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# Shaken but unstirred? Effects of micronutrients on stress and trauma after an earthquake: RCT evidence comparing formulas and doses

Julia J Rucklidge[1]*, Rebecca Andridge[2], Brigette Gorman[1], Neville Blampied[1], Heather Gordon[1] and Anna Boggis[3]

[1]*Department of Psychology, University of Canterbury, Christchurch, New Zealand*
[2]*Division of Biostatistics, College of Public Health, Ohio State University, Columbus, Ohio, USA*
[3]*West Coast District Health Board, Greymouth, New Zealand*

**Objective** To compare two micronutrient (vitamins and minerals) formulas (Berocca™ and CNE™) and assess their impact on emotions and stress related to the 6.3 earthquake on February 22nd 2011 in Christchurch, New Zealand.
**Methods** 91 adults experiencing heightened anxiety or stress 2–3 months following the earthquake were randomized to Berocca™, CNE™ low dose (CNE4), or CNE™ high dose (CNE8), for 28 days and monitored weekly via on-line questionnaires and followed 1 month post-trial. A nonrandomized control group (n = 25) completed questionnaires at baseline and 4 weeks.
**Results** All treatment groups experienced significant declines in psychological symptoms ($p < .001$). CNE™ groups experienced greater reduction in intrusive thoughts as compared with Berocca™ ($p = .05$), with no group differences on other measures of psychological symptoms. However, CNE8 group reported greater improvement in mood, anxiety, and energy ($p < .05$) with twice as many reporting being "much" to "very much" improved and five times more likely to continue taking CNE™ post-trial than Berocca™ group. Treated participants had better outcomes on most measures over 4 weeks as compared to controls.
**Conclusions** This study supports micronutrients as an inexpensive and practical treatment for acute stress following a natural disaster with a slight advantage to higher doses ACTRN 12611000460909. 

KEY WORDS—earthquake; micronutrients; trauma; disaster; stress; vitamins

Psychological distress, including heightened anxiety, fear, and depression, in those who survive a natural disaster such as an earthquake is well supported by research (Suhail *et al*., 2009; Bonanno *et al*., 2010; Wang *et al*., 2010). A range of factors impact the distress experienced by survivors, including severity of injury to self and important others, level of destruction of one's home and place of business, and general loss of resources (Sattler *et al*., 2006; Kuwabara *et al*., 2008). Long-term impacts on psychological well-being include the development of Post-traumatic Stress Disorder (PTSD), with incidence of PTSD likely up to 30%, depression, anxiety, traumatic grief, suicide risk, substance abuse, and stress-related health problems (Bonanno *et al*., 2010).

How might these adverse outcomes be prevented or ameliorated? To be effective for an entire community affected by a natural disaster, such measures have to be inexpensive to provide, easy to distribute and administer, and unlikely to have their own adverse side effects. One potential intervention that has not been adequately researched is the impact that nutrient supplementation may have on resilience and overall reduction of anxiety, stress, and trauma symptoms. Research in the field of micronutrients (vitamins and minerals) is receiving growing international attention in other areas, especially for the treatment of psychiatric symptoms (Glatthaar, 1999; Kaplan *et al*., 2007; Rucklidge *et al*., 2009). Many studies have documented the positive effect of broad spectrum micronutrients on mental disorders such as Attention Deficit/Hyperactivity Disorder (ADHD), autism, and bipolar disorder (Gately and Kaplan, 2009; Mehl-Madrona *et al*., 2010; Rucklidge *et al*., 2011b), on psychological symptoms such as stress and anxiety (Carroll *et al*., 2000; Schlebusch *et al*., 2000; Kennedy *et al*., 2010; Stough *et al*., 2011), and on physical illness such as infectious disease and stroke recovery (Barringer *et al*., 2003; Sato *et al*., 2005; Gariballa and Forster, 2007; Chen *et al*., 2011).

Vitamins and minerals play an important role in brain health, acting as cofactors in the synthesis and

*Correspondence to: J. Rucklidge, Department of Psychology, University of Canterbury, Private Bag 4800, Christchurch, New Zealand. Tel: 64 3 364 2987 ext 7959; Fax: 64 3 364 2181. E-mail: julia.rucklidge@canterbury.ac.nz
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metabolism of neurotransmitters, which regulate our neuronal systems. According to McCann and Ames (2009), the stress response imposes high nutritional needs, and these can take precedence over other biological needs, thereby impacting other normal biological activity during periods of prolonged stress. Vitamins have been well documented to act as neurotransmitter cofactors essential for the regulation of the stress response (Kaplan *et al*., 2007). For example, thiamine ($B_1$) protects the adrenal glands from exhaustion; niacinamide ($B_3$) shunts tryptophan to serotonin; pyridoxal 5 phosphate ($B_6$) acts as a cofactor for the synthesis of gamma-aminobutyric acid, serotonin, and dopamine; methylcobalamin ($B_{12}$) normalizes cortisol production; ascorbic acid (vitamin C), given in higher than recommended dietary allowance values, supports adrenal function and decreases high cortisol levels; and 5-methyltetrahydrofolate regenerates tetrahydrobiopterin, which is essential for neurotransmitter formation (see Head and Kelly, 2009). Folate, vitamin $B_{12}$, and $B_6$ are involved in the metabolism of homocysteine, which is a by-product of methionine metabolism. Recent research shows that there is a clear relationship between homocysteine levels and stress (Kang *et al*., 2005), possibly caused by a reduction in $B_6$ levels by acute stressors and that supplementation with $B_6$ may result in reductions in stress. With these physiological mechanisms, supplementation with B vitamins may be sufficient to decrease stress levels, at least in the short-term.

The 2010–2011 earthquakes in Christchurch offered a unique opportunity to study the impact of nutrients on mental health symptoms post-disaster. Fortuitously, the 7.1 magnitude earthquake on 4 September 2010 occurred in the context of ongoing trials of New Zealand adults with ADHD taking a micronutrient supplement called EMPowerplus™ (EMP+), which supplies 36 ingredients (vitamins, minerals, amino acids, and antioxidants). A comparison of the self-reported depression, anxiety, and stress responses of adults with ADHD who were and were not taking the micronutrient supplement at the time of the earthquake showed at 2 weeks post-quake that those taking EMP+ reported feeling significantly less anxious and stressed than those not taking it, showing a medium to large effect size, suggesting that the micronutrients provided resilience to the on-going stress of the earthquake and subsequent aftershocks (Rucklidge *et al*., 2011a). These data are consistent with other trials investigating the impact of nutrients on mental health symptoms such as stress. For example, Schlebusch *et al*. (2000), Carroll *et al*. (2000), and Kennedy *et al*. (2010), using double blind placebo-controlled designs with both healthy and stressed adults, all found that those taking an over-the-counter high vitamin B complex formula (Berocca™) were less stressed and anxious after 30 days than those taking the placebo.

Research following the initial September quake established that anxiety and stress were high among the general population (Kemp *et al*., 2011), but there are no studies yet that have investigated the impact of nutrient supplementation on post-earthquake emotional resilience and recovery within the general public (i.e., as distinct from those with known pre-existing mental health problems). To meet this gap in research, following the devastating 6.3 aftershock on 22 February 2011, which killed 185 people and caused extensive destruction in Christchurch city, we compared two doses (four capsules or eight capsules per day) of a product that is the identical formula as EMP+ called CNE™ and is marketed for general health. These two dosage levels were compared with Berocca Performance™ (one pill per day), given that Berocca™ had already been established as efficacious in the treatment of stress and anxiety through three randomized trials (Carroll *et al*., 2000; Schlebusch *et al*., 2000; Kennedy *et al*., 2010). Under the circumstances following this natural disaster (e.g., on-going intermittent loss of power, no permanent space from which to run the study because of the closure of buildings on campus, transportation challenges, persistent aftershocks, lack of telephone contact with the researchers because of their own transient living situations, desire for a short recruitment period to ensure similar environmental stressors across groups, and substantial and ongoing stressors in the community), we felt that a comparison with an established treatment was the best design over a placebo-controlled study. Indeed, ethically, in contemporary randomized controlled trial research, where there is an established effective treatment, new treatments are expected to be compared head to head with that treatment rather than an inert placebo (Coulter, 2011). The ethics committees concurred with this decision.

We were interested in the impact of nutrients on stress, anxiety, mood, and post-traumatic symptoms such as intrusive thoughts, avoidance, and hyperarousal. We also included a nonrandomized group from the community who did not take the micronutrients but who completed the same screening questionnaires.

## METHODS

### *Design*

The study used a randomized controlled design in which participants were assigned to one of the three



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conditions in an equal ratio: (i) Berocca Performance™ (Berocca™—one pill a day); (ii) four capsules of CNE™ (CNE4); or (iii) eight capsules of CNE™ (CNE8). The ingredients and dosage of these different treatments are detailed in Table 1, and both products were purchased for the purposes of the study. The randomization scheme was generated by using the website randomization.com (http://www.randomization.com) in seven blocks of 15. Assignment of the next recruited participant was placed in a concealed folder, and once informed consent had been reviewed, the assignment was revealed, and the participant provided with the pills to which they had been assigned. The study received ethical approval from both the Lower South Health and Disability Ethics Committee and the Human Ethics Committee at the University of Canterbury.

### *Participants*

The final sample consisted of 91 participants, 30 assigned to Berocca™, 31 to CNE4, and 30 to CNE8 (see Figure 1 for the CONSORT diagram and Table 2 for demographic information). Participants were recruited from the general population through advertisements in newspapers, websites dedicated to the Christchurch relief process (e.g., community websites, Facebook pages, and online auction sites), links on workplace websites, and word of mouth. To expedite the screening procedure, potential participants were first directed to a website (www.mentalhealthandnutrition.co.nz) that provided more information about the study, other treatment options for symptoms of stress, and a link to a survey developed using Qualtrics (www.qualtrics.com) that asked some brief screening questions (see Inclusion Criteria section), demographic information, and also asked potential participants to complete the measures of emotions, stress, and exposure to trauma (see Measures section). The survey reviewed some exclusion criteria (see Exclusion Criteria section), and if a potential participant endorsed one of those (e.g., being pregnant), the survey ended,

Table 1. Ingredient list of CNE™ and Berocca™

| | Four caps CNE™ | | %DV | Eight caps CNE™ | | %DV | Berocca™ | | %DV |
|---|---|---|---|---|---|---|---|---|---|
| Vitamin A | 1536.0 | IU | 30 | 3072.0 | IU | 60 | | | |
| Vitamin C | 160.0 | mg | 270 | 320.0 | mg | 540 | 500 | mg | 847 |
| Vitamin D | 384.0 | IU | 100 | 768.0 | IU | 200 | | | |
| Vitamin E | 96.0 | IU | 320 | 192.0 | IU | 640 | | | |
| Vitamin B1 | 4.8 | mg | 320 | 9.6 | mg | 640 | 15 | mg | 1000 |
| Vitamin B2 | 3.6 | mg | 210 | 7.2 | mg | 420 | 15 | mg | 882 |
| Vitamin B3 | 24.0 | mg | 120 | 48.0 | mg | 240 | 50 | mg | 250 |
| Vitamin B5 | 5.8 | mg | 60 | 11.5 | mg | 120 | 23 | mg | 240 |
| Vitamin B6 | 9.6 | mg | 480 | 19.2 | mg | 960 | 10 | mg | 500 |
| Vitamin B9 | 384.0 | µg | 100 | 768.0 | µg | 200 | 400 | µg | 104 |
| Vitamin B12 | 240.0 | µg | 4000 | 480.0 | µg | 8000 | 10 | µg | 167 |
| Vitamin H | 288.0 | µg | 100 | 576.0 | µg | 200 | 150 | µg | 52 |
| Calcium | 352.0 | mg | 35 | 704.0 | mg | 70 | 100 | mg | 10 |
| Iron | 3.7 | mg | 20 | 7.3 | mg | 40 | | | |
| Phosphorus | 224.0 | mg | 20 | 448.0 | mg | 40 | | | |
| Iodine | 54.4 | µg | 40 | 108.8 | µg | 80 | | | |
| Magnesium | 160.0 | mg | 40 | 320.0 | mg | 80 | 100 | mg | 25 |
| Zinc | 12.8 | mg | 90 | 25.6 | mg | 180 | 10 | mg | 70 |
| Selenium | 54.4 | µg | 80 | 108.8 | µg | 160 | | | |
| Copper | 1.9 | mg | 100 | 3.8 | mg | 200 | | | |
| Manganese | 2.6 | mg | 130 | 5.1 | mg | 260 | | | |
| Chromium | 166.4 | µg | 140 | 332.8 | µg | 280 | | | |
| Molybdenum | 38.4 | µg | 50 | 76.8 | µg | 100 | | | |
| Potassium | 64.0 | mg | 2 | 128.0 | mg | 4 | | | |
| dl-Phenylalanine | 96.0 | mg | 10 | 192.0 | mg | 20 | | | |
| Glutamine | 48.0 | mg | | 96.0 | mg | | | | |
| Citrus bioflavanoids | 64.0 | mg | | 128.0 | mg | | | | |
| Grape seed | 12.0 | mg | | 24.0 | mg | | | | |
| Choline bitartrate | 144.0 | mg | 26 | 288.0 | mg | 52 | | | |
| Inositol | 48.0 | mg | 120 | 96.0 | mg | 240 | | | |
| Ginkgo biloba | 9.6 | mg | | 19.2 | mg | | | | |
| Methionine | 16.0 | mg | | 32.0 | mg | | | | |
| Germanium sesquioxide | 5.5 | mg | 180 | 11.0 | mg | 360 | | | |
| Boron | 640.0 | µg | | 1280.0 | µg | | | | |
| Nickel | 7.8 | µg | | 15.7 | µg | | | | |
| Vanadium | 318.4 | µg | | 636.8 | µg | | | | |

DV, daily value.



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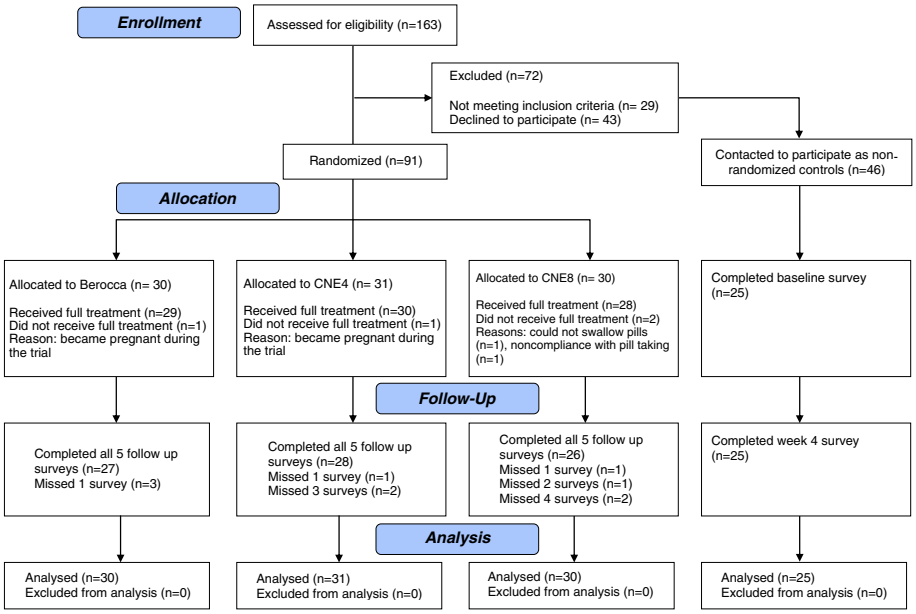


Figure 1. Screening, randomization, and participant flow by group

Table 2. Baseline characteristics of study participants

| Characteristic | Berocca™ | | CNE4 | | CNE8 | | Control | |
|---|---|---|---|---|---|---|---|---|
| Number of participants | 30 | | 31 | | 30 | | 25 | |
| Age (mean, SD)[a] | 41.8 | 14.5 | 35.6 | 10.9 | 46.6 | 17.8 | 40.1 | 9.6 |
| Female | 24 | 80% | 28 | 90% | 26 | 87% | 23 | 92% |
| Income | | | | | | | | |
| <$20,000 | 4 | 13% | 7 | 23% | 5 | 17% | 3 | 12% |
| $20,000–$40,000 | 6 | 20% | 6 | 19% | 8 | 27% | 5 | 20% |
| $40,000–$60,000 | 10 | 33% | 4 | 13% | 7 | 23% | 4 | 16% |
| $60,000–$80,000 | 3 | 10% | 6 | 19% | 5 | 17% | 8 | 32% |
| >$80,000 | 7 | 23% | 8 | 26% | 5 | 17% | 5 | 20% |
| Education | | | | | | | | |
| No school certificate | 3 | 10% | 2 | 6% | 3 | 10% | 2 | 8% |
| School certificate in one or more subjects | 1 | 3% | 2 | 6% | 5 | 17% | 4 | 16% |
| Sixth form certificate or university entrance in one or more subjects | 4 | 13% | 3 | 10% | 3 | 10% | 7 | 28% |
| University bursary or scholarship | 2 | 7% | 0 | 0% | 2 | 7% | 0 | 0% |
| Overseas qualification | 0 | 0% | 0 | 0% | 0 | 0% | 1 | 4% |
| Post-secondary (e.g., diploma and trade certificate) university degree | 9 | 30% | 8 | 26% | 7 | 23% | 4 | 16% |
| Other qualification | 8 | 27% | 15 | 48% | 7 | 23% | 5 | 20% |
| Other | 3 | 10% | 1 | 3% | 3 | 10% | 2 | 8% |
| Ethnic origin | | | | | | | | |
| New Zealanders of European descent | 25 | 83% | 22 | 71% | 27 | 90% | 22 | 88% |
| Maori | 3 | 10% | 4 | 13% | 0 | 0% | 2 | 8% |
| Other | 2 | 7% | 5 | 16% | 3 | 10% | 1 | 4% |
| History of mental illness | 14 | 47% | 8 | 26% | 15 | 50% | 13 | 52% |
| Smoker | 6 | 20% | 7 | 23% | 6 | 20% | | |
| TESS occurrence (mean, SD) | 5.3 | 3.2 | 7.0 | 3.2 | 7.2 | 2.4 | 6.1 | 2.9 |
| TESS distress (mean, SD)[b] | 18.5 | 12.8 | 25.3 | 14.4 | 27.8 | 11.9 | 23.0 | 14.2 |
| Cannabis user | 3 | 10% | 0 | 0% | 0 | 0% | | |
| Alcohol abuse[c] | 5 | 17% | 4 | 13% | 6 | 20% | | |
| Caffeine use (mean, SD)[d] | 17.2 | 12.3 | 23.2 | 13.4 | 26.1 | 13.3 | | |
| Receiving counseling | 5 | 17% | 4 | 13% | 1 | 3% | | |

[a]CNE4 group significantly different from CNE8 group.
[b]Berroca group significantly different from CNE8 group.
[c]Determined by New Zealand guidelines and defined as either a binge drinker (women consuming more than four drinks in one sitting and men more than five drinks in one sitting) or anyone whose weekly consumption did not include two alcohol free days and men reported drinking more than three standard drinks a day and women drinking more than two standard drinks a day.
[d]Caffeine assessed as number of caffeinated drinks (coffee, red bull, tea, coke, etc.) consumed over the week prior to the trial. CNE8 group significantly different than Berocca™ group.



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and the individual was provided with a list of counseling services and other treatment options in Christchurch. On submission of the information electronically, the questionnaires to assess eligibility were electronically scored (see the following text).

*Inclusion criteria.* Participants had to have been in Christchurch at the time of the 22 February earthquake. They had to be free of psychotropic medications for the trial (established through the online screening questionnaire) and must have been off psychotropic medications for a minimum of 4 weeks prior to the trial. They had to be at least 18 years of age, possess a level of language comprehension sufficient to complete the questionnaires, and be considered reliable and compliant with the protocol, which included taking the pills with food and water. They also had to have *at least* one score above the cut-off scores of the measures of depression, anxiety, stress, and trauma symptoms (see Measures section).

*Exclusion criteria (established through the screening questionnaire).* (i) Neurological disorder involving brain or other central nervous system function (e.g., epilepsy and multiple sclerosis); (ii) any serious medical condition requiring intervention during the trial; (iii) pregnant or breastfeeding; (iv) evidence of untreated or unstable thyroid disease; (v) any known abnormality of mineral metabolism (e.g., Wilson's disease and hemochromatosis); and (vi) any participant judged clinically to be at serious risk for suicide or violence in the opinion of the researchers (established through the face-to-face meeting at the university with clinical psychologists). If any medical concerns were raised, these were reviewed by the study physician to establish eligibility.

### *Nonrandomized controls*

To compare the responses of the trial participants with people who did not participate but could provide us with a sample of changes in stress within Christchurch over the same period, we contacted all those who had been eligible for the trial, had completed the online screening survey, but who had decided not to partake in the study ($n = 37$). We also contacted those who were taking psychotropic medications and as such were ineligible for the trial ($n = 9$). Of these 46 people contacted, 25 (seven were taking medications) completed an online survey approximately 4 weeks after the completion of the first survey. They were compensated with a $10 grocery voucher.

### *Measures*

*Demographic information.* Participants were asked their level of education (assessed on a scale from 1 "no school certificate" to 7 "post-graduate degree"), age, occupation, income (measured on a five-point scale from 1 "less than $20,000" to 5 "more than $80,000"), history of mental illness (e.g., anxiety disorder and ADHD), and ethnicity.

*The Depression Anxiety and Stress Scale (DASS-42; Lovibond and Lovibond, 1995).* The DASS is a 42-item questionnaire that assesses an individual's current severity of symptoms relating to depression, anxiety, and stress. Cut-offs have been provided to indicate mild, moderate, or severe problems; anything below 10 (for depression), 7 (for anxiety), and 14 (for stress) is considered within the normal range, and these scores were used as cut-offs for inclusion.

*Impact of Event Scale (IES-R; Weiss and Marmar, 1997).* The IES-R is a self-report measure designed to assess current subjective distress for any specific life event, in this case the 22 February earthquake. Participants indicated from 0 (not at all) to 4 (extremely) their distress over the last 7 days. The IES-R has 22 items with three subscales: intrusive thoughts (eight items; e.g., other things kept making me think of it), avoidance (eight items; e.g., I stayed away from reminders of it), and hyperarousal (six items; e.g., I felt irritable and angry), and a total score, providing four mean scores ranging from 0 to 4. Creamer *et al*. (2003) suggested a cut-off of 1.5 on the total score (equivalent to a total score of 33) has good diagnostic accuracy for identifying individuals who would likely be identified with PTSD if assessed with a clinical interview.

*Perceived Stress Scale (PSS; Cohen et al*., 1983). The PSS assesses the degree to which situations in people's lives are appraised as stressful. It comprises 14 items, each scored on a five-point Likert scale; total scores range from 0–56.

*Traumatic Exposure Severity Scale (TESS; Elal and Slade, 2005).* The TESS was developed to specifically address dimensions of exposure to an earthquake disaster in adults. There are 24 items that assess a wide range of stressors across five subscales: Resource Loss (e.g., did you need food), Damage to Home and Goods (e.g., did you have to relocate), Personal Harm (e.g., were you buried under the rubble), Concern for Significant Others (e.g., were any members of your family physically injured), and Exposure to the Grotesque



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(e.g., did you see any dead bodies). The scale assesses both occurrences (i.e., did you need shelter after the earthquake; range 0–24) and distress [how distressing was this for you from 1 (not at all) to 5 (extremely); range 0–120].

*Modified Clinical Global Impressions (CGI-I; Spearing et al.*, 1997). At 4 and 8 weeks, we asked participants to rate how much they thought their mood, anxiety, stress, and energy had changed since they started the trial (or for controls, since they had completed the initial screening questionnaire). They were asked to indicate on a seven-point scale, which statement best applied, from 1 (very much improved) to 7 (very much worse). This rating scale is widely used for clinical trials and is typically completed by a clinician. As participants could not be tracked face-to-face, it was adapted such that participants could rate their own impressions of change.

*Adverse events.* Participants were asked about common side effects associated with taking medications (e.g., headaches, rash, and nausea). They were also asked to comment on any other changes they attributed to the pills.

*Weekly diet intake questionnaire (Baker et al., 2003).* Participants were asked to indicate from 1 (less than once a week) to 5 (daily) how often over the previous 2 weeks they ate breakfast, ate a balanced meal, ate even when full, and ate fast foods or snack foods such as potato chips or candy bars, and we also asked about average daily servings of fruit and vegetables [from 1 (less than one serving) to 5 (4 or more servings)]. Participants were also asked to indicate from 1 (not very healthy) to 7 (very healthy) how healthy they thought their diet is. A total score ranged from 9 to 47, with a higher score indicative of a healthier diet (two items were reverse scored). This questionnaire was completed at baseline, 4 weeks, and 1 month follow-up. Further, every week (starting with baseline), participants were asked to record the amount of alcohol, caffeinated beverages (coffee, tea, coke, etc.), cigarettes, and illicit drugs consumed over the previous week. Participants were asked to limit their consumption of these products to maximize response to the micronutrients. These dietary related questions were not completed by the control group.

### *Procedures*

Eligible participants were contacted by e-mail and offered a convenient appointment time (30 min) at the university. As university buildings were closed because of earthquake damage for most of the recruitment period (22 May to 9 June 2011), interviews were held in a relocatable building on the university's suburban campus. Recruitment came to a natural end following the 13 June 6.3 magnitude earthquake because of the complete closure of the university and further disruption to the city and its infrastructure.

At the allocated appointment, the information sheet was reviewed, informed consent obtained, the DASS-42, PSS, and IES-R were repeated if it had been at least 1 week since the completion of the online survey, additional information was obtained on current and past mental health symptoms (prior mental health consultation or psychiatric diagnosis), the diet intake questionnaire was completed, and the pills were provided for the duration of the study. All participants received a $10 petrol voucher to cover the cost of coming to the university.

The trial lasted for a 4-week period. Those in the low dose CNE™ group started with the full dose of four capsules a day (taken as one dose). To allow the body time to adjust to the consumption of a large number of nutrients, those in the higher dose group began at four capsules a day (two twice a day) and increased their dose to eight (four twice a day) at day 4 and continued at this dose until the end of the 4-week period. Participants were monitored every week via the internet by using the same questionnaires as baseline for the 4-week period. Participants were asked to monitor compliance with taking the pills and to indicate the number of doses missed and also any adverse events. We offered participants daily text messages to remind them to take their pills [22 participants (24%) opted for these]. The 4-week questionnaire also included the diet intake questionnaire and the CGI-I as well as whether they had received any counseling over the trial or had changed their amount of exercise. At the completion of the 4-week trial, participants were offered a choice of either a further month's supply of Berocca™, CNE™, or a grocery voucher; all of which were sent to participants by post. They were then contacted by e-mail 1 month later and again asked to complete the same questionnaire as completed at 4 weeks with additional questions assessing if they had stayed on micronutrients (and which one and at which dose), switched to medications, or stopped completely.

### *Statistical analysis*

The primary outcomes were changes in DASS-42, IES-R, and PSS scores from baseline to week 4. The secondary outcome was the CGI-I scale completed at week 4. Mixed models were used to test the effects of micronutrient supplementation (Diggle *et al.*, 2002). This type of model accounts for the within-subject correlation arising from repeated measurements



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and accommodates intermittent missing data, thus all participants' data could be used in an intent-to-treat analysis. A compound-symmetric variance–covariance structure was used to estimate error variance, using the PROC MIXED procedure in SAS 9.1 with a REPEATED statement (SAS Institute, Cary, NC, USA) and the Kenward–Roger adjustment to the degrees of freedom (Kenward and Roger, 1997). To test for treatment group differences, models included the effects of week (categorical), treatment group, and their interaction. Secondary analyses adjusted for baseline characteristics that differed between the groups. As appropriate, chi-square tests, Fisher's exact tests, and analysis of variance were used to compare the treatment groups on baseline characteristics and changes in these characteristics over the course of the trial. Post hoc group comparisons were adjusted for multiple comparisons by using Tukey's test. The primary analyses were comparisons of randomized groups; secondary analyses compared randomized treatment groups with nonrandomized controls, and these were adjusted for multiple testing by using a Bonferroni correction to protect against an inflated risk of type 1 error.

## RESULTS

### *Study population*

Characteristics of the study sample at baseline are shown in Table 2. Comparison with the nonrandomized control group revealed no significant differences in these baseline measures between control and treatment groups. For the purposes of determining if any chance imbalance between the groups occurred that could affect outcome measures, we compared groups at baseline. The analysis revealed differences in age, TESS distress, and caffeine use. Post hoc comparisons showed the CNE4 group was younger than the CNE8 group, the Berocca™ group reported lower TESS distress than the CNE8 group, and the CNE8 group had higher caffeine use than the Berocca™ group. Subsequently, these variables were used as covariates in secondary analyses of treatment effects to guard against confounding.

During the trial period, the NZ government made some significant decisions about residential land that was a substantial stressor during this time. We examined the addresses identifying where our participants lived and whether they had received information from the government about the fate of their land and whether they could rebuild on it. Twenty-three (76.7%) of those in the Berocca™ group, 26 (80.6%) of the CNE4 group, 18 (60%) of the CNE8 group, and 20 (80%) of the control group were told their land could be rebuilt on, with no differences among the groups ($\chi^2$ (3, $n = 116$) = 5.279, *ns*). There was also an equal distribution of participants who completed the 4 week questionnaire in the week following the 13 June 6.3 aftershock with about 23% of the sample completing the study around that time ($\chi^2$ (3, $n = 116$) = 1.067, *ns*).

Paired *t*-tests comparing those who completed the baseline assessment twice ($n = 31$) suggested that the overall functioning, specifically stress ($t(30) = 2.429$, $p < .05$) and intrusions ($t(30) = 2.124$, $p < .05$), worsened from when they completed the online questionnaire to when they entered the study, although mood significantly improved over the same period ($t(30) = 2.170$, $p < .05$). The mean period was 10 days with a range from 7 to 24 days. The second baseline (closest to the start of the study) was utilized as the baseline measurement for these participants. There was no difference in the percent of participants with multiple baselines across the three randomized groups ($\chi^2$ (2, $n = 91$) = 3.97, *ns*), and there was no difference in average time between baseline assessments ($F(2, 28) = 2.04$, *ns*).

### *Side effects and compliance*

Adverse effects reported by at least 5% of a study group are summarized in Table 3. There were

Table 3. Treatment-emergent adverse effects reported by at least 5% of the participants in a treatment group during trial

| | Berocca™ ($n = 30$) | | CNE4 ($n = 31$) | | CNE8 ($n = 30$) | | *p*-value |
|---|---|---|---|---|---|---|---|
| Dry mouth | 5 | 17% | 7 | 23% | 4 | 13% | .78 |
| Urinary retention | 0 | 0% | 0 | 0% | 2 | 7% | .10 |
| Constipation | 4 | 13% | 3 | 10% | 6 | 20% | .45 |
| Sedation | 1 | 3% | 3 | 10% | 0 | 0% | .32 |
| Sleep disruptions | 3 | 10% | 2 | 6% | 8 | 27% | .04 |
| Weight gain | 3 | 10% | 0 | 0% | 5 | 17% | .04 |
| Headache | 4 | 13% | 6 | 19% | 4 | 13% | .82 |
| Nausea | 2 | 7% | 7 | 23% | 4 | 13% | .20 |
| Gastrointestinal disturbances/diarrhea | 3 | 10% | 5 | 16% | 6 | 20% | .51 |
| Abdominal pain | 1 | 3% | 3 | 10% | 1 | 3% | .61 |
| Anxiety | 0 | 0% | 1 | 3% | 4 | 13% | .04 |

Data are *n* (%). *p*-values by Fisher's exact test.



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significant differences in the experience of sleep disruptions (Fisher's exact test, $p < .05$), weight gain (Fisher's exact test, $p < .05$), and anxiety (Fisher's exact test, $p < .05$) across the treatment groups, with the CNE8 group reporting the largest number of side effects. One person dropped out (CNE8) within the first week because of difficulty swallowing the pills. We assessed compliance with taking all doses across the 4-week period, and there was a group difference ($F(2, 85) = 3.32$, $p < .05$), post hoc analyses revealing that the CNE8 group was less compliant with taking all doses compared with the Berocca™ group. However, average compliance across the groups was actually high at 97% for the Berocca™ group, 96% for the CNE4 group, and 92% for the CNE8 group. Other than one participant in the CNE8 group (who also did not complete any surveys until the 1-month follow-up), all participants consumed at least 50% of the doses over the 4 weeks with the lowest compliance at 61% in CNE4.

*Primary outcomes for randomized groups*

Results for the primary outcomes of DASS-42, IES-R, and PSS for randomized participants are summarized in Table 4. There were no significant differences at baseline by group for any measure. All three treatment groups showed significant decreases in all measures over the 4 weeks of the trial ($p < .001$ for all outcomes). The pattern of change was similar for all outcome measures; Figures 2 and 3 show the change over time in IES-R intrusions and DASS-42 stress. There were no significant differences between the treatment groups in the change over time, although there was a borderline effect of treatment on the change in IES-R intrusion, with the CNE4 and CNE8 groups showing greater benefit in terms of reduced intrusive thoughts related to the trauma as compared with the Berocca™ group.

Because baseline analyses revealed that the treatment groups differed on age, distress, and caffeine use at baseline, secondary analyses that controlled for these variables were conducted. Results were not substantially different from the primary analyses, with the effect of week remaining significant for all outcomes and only a borderline significant group-by-time interaction for IES-R intrusion ($p = .06$ for group-by-time interaction, results not shown).

To further clarify results, we calculated the percent change from baseline (week 0) for all participants who provided week 4 data and took a reduction of 50% or more from the baseline to be clinically

Table 4. Differential effects of three supplement types on DASS, IES-R, and PSS[a]

| Outcome | Treatment | Baseline | Change baseline to 4 weeks | Percent change (%) | *p* for change | *p* for week by treatment interaction |
|---|---|---|---|---|---|---|
| DASS depression | Berocca™ | 17.8 (1.4) | −9.0 (1.5) | −51 | <.0001 | .76 |
| | CNE4 | 14.2 (1.4) | −7.4 (1.5) | −52 | <.0001 | |
| | CNE8 | 15.4 (1.4) | −6.8 (1.5) | −44 | <.0001 | |
| DASS anxiety | Berocca™ | 9.8 (1.1) | −5.0 (1.1) | −51 | <.0001 | .22 |
| | CNE4 | 12.1 (1.1) | −8.3 (1.1) | −69 | <.0001 | |
| | CNE8 | 12.2 (1.1) | −7.1 (1.2) | −58 | <.0001 | |
| DASS stress | Berocca™ | 21.0 (1.5) | −8.7 (1.5) | −41 | <.0001 | .48 |
| | CNE4 | 22.2 (1.4) | −12.1 (1.5) | −55 | <.0001 | |
| | CNE8 | 22.0 (1.5) | −10.8 (1.6) | −49 | <.0001 | |
| DASS total | Berocca™ | 48.6 (3.4) | −22.6 (3.6) | −47 | <.0001 | .63 |
| | CNE4 | 48.5 (3.4) | −27.8 (3.5) | −57 | <.0001 | |
| | CNE8 | 49.6 (3.4) | −24.7 (3.7) | −50 | <.0001 | |
| IES-R avoid | Berocca™ | 1.3 (0.1) | −0.6 (0.1) | −49 | <.0001 | .76 |
| | CNE4 | 1.6 (0.1) | −1.0 (0.1) | −60 | <.0001 | |
| | CNE8 | 1.5 (0.1) | −0.8 (0.1) | −51 | <.0001 | |
| IES-R intrusion | Berocca™ | 1.6 (0.2) | −0.5 (0.1) | −31 | .001 | .05 |
| | CNE4 | 2.0 (0.2) | −0.8 (0.1) | −40 | <.0001 | |
| | CNE8 | 2.1 (0.2) | −0.9 (0.2) | −42 | <.0001 | |
| IES-R arousal | Berocca™ | 1.8 (0.2) | −0.6 (0.2) | −33 | .0002 | .09 |
| | CNE4 | 2.2 (0.2) | −1.1 (0.2) | −49 | <.0001 | |
| | CNE8 | 2.2 (0.2) | −0.9 (0.2) | −43 | <.0001 | |
| ES-R total | Berocca™ | 34.2 (2.9) | −12.6 (2.7) | −37 | <.0001 | .12 |
| | CNE4 | 42.4 (2.9) | −20.8 (2.7) | −49 | <.0001 | |
| | CNE8 | 42.0 (2.9) | −18.8 (2.8) | −45 | <.0001 | |
| PSS stress | Berocca™ | 21.8 (1.3) | −4.5 (1.3) | −21 | .0007 | .28 |
| | CNE4 | 23.1 (1.3) | −7.8 (1.3) | −34 | <.0001 | |
| | CNE8 | 22.7 (1.3) | −6.1 (1.4) | −27 | <.0001 | |

DASS, Depression and Anxiety Scale; IES-R, Impact of Event Scale-Revised; PSS, Perceived Stress Scale.
[a]All values are mean (SE), derived from tests for orthogonal contrasts in mixed effects models.



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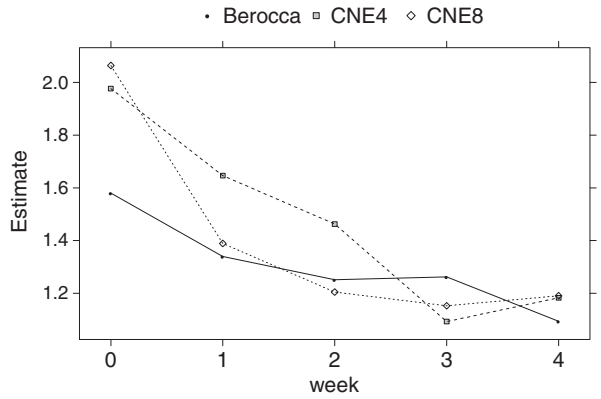


Figure 2. Change in IES-R intrusions during the trial, by treatment group. Results from mixed effects regression models

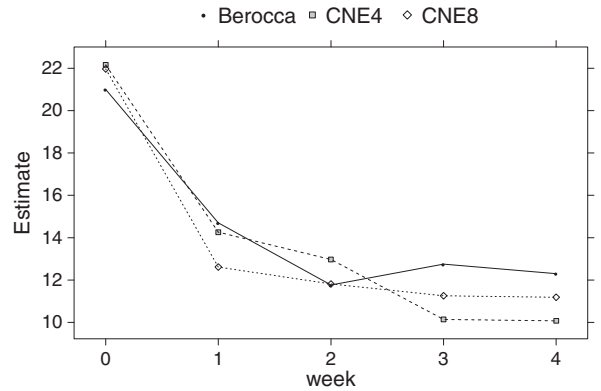


Figure 3. Change in DASS stress during the trial, by treatment group. Results from mixed effects regression models

significant. To obtain a conservative estimate of the treatment effects, for the six participants who did not complete the questionnaires at week 4 (1 Berocca™, 1 CNE4, 4 CNE8, and 0 control) we assumed there was not a 50% reduction. There was a borderline significant difference by treatment in the proportion of participants who achieved a 50% reduction in the total DASS score ($\chi^2$ (2, $n = 91$) = 6.03, $p = .05$), with a smaller proportion of the Berocca™ group experiencing a 50% or greater reduction (Table 5). There were no other differences across treatment groups.

### *Comparison to nonrandomized controls*

Nonrandomized controls were only assessed at baseline and week 4. To compare these participants to the treatment groups, models for primary outcomes were repeated using only data from these two time points. Because we did not find significant differences in primary outcomes among the treatment groups, these groups were pooled for the purposes of comparison with controls. There were significant differences between treated and control participants for almost all measures (Table 6), with the treatment groups experiencing larger decreases. These differences were also seen when taking a reduction of 50% or more from the baseline to be clinically significant (Table 4). There were significant differences for both the total DASS and total IES-R in that a greater percent of the treated participants had at least 50% reduction.

By using a cut-off of 33 on the total score for IES-R, as suggested by Creamer *et al*. (2003), participants were classified as having likely PTSD at baseline and at the 4-week follow-up (participants with missing scores were conservatively classified as no PTSD). At baseline, 70 of the 116 (60%) participants had probable PTSD, with no significant differences across the study groups ($\chi^2$ (3, $n = 116$) = 6.39, *ns*), although the control group tended to have fewer participants with

Table 5. Percent of participants with at least a 50% reduction in outcomes, by treatment group and with comparison with nonrandomized control group[a]

| | Berocca™ | | CNE4 | | CNE8 | | *p* for treatment comparison[a] | Combined treatment groups | | Control | | *p* for treatment versus control[b] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Number of participants | 30 | | 31 | | 30 | | | 91 | | 25 | | |
| DASS | | | | | | | | | | | | |
| Depression | 15 | 50% | 19 | 61% | 13 | 43% | .36 | 47 | 52% | 9 | 36% | >.99 |
| Anxiety | 14 | 47% | 23 | 74% | 17 | 57% | .09 | 54 | 59% | 7 | 28% | .05 |
| Stress | 13 | 43% | 18 | 58% | 15 | 50% | .51 | 46 | 51% | 5 | 20% | .06 |
| Total | 13 | 43% | 23 | 74% | 18 | 60% | .05 | 54 | 59% | 5 | 20% | .004 |
| IES-R | | | | | | | | | | | | |
| Avoid | 14 | 47% | 19 | 61% | 13 | 43% | .33 | 46 | 51% | 2 | 8% | .001 |
| Intrusion | 11 | 37% | 14 | 45% | 14 | 47% | .70 | 39 | 43% | 6 | 24% | .78 |
| Arousal | 11 | 37% | 14 | 45% | 13 | 43% | .78 | 38 | 42% | 4 | 16% | .16 |
| Total | 11 | 37% | 15 | 48% | 16 | 53% | .41 | 42 | 46% | 3 | 12% | .02 |
| PSS stress | 5 | 17% | 9 | 29% | 6 | 20% | .48 | 20 | 22% | 2 | 8% | >.99 |

DASS, Depression and Anxiety Scale; IES-R, Impact of Event Scale-Revised; PSS, Perceived Stress Scale.
Dropouts are assumed to not show 50% improvement. There were six dropouts: Berocca™ = 1, CNE4 = 1, and CNE8 = 4.
[a]Chi-square tests with two degrees of freedom.
[b]Chi-square tests with one degree of freedom. *p*-values are Bonferroni adjusted.



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Table 6. Comparison of average treatment effect to changes in nonrandomized control group for DASS, IES-R, and PSS[a]

| Outcome | Group | Baseline | Change baseline to 4 weeks | % change | $p$ for comparison of changes[b] |
|---|---|---|---|---|---|
| DASS depression | Treatment | 15.8 (0.9) | −7.7 (1.0) | −49 | .31 |
| | Control | 13.4 (1.8) | −3.3 (1.8) | −24 | |
| DASS anxiety | Treatment | 11.4 (0.8) | −6.8 (0.7) | −59 | .009 |
| | Control | 10.5 (1.5) | −1.6 (1.3) | −15 | |
| DASS stress | Treatment | 21.7 (0.9) | −10.5 (1.0) | −49 | .002 |
| | Control | 18.5 (1.7) | −2.6 (1.8) | −14 | |
| DASS total | Treatment | 48.9 (2.3) | −25.0 (2.3) | −51 | .005 |
| | Control | 42.4 (4.3) | −7.4 (4.3) | −18 | |
| IES-R avoid | Treatment | 1.5 (0.1) | −0.80 (0.1) | −54 | .001 |
| | Control | 1.1 (0.2) | −0.02 (0.2) | −2 | |
| IES-R intrusion | Treatment | 1.9 (0.1) | −0.7 (0.1) | −39 | .61 |
| | Control | 1.9 (0.2) | −0.3 (0.2) | −18 | |
| IES-R arousal | Treatment | 2.1 (0.1) | −0.9 (0.1) | −42 | .0003 |
| | Control | 1.7 (0.2) | 0.1 (0.2) | 3 | |
| IES-R total | Treatment | 39.5 (1.7) | −17.5 (1.8) | −44 | .002 |
| | Control | 34.5 (3.5) | −2.5 (3.5) | −7 | |
| PSS | Treatment | 22.5 (0.8) | −6.2 (0.9) | −27 | .68 |
| | Control | 21.0 (1.6) | −2.7 (1.7) | −13 | |

DASS, Depression and Anxiety Scale; IES-R, Impact of Event Scale-Revised; PSS, Perceived Stress Scale.
[a]All values are mean (SE), derived from tests for orthogonal contrasts in mixed effects models.
[b]$p$-values are Bonferroni adjusted.

PTSD compared with the treatment groups (44 vs 65%). At 4 weeks, only 19% of the participants in the treatment groups had probable PTSD (17 of the 91), compared with 48% (12 of the 25) of the controls ($\chi^2$ (3, $n = 116$) = 9.15, $p < .05$). There were no significant differences in rates of PTSD across the treatment groups, with 20, 16, and 20% in the Berocca™, CNE4, and CNE8 groups, respectively ($\chi^2$ (2, $n = 91$) = 0.20, *ns*).

### *Secondary outcome*

Results from the participants' CGI-I ratings of change in mood, anxiety, stress, and energy since starting the trial are displayed in Table 7 and Figure 4. Among the treatment groups, there were significant treatment differences in mood ($F(2, 80) = 3.60$, $p < .05$), anxiety ($F(2, 80) = 3.780$, $p < .05$), and energy ($F(2, 80) = 5.91$, $p < .01$). There was no treatment difference for the change in stress ($F(2, 80) = 2.30$, *ns*). Post hoc analyses revealed that the CNE8 group had significantly improved mood ($p < .05$), anxiety ($p < .05$), and energy ($p < .01$) compared with the Berocca™ group. Comparison of the treatment groups with the nonrandomized control group showed that the treatment groups reported greater improvement in mood ($p < .001$), anxiety ($p < .001$), and stress ($p < .0001$) compared with the controls (energy was not measured in the controls).

### *Other variables*

We assessed changes in behavioral and dietary characteristics over the length of the trial as secondary analyses. There was a significant reduction in caffeine use overall during the trial ($F(4, 328) = 13.17$, $p < .001$), but there were no significant differences in reduction by treatment group ($F(8, 328) = 1.38$, *ns*). At the end of the trial, there were no differences across treatment groups in the percent of participants receiving counseling, with two

Table 7. Change in mood, anxiety, stress, and energy at week 4, by treatment group[a] from the CGI-I scale (1 = very much improved to 7 = very much worse). A larger number indicates a worse outcome

| Characteristic | Berocca™ | | CNE4 | | CNE8 | | $p$ for treatment comparison[b] | Control | | $p$ for treatment vs. Control[c] |
|---|---|---|---|---|---|---|---|---|---|---|
| Number of participants | 28 | | 30 | | 25 | | | 25 | | |
| CGI-I change in[a]: | | | | | | | | | | |
| Mood | 3.0 | 0.9 | 2.5 | 1.0 | 2.4 | 0.9 | .03 | 3.5 | 1.1 | .001 |
| Anxiety | 3.3 | 0.9 | 2.7 | 1.1 | 2.6 | 1.0 | .03 | 3.8 | 1.4 | <.001 |
| Stress | 3.2 | 0.8 | 2.6 | 1.0 | 2.8 | 1.4 | .11 | 4.1 | 1.2 | <.0001 |
| Energy | 3.1 | 0.9 | 2.6 | 1.0 | 2.2 | 0.8 | .004 | | | |

CGI-I, Modified Clinical Global Impressions.
[a]Data are means and standard deviations from the participants who completed the 4-week assessment.
[b]Results from analysis of variance model.
[c]Results from orthogonal contrast in analysis of variance model. $p$-values are Bonferroni adjusted.



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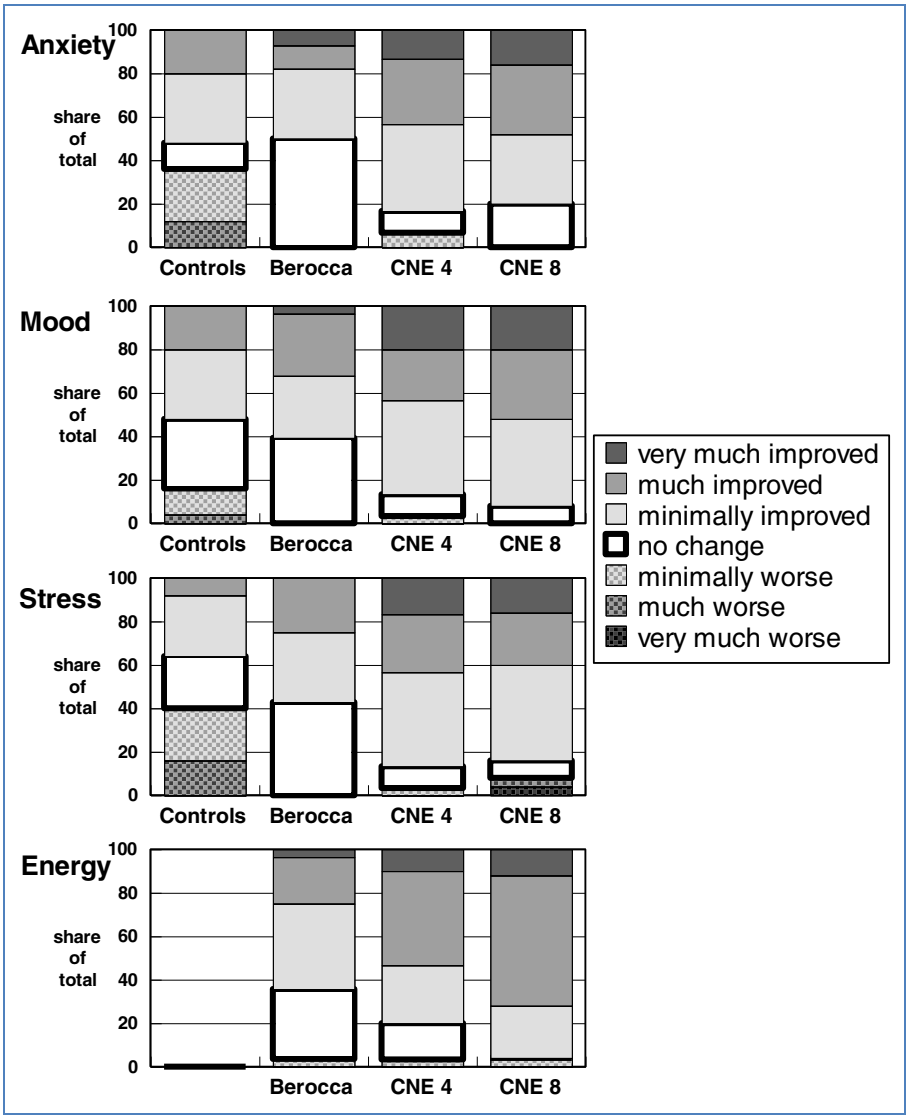


Figure 4. Percent of participants in each group endorsing the different ratings on the Clinical Global Impression Scale at 4 weeks post-baseline (change in energy not measured for controls)

(7%) of the Berocca™ group, one (3%) of the CNE4 group, and one (4%) of the CNE8 group receiving counseling (Fisher's exact test, *ns*). In contrast, six (24%) of the control group were receiving counseling (borderline significance; Fisher's exact test, $p = .06$).

There was no change in cigarette use, alcohol, or cannabis use over the trial across the groups. There were no group differences among the treatment groups in how much participants thought that their exercise changed over the duration of the trial (Fisher's exact test, *ns*). With the weekly diet questionnaire, the three groups showed very similar eating patterns among groups at both baseline ($F(2, 88) = 0.03$, *ns*) and 4 weeks ($F(2, 80) = 0.90$, *ns*). Further, the means within groups did not change over the trial period.

*One-month follow-up.* At the completion of the 1 month follow-up, there were many changes in dose and micronutrient type; thus, we grouped those who stayed on micronutrients and compared them with those who came off the micronutrients or switched to medications. Of the 84 who completed the 1-month follow-up questionnaire, 50 stayed on, and 34 came off the micronutrients (with three of these switching to medications). There was a treatment group difference between those who stayed on the micronutrients and those who came off at follow-up ($\chi^2$ (2, $n = 84$) = 8.18, $p < .05$), with the CNE8 group being more likely to stay on micronutrients than the Berocca™ group (odds ratio = 5.2, $p < .01$). Participants who stayed on micronutrients showed greater continued improvement in depression compared



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with participants who came off ($t(80) = 2.23$, $p < .05$). Borderline differences in stress were found between those who stayed on and those who came off micronutrients (DASS: $t(80) = 1.77$, $p = .08$; PSS: $t(80) = 1.67$, $p = .10$), with those staying on showing greater decrease in stress. There were significant group differences in the amount of change that the participants reported in anxiety ($t(82) = 3.48$, $p < .001$), stress ($t(84) = 2.70$, $p < .01$), and energy ($t(82) = 4.12$, $p < .001$) with those staying on the micronutrients reporting greater positive improvement in anxiety, stress, and energy than those who came off.

## DISCUSSION

All three treatments conferred large and clinically meaningful changes in the psychiatric symptoms presenting in a sample from the general population following the 22 February earthquake on all primary and secondary measures assessed over the 4-week trial. There was a slight advantage to taking the broader based nutrient supplement (CNE™) over taking the high vitamin B complex supplement (Berocca™) for the reduction of intrusive thoughts related to the earthquake, although this difference may have been caused by a regression to the mean. Participants taking the higher dose of CNE™ also reported significantly greater improvement on the CGI in mood, anxiety, and energy over the 4 weeks as compared with those taking Berocca™; for example, at 4 weeks, 52% of those taking CNE8 reported their anxiety levels as "much" to "very much" improved since baseline in contrast to only 17% of those taking Berocca™ (Figure 4). The CGI may be better able to capture the change occurring over the entire duration of the trial as it is not bound to experiences in the previous week. No other differences between treatment groups were identified. There were no group differences between the high dose and low dose of CNE™, suggesting that there was not a dose response; the lower dose of CNE™ appears as effective as the higher dose. It may be that a floor effect occurred, which resulted in a reduced ability to detect differences in both treatments and doses.

In comparison to a nonrandomized control group not taking the nutrients, all three treatment groups were significantly improved in stress, anxiety, avoidance, and arousal after 4 weeks of consumption of micronutrients. Another way to assess change is to look at what percent of the group showed at least a 50% reduction in the symptom as this is often used as a marker for assessing clinically significant improvement. This percent ranged from 22 to 59% for the combined treatment groups, whereas this ranged from 8 to only 36% for the control group.

Our retention rate was high (93.4% to 4 weeks), the side effect profile was mild with only a small percent of participants experiencing side effects (sleep disruption was the highest reported side effect at 27% for the CNE8 group), compliance was good (over 90% for all groups), and finally, only one person dropped out because of difficulties swallowing the pills. Overall, the CNE8 group was less compliant (likely because of having to take more pills) and reported more side effects, possibly because of taking the pills too late at night (as the pills can energize and hence disrupt sleep).

We looked at variables that might explain group differences and established that they were not contributing to the differences found. These variables included change in diet, exercise, initial trauma exposure, residential zoning, ethnicity, gender, history of mental illness, and caffeine, cigarette, and alcohol use. The group taking Berocca™ was slightly better functioning than the other two groups at baseline.

At the 1-month follow-up, we observed that those who stayed on the nutrients were functioning better than those who chose to come off, consistent with previous research (Rucklidge *et al*., 2011b). There appeared to be a preference for the higher dose of CNE™ in that five times more of these participants stayed on the micronutrients compared with those in the Berocca™ group. Perhaps with greater time we would have seen a differentiation of the three groups in that those taking the additional minerals contained in CNE™ may have shown greater benefit than those not taking the added minerals. However, because the majority of trial participants who stayed on the micronutrients chose CNE™ over Berocca™, we could not compare longer exposures across the different treatments.

These results are at least comparable with changes observed with other treatments for stress related to traumas such as medications (Önder *et al*., 2006), single session behavioral treatment using an earthquake simulator (Başoğlu *et al*., 2007), and eye movement desensitization and reprocessing (Konuk *et al*., 2006; Abbasnejad *et al*., 2007), with fewer side effects and better retention rates. Despite their efficacy, exposure therapy programs are more challenging to implement in post-disaster settings and require high treatment fidelity to be maintained. Benzodiazepines have been shown to increase the likelihood of PTSD among symptomatic trauma survivors (Gelpin *et al*., 1996). Given its simplicity of administration and ability to reach a larger proportion of the stressed population at one time, the use of micronutrients presents as an ecologically viable treatment option for stress following a natural disaster.



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The rationale for why B vitamins might reduce stress was outlined in the introduction. However, the role of minerals needs to also be considered. Chronic stress has been documented to impact mineral bone density (Furlan *et al*., 2005), and therefore, further research into whether the additional minerals contained in CNE™ can curb such deterioration would be important. Given that minerals are well documented to play vital roles in physiological processes, it is reasonable to expect that minerals would confer a positive and additive benefit to B vitamins in improving mental health symptoms. For example, iron functions in the enzyme system involved in the production of serotonin, norepinephrine, epinephrine, and dopamine and is a cofactor in the metabolism of tyrosine to dopamine, selenium serves as an essential trace mineral that is part of antioxidant enzymes that protect cells from effects of free radicals, and of course magnesium, zinc, and calcium, present in both formulas, play essential roles as coenzymes in hundreds of biochemical reactions in the body (Kaplan *et al*., 2007). A longer trial could establish whether the broader spectrum approach with higher mineral content confers a meaningful advantage over a formula with fewer nutrients.

Is it possible that the symptoms would have remitted anyway over time? This is always a possibility (see Bonanno *et al*., 2010); however, there are a few reasons why we think that it is unlikely. For one, the stresses on the general population were maintained or even increased during the period of data collection. Twenty (23.5%) of our trial participants completed the 4-week questionnaire the week following the 13 June 6.3 earthquake that caused further damage and disruption to essential services such as sewerage, power, and water and also resulted in increased aftershock activity. Ongoing aftershocks continued throughout the study (there were 45 aftershocks greater than magnitude 4 during the trial period meaning on average, participants experienced a noticeable earthquake once to twice *per day* (source: www.geonet.co.nz)). About 30% of our participants completed baseline twice because of a delay in getting them to start the trial, and overall, these individuals became more stressed over this period. Decisions were also made about the status of private land the week following the 13 June quake (determining if individuals could rebuild on the land or be forced to relocate). Twenty-two (25.9%) of our participants (equally distributed across the groups) received notification that either they had to move off their land or that there was continued uncertainty about the land they were living on. The strongest evidence against our data reflecting only spontaneous remission of symptoms is the evidence from our control group. The control group, although not randomized because of the circumstances under which the data were collected, was equivalent to the treatment groups in terms of stress and exposure to trauma at baseline. However, they did not show the same level of improvement within the same time frame as those who entered the study despite about 25% of them receiving standard treatment during the 4-week period (e.g., counseling and medications).

Are we simply reporting on a large placebo effect? It is very difficult to specify, when change occurs, what caused the change even in placebo trials. The strongest argument against a placebo effect is that there have been three well-conducted randomized controlled trials (Carroll *et al*., 2000; Schlebusch *et al*., 2000; Kennedy *et al*., 2010) showing that Berocca™ is more effective that placebo at reducing stress, establishing Berocca™ as an efficacious treatment for stress. This current study extends the range of benefits to include post-earthquake stress and trauma symptoms and also confirms CNE™ as a probably efficacious treatment given that it was found to be as effective if not more effective than an established treatment. Overreliance on placebo studies for establishing the expected response when applied within the general population can in itself be problematic (Kaplan *et al*., 2011); this study provides some insight as to how the treatments might perform under normal conditions.

Further, the fact that there were group differences in some outcome measures gives some confidence that the effects observed are not simply attributable to nonspecific trial effects. Contact with investigators was minimal, and completion of the questionnaires was viewed by many as tedious. Further, that those who continued to take the pills at follow-up showed further improvement, whereas those who stopped did not show further benefit, suggests that the micronutrients did exert an ongoing positive health benefit. Finally, the study tracked changes in trauma symptoms, showing large effects on these symptoms (from 65% having probable PTSD down to 19% 4 weeks later across the three treatment groups). Note that current treatments for PTSD require specialist and labor intensive resources to reliably achieve positive effects, and absent of such treatment, it is unlikely that the trauma symptoms in our sample were reducing unless some other treatment effect was operating. This confers confidence that the changes reported are attributable to the consumption of nutrients, although we cannot rule out some positive benefit of completing an online questionnaire—perhaps it served as an exposure to the trauma and as such, reduced symptoms in its own right. We also do not know if those taking more pills would have an expectation of greater benefit, which was



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reflected in the greater reported improvement for the CNE8 group on the basis of the CGI ratings.

This study may have been underpowered to detect group differences. Under normal nondisaster conditions, it would have been better to have tracked the participants more closely with standardized clinical interviews to assess more directly acute stress symptoms and to provide a more standard rating for the clinical global assessment of change, although a recent study suggested that web-based assessments of depression symptoms are reliable and valid (Zimmerman and Martinez, 2012). Alcohol abuse information may not be accurate as it was only on the basis of alcohol consumption during the trial period, and a more standardized interview could have established the extent alcohol was impacting on life as well as whether the intake observed over the 4 weeks was typical for these participants. A further limitation of the study pertains to how generalizable the results are to the wider population; all participants had to have access to a computer to participate in the study, possibly excluding people from lower decile communities as well as those unable to comply with the demands of a trial.

The results need to be interpreted cautiously given the lack of a placebo group, the lack of blinding, and the nonrandomized nature of the control group. The control group partially reflects a group of individuals who could not follow through with the study and therefore is not an ideal comparison with those who were randomized and completed the trial. Nevertheless, this trial has provided some evidence that a simple intervention of giving micronutrients and completing weekly online questionnaires can result in substantial symptom reduction for many of the participants with only minor side effects. The impact of a large scale disaster such as the Christchurch earthquakes is substantial and enduring. This study and our previous one on adults with ADHD (Rucklidge and Blampied, 2011; Rucklidge *et al*., 2011a) suggest that nutritional supplementation is one possible direction for first line intervention to reduce the emotional impact on the general population. Long-term health is essential for a community to recover. Supplementation provides the body with the essential nutrients that it may require to overcome chronic stress at a time when nutritional intake is likely compromised; indeed, stress is metabolically demanding (McCann and Ames, 2009). This study is consistent with a growing body of literature supporting nutrients as important for improving psychological functioning. Fortunately, nutritional supplementation is relatively inexpensive and if substantiated with further trials, may prove to be a practical intervention in disaster situations.

## CONFLICT OF INTEREST

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