Optimal Serum Selenium Concentrations Are Associated with Lower Depressive Symptoms and Negative Mood among Young Adults¹⁻³

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Abstract

Background: There is evidence that low, and possibly high, selenium status is associated with depressed mood. More evidence is needed to determine whether this pattern occurs in young adults with a wide range of serum concentrations of selenium.

Objective: The aim of this study was to determine if serum selenium concentration is associated with depressive symptoms and daily mood states in young adults.

Methods: A total of 978 young adults (aged 17–25 y) completed the Center for Epidemiological Studies–Depression scale and reported their negative and positive mood daily for 13 d using an Internet diary. Serum selenium concentration was determined by inductively coupled plasma mass spectrometry. ANCOVA and regression models tested the linear and curvilinear associations between decile of serum selenium concentration and mood outcomes, controlling for age, gender, ethnicity, BMI, and weekly alcohol intake. Smoking and childhood socioeconomic status were further controlled in a subset of participants.

Results: The mean ± SD serum selenium concentration was 82 ± 18 μg/L and ranged from 49 to 450 μg/L. Participants with the lowest serum selenium concentration (62 ± 4 μg/L; decile 1) and, to a lesser extent, those with the highest serum selenium concentration (110 ± 38 μg/L; decile 10) had significantly greater adjusted depressive symptoms than did participants with midrange serum selenium concentrations (82 ± 1 to 85 ± 1 μg/L; deciles 6 and 7). Depressive symptomatology was lowest at a selenium concentration of 85 μg/L. Patterns for negative mood were similar but more U-shaped. Positive mood showed an inverse U-shaped association with selenium, but this pattern was less consistent than depressive symptoms or negative mood.

Conclusions: In young adults, an optimal range of serum selenium between 82 and 85 μg/L was associated with reduced risk of depressive symptomatology. This range approximates the values at which glutathione peroxidase is maximal, suggesting that future research should investigate antioxidant pathways linking selenium to mood. This trial was registered with the Australian New Zealand Clinical Trials Registry as ACTRN12613000773730. J Nutr. 2015;145:59–65.

Keywords: selenium, micronutrients, mood, depression, young adults, daily diary method

Introduction

There is growing evidence for the role of micronutrients in mental health, although the links between multivitamin-mineral supplements, specific micronutrients, and mood remain inconclusive (1, 2). In a recent review, 4 of 8 trials demonstrated decreases in depressed mood after supplementation with multivitamin-mineral supplements in nonclinical populations. Research also linked low concentrations of specific micronutrients such as vitamin B-12 and folate to increased levels of depressive symptomatology (3, 4), although not consistently (1, 2). In this report, we investigated whether low concentrations of selenium may also be implicated in depressive symptomatology. Selenium is an essential nutrient required for the optimal functioning of several selenoproteins involved in antioxidant defenses within the brain and nervous system, including the glutathione peroxidase antioxidant enzymes (GPx)⁶ (5). Several studies found lower GPx activity among those with major

¹ Supported by a Health Research Council Emerging Researcher First Grant (12/709) and a University of Otago Research Grant to TS Conner.
² Author disclosures: TS Conner, AC Richardson, and JC Miller, no conflicts of interest.
³ Supplemental Tables 1–3 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.
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⁵ Abbreviations used: CES-D, Center for Epidemiological Studies–Depression; GPx, glutathione peroxidase antioxidant enzyme; RCT, randomized controlled trial; ROS, reactive oxygen species; SES, socioeconomic status.
depression vs. controls (6), suggesting that lower selenium could be a risk factor for depression via antioxidant pathways. Observational research in adult and elderly populations has shown a higher risk of depression among those with lower selenium intake (7), less selenium groundwater exposure (8), and lower selenium status as determined by nail samples (9). Few studies have tested the association between selenium and depressive symptoms in young adult populations (aged 18–25 y). The one study with the youngest age range of adults aged 20–35 y found that higher, not lower, selenium status was associated with higher risk of depressive symptoms 3 y later (10). Randomized controlled trials (RCTs) have found improvements in mood (11, 12) and improvement in postpartum depression (13) with selenium supplementation in adult populations. However, the largest RCT to date found no effect of selenium supplementation on mood in an elderly population (14). Older age could limit the antioxidant benefits of selenium supplementation through years of exposure to free radicals, which could explain why supplementation shows stronger benefits in adult rather than in elderly populations. Nevertheless, it is still unclear how selenium status and depressive symptoms are associated in young adults. Current observational studies focus on older ages and are limited by the methods to determine selenium intake and concentrations. For example, measures of selenium intake may not be reliable because of large variations in the selenium content of foods, which may not be accurately reflected in food composition tables (15), and nail samples tested for selenium reflect long-term selenium exposure; yet, studies using this approach typically measure mood symptoms in the past week (9, 10). Past-week mood symptoms may be more closely aligned with an acute measure of selenium, such as serum selenium, rather than a long-term measure of selenium exposure. Moreover, mood symptoms recalled over the past week can reflect memory biases; therefore, it would be useful to determine whether selenium status predicts mood measured accurately by using real-time data-capture techniques (16, 17). Our aim was to determine whether serum selenium concentration is associated with depressive symptoms and daily mood states in a large nonclinical sample of young adults. We predicted that young adults with lower selenium concentrations would report greater depressive symptoms and negative mood. We also tested whether higher selenium concentrations would also be associated with greater depressive symptoms and negative mood, given recent evidence (10).

Methods

Participants and inclusion/exclusion criteria. Participants were recruited as part of the Daily Life Study, a large cross-sectional study of the biological and genetic markers of well-being in a population of young adults living in Dunedin, New Zealand. Participants were recruited through flyers, an on-campus employment agency, or human nutrition classes and reimbursed with a small payment, or through the University of Otago Psychology Department’s experimental participation program and reimbursed with course credit. The data were collected in the fall months of March to May in 2011, 2012, and 2013 and in the winter months of July and August 2013.

Participants were eligible to participate in the Daily Life Study if they were at least part-time students at the University of Otago, were aged ≤25 y, and had regular access to the Internet (n = 1061). We excluded from analysis any study participants who reported current antidepressant medication use (n = 36) or who failed to provide sufficient data (no blood sample, n = 17; <1 wk of daily diaries, n = 30). No other inclusion or exclusion criteria were applied due to the broad focus of the Daily Life Study. Participants taking selenium supplements or other multivitamin supplements were not excluded from the study. The final sample consisted of 978 young adults (36.5% male) who identified as European (80%), Asian (10.1%), Māori or Pacific Islander (3.6%), or another ethnicity (6.3%). The study was approved by the University of Otago Human Ethics Committee (no. 10/177), and all participants provided written informed consent. This observational study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000773730).

Procedure. In an initial clinic visit, participants completed informed consent and information on demographic characteristics [gender, ethnicity, socioeconomic status (SES)], and depressive symptoms were collected with a self-administered computerized questionnaire. Participants were informed that the study aim was to understand how genes, hormones, and other biomarkers were related to daily health and well-being. Before enrolling in the study, participants were told that they would be answering questions each day about common experiences in the lives of young adults, such as their health behaviors and emotional states. They also received training for the daily diary procedure that began the following day. For the next 13 d, participants completed an online daily survey between 1500 and 2000 h every day. This daily survey included measures of negative and positive mood and alcohol consumption, among a large range of other health and well-being variables (daily exercise, sleep, stress, etc.). On the final day of the study, participants attended the Department of Human Nutrition, University of Otago, clinic where a nonfasting blood sample was drawn into additive-free Vacutainers (Becton Dickinson) for serum. Samples were refrigerated and centrifuged within 2.5 h of collection. Aliquots of serum were stored in cryovials at −80°C until analysis. Height and weight measures were taken in duplicate by using standardized procedures. On this day, participants also completed a final questionnaire to measure their current use of antidepressant medication and multivitamins. Participants recruited during the 2013 phase of the study were also asked about current smoking status.

Depressive symptoms and mood. Depressive symptoms were measured by using the Center for Epidemiological Studies–Depression (CES-D) scale (18). This scale is designed for use in the general population and contains 20 items that are self-rated on a scale of 0 (“Rarely or none of the time,” <1 d) to 3 (“Most or all of the time,” 5–7 d), such as “I thought

### TABLE 1 Participant characteristics and descriptive statistics for the young adult sample

<table>
<thead>
<tr>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td><strong>n</strong></td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
</tr>
<tr>
<td><strong>Gender, % men</strong></td>
</tr>
<tr>
<td><strong>Ethnicity, % European</strong></td>
</tr>
<tr>
<td><strong>BMI, kg/m²</strong></td>
</tr>
<tr>
<td><strong>Alcohol intake, standard drinks/wk</strong></td>
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<tr>
<td><strong>Current smoker, %</strong></td>
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<tr>
<td><strong>Childhood SES</strong></td>
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<tr>
<td><strong>Multivitamin use, % currently taking</strong></td>
</tr>
<tr>
<td><strong>Serum selenium, μg/L</strong></td>
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<tr>
<td><strong>Depressive symptoms, CES-D score</strong></td>
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<tr>
<td><strong>Negative mood score</strong></td>
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<tr>
<td><strong>Positive mood score</strong></td>
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</tbody>
</table>

1 Values are means ± SDs unless otherwise indicated. CES-D, Center for Epidemiological Studies–Depression; SES, socioeconomic status.
2 Smoking and SES data available for only a subset of participants: n = 379 for smoking and n = 352 for SES.
3 SES rating of 4.4 corresponded to an average childhood household income of $72,500 in New Zealand dollars.
4 Average mood scores ranged from 1 (not at all) to 5 (extremely). A midpoint score of 3 indicated moderately intense negative or positive mood.
### TABLE 2

Characteristics of the young adult participants (n = 978) categorized by decile of serum selenium concentration.

<table>
<thead>
<tr>
<th>Decile of serum selenium concentration</th>
<th>1 (n = 97)</th>
<th>2 (n = 99)</th>
<th>3 (n = 97)</th>
<th>4 (n = 98)</th>
<th>5 (n = 98)</th>
<th>6 (n = 99)</th>
<th>7 (n = 97)</th>
<th>8 (n = 98)</th>
<th>9 (n = 98)</th>
<th>10 (n = 98)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selenium, µg/L</td>
<td>7.5 ± 2.3</td>
<td>8.0 ± 2.4</td>
<td>8.5 ± 2.4</td>
<td>9.0 ± 2.4</td>
<td>9.5 ± 2.4</td>
<td>10.0 ± 2.4</td>
<td>10.5 ± 2.4</td>
<td>11.0 ± 2.4</td>
<td>11.5 ± 2.4</td>
<td>12.0 ± 2.4</td>
</tr>
<tr>
<td>Age (y)</td>
<td>17.5 ± 0.5</td>
<td>17.5 ± 0.5</td>
<td>17.5 ± 0.5</td>
<td>17.5 ± 0.5</td>
<td>17.5 ± 0.5</td>
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<td>17.5 ± 0.5</td>
<td>17.5 ± 0.5</td>
</tr>
<tr>
<td>Gender, %</td>
<td>49.5 ± 2.5</td>
<td>50.5 ± 2.5</td>
<td>51.5 ± 2.5</td>
<td>52.5 ± 2.5</td>
<td>53.5 ± 2.5</td>
<td>54.5 ± 2.5</td>
<td>55.5 ± 2.5</td>
<td>56.5 ± 2.5</td>
<td>57.5 ± 2.5</td>
<td>58.5 ± 2.5</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>19.6 ± 2.6</td>
<td>19.8 ± 2.6</td>
<td>20.0 ± 2.6</td>
<td>20.2 ± 2.6</td>
<td>20.4 ± 2.6</td>
<td>20.6 ± 2.6</td>
<td>20.8 ± 2.6</td>
<td>21.0 ± 2.6</td>
<td>21.2 ± 2.6</td>
<td>21.4 ± 2.6</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>7.5 ± 4.5</td>
<td>8.0 ± 4.5</td>
<td>8.5 ± 4.5</td>
<td>9.0 ± 4.5</td>
<td>9.5 ± 4.5</td>
<td>10.0 ± 4.5</td>
<td>10.5 ± 4.5</td>
<td>11.0 ± 4.5</td>
<td>11.5 ± 4.5</td>
<td>12.0 ± 4.5</td>
</tr>
<tr>
<td>Smoker, %</td>
<td>12.5 ± 2.5</td>
<td>12.5 ± 2.5</td>
<td>12.5 ± 2.5</td>
<td>12.5 ± 2.5</td>
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</tr>
</tbody>
</table>

### Data analysis

Before analysis, serum selenium values were categorized into deciles ranging from 1 to 10, from the lowest to highest 10% of values. The use of deciles mitigated the influence of outliers and afforded greater sensitivity than quintiles for detecting curvilinear patterns. An ANCOVA general linear model was constructed to test the association between serum selenium decile as the classification variable (predictor) and depressive symptoms as the dependent variable, adjusting for age, gender, ethnicity, BMI, and mean weekly alcohol intake as covariates. This analysis yielded the adjusted least-squares mean CES-D (or mood) scores for participants in each serum selenium decile. Assumptions of

Daily mood was measured each day for 13 d by using an 18-item scale (19). The scale contained 9 adjectives assessing negative mood (irritable, hostile, angry, nervous, tense, anxious, depressed, sad, unhappy) and 9 adjectives assessing positive mood (excited, energetic, enthusiastic, pleasant, happy, cheerful, content, calm, relaxed). Mood adjectives were based on the affective circumplex and captured a range of high- and low-activation states (19). Participants were required to rate each adjective on the basis of how they “felt today” on a 5-point Likert scale: 1 (not at all), 2 (slightly), 3 (moderately), 4 (very much), or 5 (extremely). Scores across the 9 adjectives were averaged each day to obtain measures of daily negative mood (α = 0.780) and positive mood (α = 0.820), which were averaged across days for analysis (α reliabilities for nested data were computed by using recommended guidelines from Næsæter; 20).

### Serum selenium status

Selenium and depressive symptoms in young adults

Before analysis, serum selenium values were categorized into deciles ranging from 1 to 10, from the lowest to highest 10% of values. The use of deciles mitigated the influence of outliers and afforded greater sensitivity than quintiles for detecting curvilinear patterns. An ANCOVA general linear model was constructed to test the association between serum selenium decile as the classification variable (predictor) and depressive symptoms as the dependent variable, adjusting for age, gender, ethnicity, BMI, and mean weekly alcohol intake as covariates. This analysis yielded the adjusted least-squares mean CES-D (or mood) scores for participants in each serum selenium decile. Assumptions of
homogeneity of covariance were analyzed for each covariate and found to be met. We tested for curvilinear patterns by saving the predicted CES-D (or mood) scores from ANCOVA, plotting them, and then predicting them from the decile of serum selenium (deciles 1–10) and the squared decile of serum selenium concentration (1–100) as simultaneous predictors. This process was repeated substituting negative mood and positive mood as the outcome variables. Statistical analyses were performed with SPSS (version 22.0). *P* values <0.05 were considered significant.

Several supplementary analyses were conducted including ANCOVA models with smoking and childhood SES added as additional covariates for the subset of participants with available data (*n* = 348). We also performed hierarchical linear regression to further test for curvilinear patterns in the relation between selenium and the mood outcomes. In the first step, age, gender, ethnicity, BMI, and mean weekly alcohol intake were entered to predict CES-D (or negative mood or positive mood) scores. In the second step, the decile of serum selenium (deciles 1–10) and the squared decile of serum selenium (1–100) were entered as simultaneous predictors of CES-D scores, controlling for the covariates. Values in the text are presented as means ± SDs unless otherwise noted.

### Results

Table 1 presents the participant characteristics and descriptive statistics for the measured variables. Serum selenium concentrations ranged from 49 to 450 μg/L with the majority of cases (99%) ranging from 49 to 158 μg/L. Depressive symptoms ranged from 0.0 to 50.0, with 33.8% (*n* = 331) of our sample reporting CES-D scores of ≥16.0, indicating significant levels of depressive symptoms. Depressive symptoms correlated with higher negative mood (*r* = 0.46, *P* < 0.001) and lower positive mood (*r* = −0.41, *P* < 0.001). Negative mood and positive mood were inversely correlated (*r* = −0.32, *P* < 0.001). Table 2 presents serum selenium concentrations and participant characteristics across the selenium deciles. Participants in the higher selenium deciles were more likely to be older, male, non-European, and of lower BMI. Participants in the middle selenium deciles reported higher childhood SES than did participants in the lower or higher selenium deciles. Table 3 presents the adjusted least-squares means of depressive symptoms, negative mood, and positive mood for each serum selenium decile. There were significant linear and curvilinear patterns across the serum selenium deciles in all 3 outcomes (all *P* < 0.001).

Figure 1 shows the relations between serum selenium decile and depressive symptoms (panel A), negative mood (panel B), and positive mood (panel C) for the full sample, adjusted for the primary covariates. For depressive symptoms, the pattern was a reverse J-shaped curve, with the lowest depressive symptoms among participants in selenium deciles 6 and 7 (82 ± 1 and 85 ± 1 μg/L serum selenium, respectively). Below and above this range, depressive symptoms increased, particularly at the lowest decile (decile 1; 62 ± 4 μg/L serum selenium). For negative mood, the pattern was a U-shaped curve with the lowest negative mood among participants in selenium decile 7 (85 ± 1 μg/L) and the highest negative mood among participants in deciles 1 and 10 (62 ± 4 and 110 ± 38 μg/L, respectively). However, the means for negative mood were all <2.0, suggesting that negative mood did not increase above the “mild” range. For positive mood, the pattern was an inverted U-shaped curve with the highest positive mood among participants in selenium decile 5 (79 ± 1 μg/L). Below and above this range, positive mood decreased. This association between serum selenium decile and adjusted positive mood was not due simply to negative mood. Results from another ANCOVA entering
negative mood as an additional covariate showed the same pattern of adjusted means in Table 3 and the same linear and curvilinear patterns shown in Figure 1C.

These relations between serum selenium decile and depressive symptoms, negative mood, and positive mood continued to be significant when including smoking status and childhood SES as additional covariates in the restricted sample of participants (Supplemental Table 1). These relations were also significant when including quadratic terms for both age and SES to control for their curvilinear relations with serum selenium decile.

Hierarchical multiple regression analyses controlling for age, gender, ethnicity, BMI, and alcohol intake confirmed these significant negative linear and curvilinear relations between serum selenium decile and depressive symptoms (linear B: $-1.071; 95\% \text{ CI: } -1.898, -0.024; P = 0.011$; curvilinear B: 0.082; 95\% CI: 0.008, 0.155; $P = 0.029$) and negative mood (linear B: $-0.052; 95\% \text{ CI: } -0.098, -0.005; P = 0.029$; curvilinear B: 0.005; 95\% CI: 0.001, 0.009; $P = 0.029$) but not positive mood (linear B: 0.029; 95\% CI: $-0.19, 0.076; P = 0.24$; curvilinear B: $-0.002; 95\% \text{ CI: } -0.006, 0.002; P = 0.31$) (Supplemental Table 2). Similar regression results were found when controlling for age and SES as additional covariates (Supplemental Table 3).

**Discussion**

The results of this study suggest that there is a nonlinear relation between serum selenium concentration and depressive symptomatology among young adults. Depressive symptomatology was lowest around selenium concentrations of 82 to 85 $\mu$g/L. Below 82 $\mu$g/L, depressive symptoms began to increase, culminating in the highest depressive symptoms for participants in the lowest decile of serum selenium (approximate serum selenium concentration of 62 $\mu$g/L). Higher serum selenium also resulted in increased depressive symptomatology, although these increases were not as sharp. This pattern suggests that although both lower and higher concentrations of serum selenium were associated with increases in depressive symptomatology, although these increases were not as sharp. This pattern suggests that although both lower and higher concentrations of serum selenium were associated with increases in depressive symptomatology, lower concentrations of serum selenium were more detrimental in this sample. Previous research also found that either low selenium exposure (7–9) or high selenium exposure (10) was associated with increased levels of depressive symptoms among adult populations. This is the first study to demonstrate that both low and high selenium statuses were associated with increased depressive symptomatology within the same sample of young adults. This is also the first study to show that selenium concentration is related to daily negative mood in a similar way to depressive symptoms. Negative mood was also lowest around a selenium concentration of 85 $\mu$g/L. Selenium concentration was less reliably related to positive mood.

The finding that higher concentrations of selenium—particularly $\geq 110$ $\mu$g/L—were associated with increased depressive symptoms may help to explain why the RCT conducted by Rayman et al. (14) found that selenium supplementation had no effect on mood or quality of life. In that RCT, there were 3 different dosage groups (100, 200, and 300 $\mu$g/d), with those in the 100-$\mu$g supplementation group having the lowest serum selenium concentration by the end of the 6-mo supplementation period (149 $\mu$g/L). This selenium value would have been associated with high depressive symptoms in our study. However, Rayman et al. (14) did not report any adverse effects on mood with selenium supplementation or with elevated serum selenium status.

The present findings may have important implications for people who eat a diet either low or very high in selenium and for people who take selenium supplements. Areas in Eastern Europe and some parts of China have lower selenium intakes than in
other areas (22). Similarly, in New Zealand, the selenium content of the soil is low and thus, historically, New Zealanders have had a low selenium intake. Although selenium status has improved since the 1990s, many New Zealanders still have serum selenium concentrations that are below what is required for maximum GPx activity, and selenium supplementation leads to increases in GPx activity (15). Our research suggests that low selenium intake may be associated with greater risk of depressive symptomatology and negative mood even among healthy young adults. However, too much selenium may also lead to increased risk. Previous research documented the detrimental effects of high selenium concentrations on physical health (23, 24) and mental health (10). Observational research demonstrated associations between higher selenium status and increased risk of type 2 diabetes (>130 μg/L; 23) and increased risk of cancer (>150 μg/L; 24). A U-shaped curve was also reported by Bleys et al. (24) in relation to selenium status and all-cause mortality (>150 μg/L). Animal research also reported a similar U-shaped curve in relation to type 2 diabetes risk (25) and heart function (26). Selenium’s role as an antioxidant may help to explain these findings. At serum selenium concentrations of 70–90 μg/L, plasma GPx enzymes are functioning at maximum activity levels (27). Below this level, the enzymes may not be performing at their maximum and thus the optimal antioxidant protection may not be achieved. This could result in increased vulnerability to oxidative stress and may explain why levels of depressive symptomatology were highest in the lowest decile with serum selenium concentrations ≤62 μg/L. Moreover, in high doses, selenium has been demonstrated to generate reactive oxygen species (ROS) (28). Although the range at which selenium begins to produce ROS in humans is not yet known, this mechanism could suggest that, in higher doses, selenium may influence depressive symptoms via the generation of ROS leading to oxidative stress. Further research is needed to examine this oxidative stress hypothesis, particularly through RCTs that monitor concentrations of ROS alongside changes in selenium status.

This study is limited by its observational design. Therefore, a causal relation between selenium status and mental health cannot be concluded. Although it is plausible that selenium status outside the optimal range leads to poorer mental health, it is also possible that those with poor mental health are less likely to eat foods high in selenium, resulting in lower selenium status, although this does not explain why higher selenium was related to increased depressive symptoms and negative mood. It is also possible that the relation between selenium and depressed mood is mediated by declines in physical health rather than any direct effect of selenium on depressive symptoms. Clinical conditions associated with high concentrations of selenium such as type 2 diabetes and cardiovascular disease are not prevalent in this population, although it is possible that subclinical differences in physical health could account for the relation between selenium and depressed mood. However, we found no relation between selenium and self-reported health as measured by physical activity and cold symptoms. In addition, the relations between selenium and depressed mood remained significant when controlling for 2 of the more relevant health factors in this population, BMI and alcohol use.

Despite being limited by its observational design, this is the only cross-sectional study of the association between serum selenium concentrations and depressive symptoms in young adults to date and, to our knowledge, the only study to have implemented a daily diary method to assess negative and positive mood. Thus, we can have more confidence that selenium is associated with experiences of negative mood that occur in daily life. This study is also the first to report that serum selenium within an optimal range is associated with lower levels of both depressive symptoms and negative mood. Below this range, symptoms of depression and negative mood were found to increase significantly. Above this range, symptoms also increased, although to a lesser extent. This latter finding adds to the evidence base that a high selenium intake may be associated with adverse health effects. Although further research is needed, care should be taken to avoid consuming a diet too low or too high in selenium.

Acknowledgments

We thank Hadyn Youens for web programming; Maria Polak and Dr. Lisa A Houghton for assistance with blood collection; and Dr. Malcolm Reid and David Barr from the University of Otago Chemistry Department for selenium processing. TSC, ACR, and JCM designed the research; JCM coordinated the selenium processing; TSC and ACR conducted the research and analyzed data; TSC, ACR, and JCM wrote the manuscript; and TSC had primary responsibility for final content. All authors read and approved the final manuscript.

References