

# Fruit, Vegetable, and Antioxidant Intakes Are Lower in Older Adults with Depression

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## ABSTRACT

Studies have shown an association between depression and both antioxidant levels and oxidant stress, but generally have not included intakes of antioxidants and antioxidant-rich fruits and vegetables. This study examined the cross-sectional associations between clinically diagnosed depression and intakes of antioxidants, fruits, and vegetables in a cohort of older adults. Antioxidant, fruit, and vegetable intakes were assessed in 278 elderly participants (144 with depression, 134 without depression) using a Block 1998 food frequency questionnaire that was administered between 1999 and 2007. All participants were aged 60 years or older. Vitamin C, lutein, and beta cryptoxanthin intakes were significantly lower among individuals with depression than in comparison participants ( $P < 0.05$ ). In addition, fruit and vegetable consumption, a primary determinant of antioxidant intake, was lower in individuals with depression. In multivariable models controlling for age, sex, education, vascular comorbidity score, body mass index, total dietary fat, and alcohol; vitamin C, beta cryptoxanthin, fruits, and vegetables remained significant. Antioxidants from dietary supplements were not associated with depression. Antioxidant, fruit, and vegetable intakes were lower in individuals with late-life depression than in comparison participants. These associations may partially explain the elevated risk of cardiovascular disease among older individuals with depression. In addition, these findings point to the importance of antioxidant food sources rather than dietary supplements.

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**D**EPRESSION IS A SERIOUS AND COMMON MENTAL disorder, and a significant burden to both individuals and society. Depression affects 121 million people, is the third leading cause of disease burden (projected to be the number-one cause by 2030), and is the leading cause of disability worldwide.<sup>1</sup> Depression is responsible for a majority of 870,000 suicides annually.<sup>1</sup> Late-life depression, occurring after age 60 years, contributes to higher risk of dementia, heart disease, and doubles health care costs.<sup>2,3</sup> Depression has been associated with poor nutrition, which may be both a contributor to and consequence of depression. One critical aspect of poor nutrition is inadequate consumption of fruits and vegetables, and the consequent low intake of antioxidant nutrients.

Antioxidants may protect against aging and chronic diseases,<sup>4,5</sup> and may have a biologic role in depression etiology. Oxidative stress has been found to be higher in individuals with depression, whereas antioxidant capacity is lower.<sup>6-8</sup> One marker of oxidative damage to DNA, 8-hydroxy-deoxyguanosine, is elevated in depression.<sup>9</sup> Antidepressant treatment may lower oxidative stress and raise serum antioxidant capacity.<sup>10</sup> Unfortunately, these studies have often ignored dietary intake, so it is not clear whether serum changes reflected dietary changes during and after a depressive episode or were due to effects of the illness or medications.

Higher consumption of fruits and vegetables has been found to lead to better cognitive test scores, fewer depressive symptoms, and lower risk of developing depression.<sup>11,12</sup> Intakes of beta carotene, vitamin C, fiber, and folate—nutrients found in fruits and vegetables—have been shown to be lower in those with depression compared with individuals without depression.<sup>13-15</sup> Lastly, although plant foods and food-derived phytochemicals have been associated with health benefits, antioxidants from dietary supplements appear to be less beneficial and may, in fact, be detrimental to health.<sup>16</sup>

Our study objective was to examine the relationship between late-life depression and intakes of fruits, vegetables, and antioxidants. We hypothesized that fruit, vegetable, and antioxidant intakes would be lower in members of a depressed group compared with a nondepressed control group. Further, we hypothesized that antioxidant differences would be limited to those from food sources.

## METHODS

### Design

This case-control study occurred within a larger longitudinal clinical examination of depression in older adults (NeuroCognitive Outcomes of Depression in the Elderly).<sup>17</sup> Nutrition-related data were collected between 1999 and 2007.

## Sample

All participants who completed a nutrition questionnaire were included in the study, and were blinded to any focus on antioxidants, although they had been informed that relationships between diet and depression would be examined. This sample included patients who met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, diagnostic criteria for major depressive disorder at study baseline, and comparison participants recruited from the community. Participants were aged  $\geq 60$  years and could speak and write English.

Exclusion criteria included a concurrent diagnosis of a psychiatric or neurologic illness, and significant cognitive impairment (as indicated by a Mini-Mental State Examination score  $< 24$  out of 30). In addition, participants with severe depression symptomatology were excluded because of concerns about subject burden given the length and difficulty of the food frequency questionnaire, and memory impairment that is common with depression and could affect accuracy of the reporting. This criterion was evaluated by the treating psychiatrist on a case-by-case basis, an approach that was used because the clinician was most familiar with a patient's limitations. Comparison participants were required to have no evidence of a depression diagnosis.

After complete description of the study to the participants, written informed consent was obtained. This research protocol has been reviewed and approved by the Duke University Institutional Review Board, and was in compliance with Health Insurance Portability and Accountability Act guidelines.

## Treatment

Depression patients received individualized treatment from a psychiatrist, who followed them throughout the study. Most participants with depression received antidepressant medication.

## Measures

**Depression and Medical Comorbidity.** At baseline a trained interviewer administered the Duke Depression Evaluation Schedule, which includes sections of the National Institute of Mental Health Diagnostic Interview Schedule, which assesses depression, as well as items on self-reported physical health.<sup>18</sup> Four conditions were included in the comorbidity score: diabetes, hypertension, arteriosclerosis, and heart trouble. Each condition was assigned a score. Score=1 if the condition was not reported, score=2 if the condition was reported as present and interfered not at all, score=3 if it interfered a little, or score=4 if it interfered a lot. The comorbidity score thus had a possible range from 4 to 16.

**Dietary Assessment.** The nutrition protocol has been described previously.<sup>19</sup> The 1998 Block Food Frequency Questionnaire (FFQ) (NutritionQuest) was self-administered to assess dietary intake during the preceding year and has been validated against other nutrition assessment instruments.<sup>20</sup> Returned questionnaires were checked for completeness and excluded if more than 15 food items were skipped. Participants who reported improbable energy intakes ( $< 500$  kcal/day or  $> 5,000$  kcal/day) were excluded from analyses. Intake estimates include total energy, servings of fruits and vegeta-

bles, and antioxidants. Antioxidant estimates include vitamin C, vitamin E ( $\alpha$ - and  $\gamma$ -tocopherol), selenium, and carotenoids (alpha carotene, beta carotene, beta cryptoxanthin, lutein/zeaxanthin, and lycopene). Vitamin C,  $\alpha$ -tocopherol, and beta carotene were estimated from both foods and dietary supplements, whereas other antioxidants were estimated only from food sources. For selenium, the FFQ provided intake estimates from both food and supplement sources, but only supplement intakes were evaluated because food estimates are inaccurate due to the high variability of selenium in the soil. Body mass index (BMI) was calculated from self-reported weight and height at time of FFQ.

## Statistical Analyses

All statistical analyses were conducted using JMP software, version 8.0 (2009, SAS Institute Inc). General descriptive statistics were calculated to examine the characteristics of the sample by group (depression vs comparison). Bivariate comparisons between group and covariates were conducted using  $\chi^2$  test if the covariates were categorical (sex and race), and  $t$  test if the variables were continuous (eg, age, education, comorbidity score, BMI, total daily energy [kilocalories], fat, and alcohol). Race was dichotomized (white/nonwhite) because of small sample sizes in nonwhite categories. To describe the depression and comparison groups in terms of intake of fruits, vegetables, and antioxidants,  $t$  tests were performed.

Logistic regression was performed to determine the effect of fruit, vegetable, and antioxidant intakes upon depression group while controlling for potential confounders. Covariates were selected by backward stepwise regression (cutoff of  $P > 0.2$  for exclusion). Covariates examined in this way included age, sex, race, education, comorbidity score, BMI, total daily energy (kilocalories), total fat, alcohol intake, and dietary supplement use.

## RESULTS AND DISCUSSION

This sample of older adults included a total of 144 participants with depression and 134 comparison participants after the exclusion of 12 participants ( $n=9$  for missing covariate data,  $n=3$  for energy intakes  $< 500$  kcal). The comparison group was older ( $t_{276} = -2.39$ ;  $P=0.0175$ ), included more women ( $\chi^2_1=8.26$ ;  $P=0.0040$ ), had more years of education ( $t_{276} = -3.63$ ;  $P=0.0003$ ), a lower comorbidity score ( $t_{276}=5.03$ ;  $P<0.0001$ ), and lower BMI ( $t_{276}=4.21$ ;  $P<0.0001$ ) than the depression group (Table 1). In addition, the comparison group consumed more alcohol ( $t_{276} = -2.52$ ;  $P=0.0123$ ) and less fat ( $t_{276}=2.63$ ;  $P=0.0089$ ). Regarding antioxidant foods and nutrients, the depression group reported a lower intake of fruits ( $t_{276} = -4.22$ ;  $P<0.0001$ ), vegetables ( $t_{276} = -2.15$ ;  $P=0.0323$ ), beta cryptoxanthin ( $t_{276} = -4.18$ ;  $P<0.0001$ ), lutein ( $t_{276} = -2.29$ ;  $P=0.0227$ ), and vitamin C from foods ( $t_{276} = -5.10$ ;  $P<0.0001$ ) (Table 2).

Separate logistic regression models were run for fruits, vegetables, and each antioxidant variable (Table 3). Fruits, vegetables, vitamin C from foods, and beta cryptoxanthin were significantly lower in the group with depression, as in the bivariate analyses, whereas lutein was no longer significant.

Overall, this study showed lower intakes of fruits, vegetables, vitamin C, and beta cryptoxanthin in older adults with depression compared with comparison participants without depression. Only food sources of antioxidants were inversely

**Table 1.** NeuroCognitive Outcomes of Depression in the Elderly Study—Participant group characteristics: Sociodemographics, medical comorbidity, body mass index, and diet

Characteristic	Total (N=278)	Depression (n=144)	Comparison (n=134)	P value <sup>a</sup>
	←————— <i>mean ± standard deviation</i> —————→			
Age (y)	70.4 ± 6.0	69.5 ± 6.2	71.3 ± 5.7	0.02
Education (y)	14.8 ± 2.3	14.3 ± 2.5	15.3 ± 2.0	0.0003
Comorbidity score <sup>b</sup>	4.9 ± 1.2	5.2 ± 1.4	4.5 ± 0.8	<0.0001
Body mass index	26.5 ± 4.6	27.6 ± 4.5	25.4 ± 4.5	<0.0001
Energy (kcal)	1,710.6 ± 673.2	1,764.1 ± 718.2	1,653.1 ± 618.7	0.2
Total fat (g)	66.8 ± 34.9	72.0 ± 37.7	61.1 ± 30.8	0.009
Alcohol (g)	7.7 ± 12.0	6.0 ± 11.6	9.6 ± 12.1	0.01
	←————— <i>n (%)</i> —————→			
Sex (female)	173 (62)	78 (54)	95 (71)	0.004
Race <sup>c</sup>				0.2
White	239 (86)	127 (88)	112 (84)	
African American	24 (9)	8 (6)	16 (12)	
Asian	7 (3)	5 (3)	2 (1)	
Native American	1 (0.4)	1 (0.7)	0 (0)	
Multiracial	7 (3)	3 (2)	4 (3)	
Dietary supplement use (yes) <sup>d</sup>	200 (80)	92 (78)	108 (82)	0.4

<sup>a</sup>Difference between groups ( $\chi^2$  test used to compare proportions; *t* test used to compare means).

<sup>b</sup>Comorbid conditions include diabetes, hypertension, arteriosclerosis, and heart disease (score of 1–4 for each condition to yield total score of 4–16).

<sup>c</sup>Percentages do not total 100% due to rounding.

<sup>d</sup>N = 250 (depression n = 118; comparison n = 132).

associated with depression. This may indicate that the form and delivery of the antioxidants are important, and that other components of fruits and vegetables may be beneficial for depression.

This study is consistent with prior work showing that individuals with depression are less likely to consume healthy diets than are individuals without depression.<sup>11,19,21</sup> One prior study showed that only naturally occurring food sources of folate were associated with depression, whereas folic acid from fortification and dietary supplements was not, again indicating that a diet rich in plant foods may be beneficial.<sup>15</sup> Consistent with this idea, several studies have found that dietary patterns rich in fruits and vegetables were associated with lower risk of depression.<sup>11,12,22–24</sup>

In terms of specific antioxidants, only vitamin C and beta cryptoxanthin were lower in elders with depression. A previous study found that dietary changes, which included increasing vitamin C intakes, were associated with a decrease in depression symptoms.<sup>25</sup> Older adults with depression also have lower serum levels of vitamin C.<sup>26</sup> Regarding beta cryptoxanthin, this finding may relate to the unique carotenoid profile of the brain. Xanthophyll concentrations are disproportionately high in the brain, compared with other organs such as the retina, and beta cryptoxanthin is the predominant xanthophyll in the brains of older adults.<sup>27</sup> In addition, beta cryptoxanthin concentrations in the frontal lobe, but not occipital lobe, decline with age. This may be particularly important for late-life depression given that dysfunction of the frontal lobe is considered central to its etiopathology.<sup>28,29</sup>

One potential mechanism to explain a protective association between antioxidants and depression is that antioxidants defend against the negative effects of oxidative stress, which has been associated with depression.<sup>6,7</sup> The brain is especially susceptible to oxidative stress due to high levels of aerobic respiration, as well as the high content of polyunsaturated fatty acids, which are susceptible to damage from reactive oxygen species. Another explanation for the antioxidant–depression relationship is that antioxidants have beneficial effects upon inflammatory markers,<sup>30</sup> which are known to be elevated in depression.<sup>31</sup> This idea is consistent with the Invecchiare in Chianti, Aging in the Chianti Area study, which showed that higher serum levels of carotenoids were associated with lower risk of depression, and that this effect was partially mediated by the inflammatory marker interleukin-1 receptor antagonist.<sup>30</sup> Alternatively, the observed associations may be due not to antioxidants but rather to other dietary factors such as folate that also occur in fruits, vegetables, and plant-rich diets.

Strengths of this study include the rigorous evaluation of depression. A psychiatrist evaluated and diagnosed individuals with major depressive disorder, and then treated and followed depressed participants for the duration of the study. This is in contrast to many studies that have examined diet and depression—not only do most studies not involve a psychiatrist, but depression is often indicated by self-report of one or two depression symptoms rather than by clinical diagnosis. Another strength is that par-

**Table 2.** Dietary intake of fruits, vegetables, and antioxidants by participant group in the NeuroCognitive Outcomes of Depression in the Elderly Study<sup>a</sup>

Food/nutrient	Sample (N=278)	Depression (n=144)	Comparison (n=134)	P value <sup>b</sup>
	← <i>mean ± standard deviation</i> →			
<b>Fruits (servings/d)</b>	1.9±1.2	1.6±1.2	2.2±1.1	<0.0001
<b>Vegetables (servings/d)</b>	3.2±1.8	3.0±1.7	3.4±1.9	0.03
<b>Vitamin C (mg/d)</b>				
Dietary	128.0±66.7	109.2±62.2	148.3±65.6	<0.0001
Supplemental	309.2±494.7	290.9±460.2	328.8±530.3	0.5
Total	437.2±503.8	400.0±464.1	477.1±542.2	0.2
<b>Vitamin E (mg/d)</b>				
<b>α-Tocopherol</b>				
Dietary	10.0±5.3	9.9±5.2	10.2±5.4	0.7
Supplemental	151.5±175.8	146.1±184.4	157.3±166.6	0.6
Total	161.5±176.1	156.0±184.5	167.5±167.1	0.6
<b>γ-Tocopherol<sup>c</sup></b>	22.0±13.4	23.3±15.0	20.6±11.4	0.1
<b>Selenium (μg/d)<sup>d</sup></b>	21.1±44.6	22.6±48.0	19.4±40.7	0.5
<b>Carotenoids (lg/d)</b>	11,225.2±7,502.9	10,699.9±7,334.3	11,789.7±7,667.3	0.2
Alpha carotene	820.3±766.6	751.8±737.0	893.8±793.3	0.1
Beta carotene				
Dietary	3,941.1±2,860.2	3,759.0±2,937.5	4,136.7±2,772.4	0.3
Supplemental	1,974.8±5,288.6	2,036.7±5,532.9	1,908.2±5,032.8	0.8
Total	5,915.8±6,431.4	5,795.7±6,889.2	6,044.9±5,923.3	0.7
Beta cryptoxanthin	172.6±139.0	140.0±137.8	207.7±132.1	<0.0001
Lutein	1,903.2±1,682.4	1,681.9±1,416.2	2,141.0±1,904.9	0.02
Lycopene	4,388.0±4,890.1	4,367.1±5,061.8	4,410.5±4,717.4	0.9

<sup>a</sup>Intake estimates derived from 1998 Block food frequency questionnaire (NutritionQuest).

<sup>b</sup>Difference between groups (t test used to compare means).

<sup>c</sup>Food sources only.

<sup>d</sup>Supplement sources only.

ticipants reported antioxidant intakes similar to national norms.<sup>32</sup>

A limitation of this study is the modest sample size (N=278), which may have limited power to detect associations. In addition, this study cannot confirm a causal relationship among depression and intakes of fruits, vegetables, and antioxidants given that the nutrition assessment was administered after depression diagnosis, as well as the lack of random assignment. Depression and treatments for depression, primarily antidepressants, are known to affect appetite and dietary intake.<sup>33,34</sup> However, kilocalories (total daily energy) were examined as a potential covariate and found to be non-significant, and there is no evidence that treatment type has effects upon antioxidant intakes. Another possible limitation is the exclusion of individuals with severe depression from the nutrition protocol, which likely would have made it more difficult to detect differences between depression and comparison participants. An added concern is that the decision to exclude these participants was made by the treating psychiatrist rather than an assessor not involved in the participants'

treatment. The rationale was that the treating psychiatrist would be in the best position to determine whether participation would represent an undue burden for a subject. An alternate approach of an unaffiliated assessor might represent a more standardized and objective approach. However, it is unclear what effect this would have had upon inclusion in the study. Self-report of diet has known limitations, including potential for inaccurate subject recall, which may have differed between groups. Finally, these results may be generalizable only to older individuals of primarily European descent with depression who receive psychiatric treatment.

## CONCLUSIONS

Intakes of fruits, vegetables, and naturally occurring antioxidants, specifically vitamin C and beta cryptoxanthin, were found to be inversely associated with depression in this sample of elderly patients with depression and comparison participants, although no association was found with antioxidant supplements. These results may indicate that components of

**Table 3.** Fruit, vegetable, and antioxidant logistic regression models for late-life depression in the NeuroCognitive Outcomes of Depression in the Elderly Study<sup>ab</sup>

Food/nutrient	Estimate (mean±standard error)	$\chi^2$	P value
<b>Fruits (servings/d)</b>	0.26±0.13	4.3	0.038
<b>Vegetables (svgs/d)</b>	0.16±0.08	4.0	0.047
<b>Vitamin C (mg/d)</b>			
Dietary	0.0083±0.0024	12.3	0.0005
Supplement	0.000078±0.00027	0.08	0.8
Total	0.00020±0.00027	0.53	0.5
<b>Vitamin E (mg/d)</b>			
Dietary <sup>c</sup>	0.027±0.017	2.47	0.12
Supplement <sup>d</sup>	-0.00030±0.00079	0.15	0.7
Total	-0.00024±0.00079	0.10	0.8
<b>Selenium (ig/d)<sup>e</sup></b>	-0.0045±0.0031	2.12	0.15
<b>Carotenoids (ig/d)</b>			
Alpha carotene	0.00016±0.00018	0.78	0.4
Beta carotene			
Dietary	0.000030±0.000049	0.38	0.5
Supplement	-0.000018±0.000025	0.55	0.5
Total	-0.0000074±0.000021	0.13	0.7
Beta cryptoxanthin	0.0028±0.0010	7.3	0.007
Lutein	0.00013±0.000093	2.0	0.2
Lycopene	0.000016±0.000029	0.3	0.6

<sup>a</sup>Separate logistic regression models (degrees of freedom=1 for all variables); models controlled for age, sex, race, education, comorbidity score, body mass index, total fat, and alcohol intake.

<sup>b</sup>Intake estimates derived from 1998 Block food frequency questionnaire (NutritionQuest).

<sup>c</sup>Includes both  $\alpha$ - and  $\gamma$ -tocopherol.

<sup>d</sup>Includes  $\alpha$ -tocopherol only.

<sup>e</sup>Includes supplement sources only.

fruits and vegetables, including specific antioxidants, are important for mental health. Antioxidants from dietary supplements may not confer the same benefits. Future studies are needed to confirm these findings, establish an etiological relationship between antioxidants and depression, and to clarify the mechanisms by which fruits and vegetables may influence depression and brain health. If low intakes of fruits, vegetables, and antioxidants are found to cause or exacerbate late-life depression, it may be possible to prevent depression or to lessen its negative effects through dietary intervention.

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## STATEMENT OF POTENTIAL CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

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