychology	13.524	4.363	12.164	14.883	10.500	4.468	7.920	13.080	-2.950	.003*
Mental Fatigue	Nutrition	13.682	4.328	12.366	14.998	11.926	5.334	9.816	14.036	-2.082	.037*
	Combined	13.846	4.345	12.637	15.056	12.613	3.827	11.209	14.017	-1.586	.113
	Total	13.696	4.315	12.969	14.422	11.944	4.568	10.871	13.018	-3.661	.001***

\*z-statistic for Wilcoxon Signed-Rank Test

Table 3. Comparisons across time within the secondary outcome measures (ME/CFS-specific)

		Baseline				3-month follow-up				Comparisons	
		Mean	SD	95% CI for Mean		Mean	SD	95% CI for Mean		z-statistic	p-value
				Lower	Upper			Lower	Upper		
CDC-CFS	Psychology	2.571	3.109	1.603	3.540	1.429	2.278	-.114	2.744	-1.365	.172
Sore Throat	Nutrition	3.977	3.776	2.829	5.125	1.741	2.087	-.915	2.566	-2.211	.027*
	Combined	3.202	4.494	1.951	4.454	1.904	2.821	-.870	2.939	-.804	.422
	Total	3.257	3.898	2.601	3.914	1.750	2.437	-1.178	2.323	-2.387	.017*
CDC-CFS	Psychology	1.976	3.382	.922	3.030	1.786	3.378	-.165	3.736	-.341	.733

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Swollen	Nutrition	5.561	6.491	3.587	7.534	5.000	6.760	2.326	7.674	-2.212	.027*
Lymph nodes	Combined	3.462	4.881	2.103	4.820	2.690	4.477	1.0458	4.332	-.725	-.468
Glands	Total	3.679	5.250	2.795	4.563	3.380	5.385	2.115	4.646	-1.684	-.092
CDC-CFS	Psychology	2.071	3.249	1.059	3.084	1.643	2.818	-.016	3.270	-.730	-.465
Diarrhea	Nutrition	2.841	4.832	1.372	4.310	1.444	3.274	-.149	2.740	-1.649	-.099
	Combined	3.135	3.773	2.084	4.185	1.631	2.483	-.720	2.542	-1.996	.046*
	Total	2.717	3.998	2.044	3.390	1.563	2.827	-.899	2.228	-2.481	-.013*
CDC-CFS	Psychology	13.286	6.271	11.331	15.240	11.071	6.673	7.218	14.925	-1.550	-.121
Fatigue after exertion	Nutrition	13.722	6.450	11.761	15.682	11.815	7.217	8.960	14.670	-2.209	-.027*
	Combined	14.154	6.270	12.408	15.899	11.436	6.275	9.134	13.738	-2.392	-.017*
	Total	13.752	6.292	12.693	14.811	11.507	6.629	9.949	13.065	-3.574	-.001***
CDC-CFS	Psychology	8.286	6.747	6.183	10.388	7.429	6.892	3.450	11.408	-2.145	-.032*
Muscle Aches or Muscle Pains	Nutrition	9.091	6.383	7.151	11.031	7.222	6.278	4.739	9.706	-2.901	-.004**
	Combined	8.519	6.932	6.589	10.449	6.188	5.528	4.160	8.215	-1.908	-.056
	Total	8.630	6.664	7.509	9.752	6.817	6.029	5.400	8.234	-3.995	-.001***
CDC-CFS	Psychology	3.476	5.334	1.814	5.138	2.786	4.458	-.212	5.360	-1.778	-.075
Pain In Joints	Nutrition	4.696	5.560	3.006	6.386	3.926	5.099	1.909	5.943	-2.022	-.043*
	Combined	5.474	6.386	3.696	7.251	3.010	4.140	1.492	4.528	-1.840	-.066
	Total	4.618	5.837	3.635	5.600	3.310	4.543	2.242	4.377	-3.141	-.002**
CDC-CFS	Psychology	1.238	2.516	-.454	2.022	1.643	4.181	-.771	4.057	-.135	-.892
Fever	Nutrition	1.394	2.562	-.615	2.173	-.630	2.041	-.178	1.437	-1.487	-.137
	Combined	1.333	3.909	-.245	2.421	-.378	-.709	-.118	.638	-1.517	-.129
	Total	1.324	3.106	-.801	1.846	-.718	2.272	-.185	1.252	-1.876	-.061
CDC-CFS	Psychology	3.357	4.637	1.912	4.802	2.571	4.398	-.032	5.111	-1.970	-.049*
Chills	Nutrition	3.750	3.924	2.557	4.943	2.222	4.098	-.601	3.843	-3.401	-.001***

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	Combined	3.192	4.343	1.983	4.402	1.908	2.797	.882	2.934	-2.049	.040*
	Total	3.420	4.283	2.699	4.141	2.155	3.614	1.306	3.004	-4.206	.001***
CDC-CFS	Psychology	12.905	6.792	10.788	15.021	10.643	6.698	6.776	14.510	-.802	.422
UnrefreshingSleep	Nutrition	12.250	7.088	10.095	14.405	9.444	7.738	6.384	12.505	-1.421	.155
	Combined	12.154	7.147	10.164	14.143	10.161	7.959	7.242	13.080	-1.513	.130
	Total	12.413	6.978	11.238	13.588	9.986	7.557	8.210	11.762	-2.295	.022*
CDC-CFS	Psychology	9.286	7.658	6.899	11.672	5.286	4.921	2.444	8.127	-1.738	.082
Sleeping Problems	Nutrition	8.614	7.317	6.389	10.838	9.482	9.200	5.842	13.121	-.190	.849
	Combined	8.904	7.681	6.766	11.042	6.529	6.749	4.053	9.004	-1.794	.073
	Total	8.928	7.509	7.664	10.192	7.394	7.585	5.612	9.177	-1.983	.047*
CDC-CFS	Psychology	5.262	5.548	3.533	6.991	4.357	3.411	2.388	6.326	-1.200	.230
Headaches	Nutrition	7.646	7.040	5.506	9.786	5.185	6.294	2.695	7.675	-2.084	.037*
	Combined	6.346	5.857	4.715	7.977	4.050	3.527	2.756	5.343	-2.807	.005**
	Total	6.431	6.200	5.387	7.474	4.535	4.708	3.429	5.642	-3.000	.003**
CDC-CFS	Psychology	6.333	4.996	4.777	7.890	3.500	3.995	1.193	5.807	-1.965	.049*
Memory Problems	Nutrition	9.409	7.183	7.225	11.593	8.667	7.681	5.628	11.705	-.338	.735
	Combined	8.173	7.610	6.055	10.292	6.148	4.905	4.349	7.947	-1.446	.148
	Total	8.007	6.835	6.857	9.158	6.578	6.189	5.123	8.032	-2.053	.040*
CDC-CFS	Psychology	8.500	6.094	6.601	10.399	5.143	5.559	1.933	8.353	-2.809	.005**
Difficulty Concentrating	Nutrition	9.822	7.641	7.499	12.145	7.778	6.941	5.032	10.524	-1.196	.232
	Combined	9.135	6.942	7.202	11.067	6.507	4.843	4.731	8.283	-1.899	.058
	Total	9.161	6.903	7.999	10.323	6.718	5.844	5.345	8.092	-3.440	.001***
CDC-CFS	Psychology	3.476	4.845	1.966	4.986	2.286	2.946	.585	3.987	-.213	.832
Nausea	Nutrition	4.769	5.135	3.208	6.330	3.407	5.746	1.134	5.681	-1.686	.092
	Combined	3.327	4.902	1.962	4.692	3.458	3.585	2.144	4.773	-.855	.392



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	Total	3.832	4.966	2.996	4.668	3.211	4.396	2.178	4.244	-584	-559
CDC-CFS	Psychology	2.548	3.270	1.529	3.567	2.786	4.003	-474	5.097	-343	-732
Abdominal	Nutrition	5.064	5.165	3.493	6.634	3.593	3.905	2.048	5.137	-1.968	.049*
Pain	Combined	3.750	4.635	2.460	5.041	2.548	2.791	1.524	3.572	-598	-550
	Total	3.803	4.535	3.040	4.566	2.986	3.470	2.171	3.801	-1.727	-.084
CDC-CFS	Psychology	3.524	4.702	2.059	4.989	2.357	2.437	.950	3.764	-724	-469
Sinus-Nasal	Nutrition	5.469	6.476	3.500	7.438	4.889	6.104	2.474	7.304	-1.400	-.162
Symptoms	Combined	4.789	6.304	3.034	6.544	3.804	6.710	1.343	6.266	-2.482	.013*
	Total	4.620	5.931	3.622	5.619	3.930	5.882	2.547	5.312	-2.971	-.003**
CDC-CFS	Psychology	3.000	4.191	1.694	4.306	1.571	2.209	-.296	2.847	-1.556	-.120
Shortness-Of	Nutrition	3.285	4.090	2.026	4.543	2.407	4.060	-.801	4.013	-1.849	-.064
Breath	Combined	3.392	4.788	2.046	4.739	2.526	3.631	1.194	3.858	-.976	-.329
	Total	3.237	4.365	2.497	3.977	2.296	3.554	1.461	3.131	-2.538	-.011*
CDC-CFS	Psychology	3.429	5.347	1.762	5.095	1.214	2.517	-.239	2.668	-1.973	.049*
Sensitivity-To	Nutrition	5.031	6.097	3.177	6.884	4.111	6.198	1.659	6.563	-2.136	.033*
Light	Combined	4.481	6.360	2.710	6.251	3.297	5.557	1.259	5.335	-.787	-.431
	Total	4.336	5.975	3.330	5.342	3.197	5.419	1.924	4.471	-2.542	-.011*
CDC-CFS	Psychology	3.952	3.938	2.725	5.180	1.571	3.228	-.292	3.435	-1.614	-.106
Depression	Nutrition	4.477	5.450	2.821	6.134	3.333	4.883	1.402	5.265	-1.584	-.113
	Combined	5.077	5.950	3.420	6.734	2.766	3.324	1.547	3.985	-1.304	-.192
	Total	4.544	5.230	3.663	5.424	2.747	3.964	1.815	3.678	-2.297	-.022*

\*z-statistic for Wilcoxon Signed-Rank Test

Table 4. Comparisons across time within the secondary outcome measures (psychological)

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		Baseline				3-month follow-up				Comparisons	
		Mean	SD	95% CI for Mean		Mean	SD	95% CI for Mean		z-statistic	p-value
				Lower	Upper			Lower	Upper		
MHLCS	Psychology	-.677	.159	-.627	-.726	-.821	.251	-.676	-.966	-2.983	.003**
Internal	Nutrition	-.622	.177	-.568	-.675	1.193	2.969	-.019	2.368	-.687	.492
	Combined	-.662	.174	-.613	-.710	-.779	.318	-.662	-.896	-1.755	.079
	Total	-.653	.171	-.624	-.682	-.942	1.822	-.514	1.371	-2.962	.003**
MHLCS	Psychology	-.368	.156	-.320	-.417	-.351	.152	-.263	-.439	-2.594	.009**
Chance	Nutrition	-.340	.133	-.299	-.380	-.911	3.020	-.284	2.105	-.143	.886
	Combined	-.354	.155	-.311	-.397	-.314	.133	-.265	-.363	-.672	.501
	Total	-.354	.148	-.329	-.379	-.545	1.853	-.109	.980	-1.552	.121
MHLCS	Psychology	-.404	.134	-.362	-.446	-.441	.315	-.259	-.624	-.000	1.000
Powerful	Nutrition	-.418	.141	-.374	-.460	-.804	2.244	-.084	1.691	-1.843	.065
Others	Combined	-.407	.101	-.379	-.436	-.434	.279	-.331	-.536	-.577	.564
	Total	-.409	.124	-.388	-.430	-.574	1.3880	-.248	.900	-1.601	.109
MHLCS	Psychology	-.169	.082	-.143	-.194	-.131	.093	-.077	-.185	-1.122	.262
Doctors	Nutrition	-.171	.089	-.144	-.197	-.657	2.668	-.398	1.713	-1.686	.092
	Combined	-.191	.147	-.150	-.232	-.153	.070	-.128	-.179	-1.384	.166
	Total	-.178	.112	-.159	-.196	-.338	1.635	-.0462	.722	-2.381	.017*
MHLCS	Psychology	-.235	.075	-.212	-.259	-.268	.189	-.159	-.377	-.118	.906
Other People	Nutrition	-.264	.129	-.225	-.304	-.739	2.652	-.311	1.788	-1.697	.090
	Combined	-.245	.074	-.224	-.265	-.252	.118	-.209	-.295	-.213	.831
	Total	-.248	.095	-.232	-.264	-.438	1.626	-.055	.820	-1.186	.236
CDC-CFS	Psychology	94.381	16.836	89.134	99.628	78.571	18.434	67.928	89.215	-3.111	.002**

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Maladaptive	Nutrition	96.386	21.946	89.714	103.059	85.259	27.665	74.315	96.203	-3.443	.001***
Stress Index	Combined	98.269	19.165	92.934	103.605	87.484	22.965	79.060	95.908	-2.215	.027*
Scale Score	Total	96.486	19.373	93.225	99.747	84.917	24.004	79.276	90.557	-5.123	.001***

\*z-statistic for Wilcoxon Signed-Rank Test

For peer review only

**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology\***  
**Checklist for cohort, case-control, and cross-sectional studies (combined)**

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	7-8
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	10-12
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	10-12
Bias	9	Describe any efforts to address potential sources of bias	20-21
Study size	10	Explain how the study size was arrived at	13-14
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	12-13
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	12-13
		(b) Describe any methods used to examine subgroups and interactions	12-13
		(c) Explain how missing data were addressed	12
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	12 & 14

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	14-15
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	13-14 & Table 1 8
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	15-17
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Tables 2-9 (IQR)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	19-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20-21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20
Generalisability	21	Discuss the generalisability (external validity) of the study results	20-21
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).