

Effects of Dehydroepiandrosterone Supplementation on Cognitive Function and Quality of Life: The DHEA and Well-Ness (DAWN) Trial

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OBJECTIVES: To examine the effects of dehydroepiandrosterone (DHEA) supplementation on cognitive function and quality of life in healthy older adults.

DESIGN: Double-blind, randomized, controlled clinical trial.

SETTING: Clinical research facility.

PARTICIPANTS: One hundred ten men and 115 women aged 55 to 85 (mean \pm standard deviation 68 ± 8).

INTERVENTION: Fifty milligrams daily oral DHEA versus placebo for 1 year.

MEASUREMENTS: Six cognitive function tests at baseline and 12 months, the Beck Depression Inventory (BDI), the Medical Outcomes Study 36-item Short Form Survey (SF-36), the Life Satisfaction Index-Z, the Satisfaction with Life Scale, the Female Sexual Function Index (in women), and the 15-item International Index of Erectile Function (in men) at baseline and 3, 6, and 12 months.

RESULTS: There were no differences between the DHEA and placebo groups in change over time in cognitive function ($P > .10$). Over time, BDI scores decreased for men ($P = .006$) and women ($P = .02$), and Satisfaction with Life Scale scores increased for women ($P = .004$), but there were no differences between the DHEA and placebo groups over time on these measures or the SF-36, Life Satisfaction Index-Z scale, or sexual function scales ($P > .10$).

CONCLUSION: DHEA supplementation has no benefit on cognitive performance or well-being in healthy older adults, and it should not be recommended for that purpose in the general population. *J Am Geriatr Soc* 56:1292–1298, 2008.

Key words: clinical trial; cognitive function; dehydroepiandrosterone; DHEA; quality of life

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DOI: 10.1111/j.1532-5415.2008.01768.x

Dehydroepiandrosterone (DHEA) and its sulfate (DHEAS) are the most abundantly found steroid hormones circulating in the human body.¹ Levels of DHEA peak between the ages of 20 and 30 and then decline progressively with age.¹ Perimenopausal women have only approximately 50% of peak DHEA levels, and that amount declines to approximately 20% once an individual reaches 70.¹

Several lines of evidence suggest that DHEA supplementation may have beneficial effects. Laboratory studies show that DHEA supplementation is associated with improved learning and memory in aged mice and rats (see²). Epidemiological studies in humans generally report that higher serum DHEA levels are associated with feelings of well-being,³ better cognitive function,⁴ and improvement over time in long-term memory,⁵ whereas lower DHEA levels are associated with depressed mood, lower life satisfaction, and poorer cognitive function.^{6–9} Early, open-label clinical trials reported improvement in libido, well-being, mood, and verbal memory after DHEA treatment.^{10–12}

In contrast, the few previous double-blind clinical trials examining the effects of DHEA supplementation on cognitive function and aspects of well-being yield inconsistent results. Although some clinical trials report improvement in memory,^{13,14} others show no differences in cognitive function between the treatment and placebo groups after 2 weeks to 4 months of supplementation with DHEAS,^{9,15–18} and a few have noted negative effects.^{14,19} For instance, a study of 75 elderly men and women supplemented with 50 mg of DHEA for 2 weeks found that, although attention was enhanced in the DHEA group, recall of previously learned material was impaired.¹⁴ Clinical trials examining outcomes related to quality of life, including mood and libido, also show mixed results, with some reporting positive effects^{13,18,20} and others reporting no effects^{9,16,17} of DHEA supplements. However, most previous clinical trials were of short duration, used small sample sizes, and did not include older men and women who were at an age when memory loss and cognitive impairment become more apparent.

The purpose of this study was to determine the effect of 50 mg daily oral DHEA replacement for 1 year on cognitive function and quality of life, including life satisfaction, mood, and sexuality, in healthy older adults not selected for lower levels of DHEA.

METHODS

Participants

The DHEA and Well-Ness (DAWN) Study is a double-blind, placebo-controlled, randomized study designed to determine the effect of a 1-year course of 50 mg daily oral DHEA replacement. Between June 2001 and May 2003, 110 men and 115 women aged 55 to 85 who were non-smokers and not currently using any hormone therapy were enrolled and randomized to treatment or placebo and followed with clinic visits at 3, 6, and 12 months post-randomization. Participants were healthy, community-dwelling individuals, not selected on the basis of DHEA level at entry. Details of rationale and design are published elsewhere.²¹ The Human Subjects Protection Program of the University of California at San Diego (UCSD) approved this study, and all participants gave written informed consent before participation.

Procedure

At baseline and each subsequent follow-up, blood samples were obtained in the morning, after a requested 12-hour fast. Serum was separated and stored at -70°C for later measurements of sex hormones. Participants were queried at baseline about their educational level and behaviors, including frequency of exercise (<3 or ≥ 3 times/week, frequency of alcohol consumption (<3 or ≥ 3 times/week), and previous smoking. Women were also queried about their menopausal history, including age at menopause and history of estrogen use.

Cognitive Function

A trained interviewer administered a battery of standardized cognitive function tests chosen to assess multiple, diverse aspects of cognitive function at baseline and at the 12-month visit. The following is a description of each measure along with the power calculated with PASS statistical software (NCSS, Kaysville, UT), to detect a 0.5 standard deviation difference between the mean of the treatment and placebo groups with two-sided tests and $\alpha = 0.05$ given a sample of 100 per group:

The Modified Mini-Mental State Examination²² assesses orientation, registration, attention, calculation, language, and recall. Scores range from 0 to 100, with higher scores indicating better performance; power is 0.94.

Trail Making Test Part B, from the Halstead-Reitan Neuropsychological Test Battery,²³ tests visuomotor tracking and attention. Participants scan a page continuously to identify numbers and letters in a specified sequence while shifting from number to letter sets. A maximum of 300 seconds is allowed. Performance is rated according to the time required to finish the test, with higher scores indicating poorer performance; power is 0.94.

In Category Fluency,²⁴ the participant names as many animals as possible in 1 minute. The score is the number of animals named correctly; power is 0.97.

In the Modified Boston Naming Test,²⁵ participants are shown a series of 15 line drawings and asked to name the objects represented; scores range from 0 to 15, with higher scores indicative of better performance; power is greater than 0.99.

In Word List Memory and Word List Recall,²⁶ participants are read a list of 10 common nouns for three trials. Scores are the sum of words correctly recalled from all three trials immediately and after a 30-minute delay; power is 0.98 and 0.89, respectively.

Quality of Life

Quality of life was assessed at baseline and at each follow-up using several self-administered measures. Depressed mood was assessed using the Beck Depression Inventory (BDI), a series of 21 sets of items.²⁷ For each set, participants choose the statement that best describes their feelings. Scores are summed over the 21 items, with higher scores indicative of more-depressed mood.

The Medical Outcomes Study 36-item Short Form Survey (SF36)²⁸ consists of 36 questions that assess eight health domains that are combined to yield physical and mental health summary scores.

General life satisfaction was ascertained according to two standardized measures: the Life Satisfaction Index-Z (LSI-Z)²⁹ and the Satisfaction with Life Scale (SWLS).³⁰ The LSI-Z consists of 13 statements with which respondents indicate whether they agree, disagree, or do not know. Two points are given for each response indicating satisfaction, 1 point for don't know, and 0 points for dissatisfaction. Points from all statements are summed, yielding a score ranging from 0 to 26, with higher scores indicating greater life satisfaction.

The SWLS consists of five statements. Respondents rate the extent of their agreement with each statement on a 1- (strongly disagree) to 7-point (strongly agree) scale. Ratings are summed for an overall score ranging from 5 to 35, with higher scores indicating greater life satisfaction.

Self-reported sexual functioning was assessed in women with the 19-item Female Sexual Function Index (FSFI)³¹ and in men with the 15-item International Index of Erectile Function (IIEF).³² The FSFI contains items concerning sexual arousal, orgasm, satisfaction, and pain, and the IIEF includes items pertaining to erectile dysfunction, intercourse satisfaction, orgasmic function, and sexual desire. For both of these measures, higher scores indicate better functioning.

Laboratory Assays

As previously described,²¹ steroid hormones were measured at baseline and 3, 6, and 12 months in the UCSD Reproductive Endocrinology Laboratory. Estradiol, testosterone, and DHEA levels were determined using radioimmunoassay after solvent extraction and celite column-chromatography; DHEAS was measured using direct radioimmunoassay. The sensitivity and intra- and interassay coefficients of variation were, respectively, 11 pmol/L, 5.9%, and 7.1% for estradiol; 0.07 nmol/L, 4.0%, and 4.9% for testosterone;

0.14 nmol/L, 6.1%, and 7.1% for DHEA; and 0.07 μ mol/L, 3.0%, and 6.3% for DHEAS. All samples for each participant were assayed side by side in the same assay, minimizing intra- and interassay variability; all analytes were measured in duplicate. Estimated normal values and ranges (Department of Reproductive Medicine, UCSD) for young men and women, respectively, were 110 (59–209) pmol/L and 135 (48–286) pmol/L for estradiol, 21.1 (12.2–37.9) nmol/L and 0.72 (0.31–1.48) nmol/L for testosterone, 15.2 (9.8–23.8) and 23.8 (7.8–35.7) nmol/L for DHEA, and 8.11 (4.07–12.75) and 5.21 (1.38–9.35) μ mol/L for DHEAS.

Safety

An independent Data Safety and Monitoring Board met eight times during the 34 months of data collection to review potential side effects and ensure participant safety.

Statistical Analysis

Analyses were performed on an intent-to-treat basis. Comparisons between groups were performed using *t*-tests for continuous variables and chi-square analysis for categorical variables. Comparisons of medians for variables that were not normally distributed were performed using Wilcoxon nonparametric tests. Baseline DHEA and testosterone levels were higher in women randomized to treatment than women randomized to placebo ($P = .003$ and $P = .01$, respectively). Analyses adjusted for baseline DHEA levels or baseline testosterone levels yielded similar results; only results of analyses adjusting for baseline DHEA levels are presented. Significance tests were two-sided, with an alpha level of 0.05. Repeated measures analyses were performed with linear mixed models to examine the cross-sectional and longitudinal comparison between the treatment and placebo groups, the independent effect of time (0, 3, 6, and 12 months), and the interaction of time by group. A more detailed explanation of the statistical analyses used in this study can be found in a previous publication.²¹ Analyses

stratified according to age group yielded similar results and are therefore not presented here.

RESULTS

At baseline, the mean age for men and women was 68.7 ± 7.9 (range = 55–85). Men had more education than women (16.7 ± 2.7 years for men vs 15.2 ± 2.4 for women). Men also had higher levels of testosterone (median (IQR) = 16.2 (7.3) vs 0.61 (0.4) nmol/L, $P < .001$), estradiol 112.0 ± 28.2 vs 38.4 ± 18.4 pmol/L, $P < .001$), and DHEAS (median (IQR) = 2.0 (1.1) vs 1.3 (1.4) μ mol/L, $P < .001$) than women; DHEA levels did not differ according to sex. In women, the median age at menopause was 50 (IQR = 7.5); 70% reported past use of estrogen replacement therapy for a median of 8 years (IQR = 15).

Comparisons of characteristics and hormone levels at baseline according to treatment status are shown in Table 1. Within each sex, there were no differences between the treatment and placebo groups in age, education, or other lifestyle variables ($P > .05$). Baseline serum testosterone and DHEA levels were higher in women randomized to treatment than placebo (median (IQR) = 0.70 (0.42) vs 0.54 (0.28) nmol/L, $P = .01$ and 6.47 (5.99) vs 5.17 (3.58) nmol/L, $P = .003$, respectively).

DHEA treatment significantly increased circulating DHEA and DHEAS levels in men and women, with levels reaching approximately two to four times higher than baseline.³³ This increase was significant after 3 months of treatment ($P < .001$), and high levels were maintained throughout the trial.³³ Testosterone increased 60% and estradiol 40% in women receiving DHEA treatment, but no changes were observed in men. These increases were significant after 3 months of treatment and stayed stable through the remainder of the trial. No changes were seen in the placebo group at any sampling interval.³³

Table 2 shows sex-specific scores on each cognitive function measure at baseline and 12 months and compar-

Table 1. Comparisons of Sample Characteristics According to Treatment Status at Baseline

Characteristic	Men			Women		
	DHEA (n = 55)	Placebo (n = 55)	P-Value	DHEA (n = 57)	Placebo (n = 58)	P-Value
Age, mean \pm SD	68.9 \pm 7.5	68.4 \pm 8.5	.74	68.9 \pm 8.1	68.5 \pm 6.7	.80
Education, years, mean \pm SD	16.7 \pm 2.7	16.6 \pm 2.6	.75	15.2 \pm 2.2	15.1 \pm 2.6	.76
Age at menopause, median (IQR)	—	—		50 (7)	50 (8)	.57
Estrogen use years, median (IQR)	—	—		8 (15)	8 (14)	.40
Endogenous hormones, median (IQR)						
Dehydroepiandrosterone, nmol/L	5.2 (3.3)	5.9 (4.8)	.51	6.5 (6.0)	5.2 (3.6)	.003
Dehydroepiandrosterone sulfate, μ mol/L	2.0 (1.2)	2.1 (1.1)	.60	1.4 (1.3)	1.1 (1.5)	.07
Testosterone, nmol/L	16.8 (9.5)	15.5 (6.7)	.15	0.7 (0.4)	0.5 (0.3)	.01
Estradiol, pmol/L	113.8 (28.2)	110.3 (28.4)	.52	41.1 (18.8)	35.7 (17.8)	.13
Previous estrogen use, %	—	—		67.2	73.7	.45
Exercise $\geq 3 \times$ /wk, %	38.2	29.1	.31	20.7	8.9	.08
Alcohol $\geq 3 \times$ /wk, %	51.0	40.0	.25	52.7	47.3	.23
Previous smoking, %	45.5	56.4	.25	51.7	51.8	.99

Comparisons of means performed using analysis of variance, comparisons of medians and interquartile ranges (IQRs) performed using Wilcoxon nonparametric tests, and comparisons of rates performed using chi-square analysis.

SD = standard deviation.

isons of the percentage change over time according to treatment status. As shown, for men and women, median scores on the cognitive function tests tended to improve over time in the treatment group, but remained the same or declined in the placebo group, although differences between the treatment and placebo groups in the amount of change over time were not statistically significant ($P > .05$).

Table 3 shows the results of age- and baseline DHEA-adjusted mixed models comparing the mean scores of the

Table 2. Comparisons of Dehydroepiandrosterone (DHEA) and Placebo Groups on Change over Time in Cognitive Function Test Scores

Cognitive Function Test	Baseline	12 Months	% Change	P-Value
	Median (Interquartile Range)			
Men				
MMSE				
Placebo	96 (5)	96 (5)	− 1.01 (5.1)	.66
DHEA	95.5 (6)	96 (5)	− 1.01 (4.4)	
Word List				
Placebo	19 (4)	20 (6)	5.56 (24.0)	.64
DHEA	20 (4)	21 (5)	0 (22.0)	
Word List recall				
Placebo	6 (3)	6 (3)	11.11 (41.7)	.85
DHEA	6 (2)	7 (3)	11.11 (57.1)	
Verbal fluency				
Placebo	19 (5)	19 (7)	− 6.64 (19.2)	.07
DHEA	20 (6)	20 (6)	5.26 (30.7)	
Boston Naming				
Placebo	15 (1)	15 (0)	0 (0)	.36
DHEA	15 (1)	15 (1)	0 (0)	
Trails B*				
Placebo	88 (38)	90 (42)	1.47 (39.0)	.20
DHEA	95 (40)	86 (29)	− 2.78 (23.6)	
Women				
MMSE				
Placebo	97 (6)	96 (6)	1.01 (5.1)	.31
DHEA	96 (7)	96 (4)	0 (5.3)	
Word List				
Placebo	21 (4)	22 (5)	0 (23.2)	.25
DHEA	22 (5)	23 (4)	0 (22.0)	
Word List recall				
Placebo	7 (2)	7 (3)	0 (37.5)	.23
DHEA	7 (3)	8 (2)	11.11 (28.6)	
Verbal fluency				
Placebo	19 (7)	19 (6)	0 (29.7)	.19
DHEA	18 (7)	19 (5.5)	5.72 (31.8)	
Boston Naming				
Placebo	15 (1)	15 (1)	0 (0)	.68
DHEA	15 (1)	15 (1)	0 (0)	
Trails B*				
Placebo	96 (43)	96 (40)	3.82 (36.2)	.26
DHEA	98 (47)	94 (53)	− 1.54 (24.9)	

Note: Comparisons performed using Wilcoxon tests.

*Higher scores indicate poorer performance.

MMSE = Mini-Mental State Examination.

treatment and placebo groups on each quality-of-life measure at baseline and at 3-, 6-, and 12-month follow-up. Men and women showed significant decreases in BDI score (indicating improved mood) over time ($P < .001$ and $P = .02$, respectively). Additionally, women had significant increases over time in life satisfaction as assessed using the SWLS ($P = .004$), but there were no treatment effects of DHEA on quality of life and no significant differences over time between the treatment and placebo groups. Similar results were obtained in analyses adjusted for baseline testosterone (data not shown).

Compliance and Adverse Effects

At the 12-month follow-up, mean compliance was 95% in the treatment group and 94% in the placebo group. During the study, 23 participants receiving DHEA and 10 participants receiving placebo experienced adverse events leading to treatment discontinuation. Events that contributed most frequently to treatment discontinuation were chest pain (3 receiving DHEA and 1 placebo), palpitations (4 receiving DHEA and 1 placebo), and a more than 1.4-ng/mL increase in prostate-specific antigen (PSA) in men (5 receiving DHEA and 2 placebo). PSA returned to normal in all but one man after discontinuing DHEA. One man was diagnosed with prostate cancer after the 3-month follow-up; it was determined that his cancer started before participation in the study.

DISCUSSION

DHEA is readily available over the counter in the United States and in other countries and has been widely touted and used by the general public as a preventive agent against many of the chronic diseases associated with aging. Unlike the participants in the majority of published studies, participants in the current study were not selected for lower levels of DHEA, enabling an examination of the effects of DHEA supplementation on cognitive function and quality of life in the general population. The results of this clinical trial provide no evidence for a beneficial effect of supplementation with 50 mg daily of DHEA on cognitive function in healthy older adults. Likewise, there were no beneficial effects of DHEA supplementation on quality of life, including mood, perceptions of physical and emotional health, life satisfaction, or sexual function.

The results of this year-long clinical trial are in accord with other shorter-term studies with smaller sample sizes that also found no effects of DHEA supplementation on cognitive function.^{9,15–18} For instance, no effects of DHEA were found on cognitive function in a nonclinical sample of 46 men aged 62 to 76 who received 50 mg DHEA daily for 13 weeks followed by placebo or the reverse.⁹ Similarly, a clinical trial of 60 symptomatic perimenopausal women aged 45 to 55 randomized to 50 mg/day of DHEA or placebo for 3 months found no differences in cognitive function, although DHEA supplementation did affect endocrine profiles.¹⁶ Furthermore, no effect of DHEA supplementation on cognitive function was observed in a clinical trial of 24 women with primary and secondary adrenal insufficiency.¹⁸ Although one study¹³ reported a beneficial effect of 2 weeks of DHEA supplementation (50 mg/day) on one of

Table 3. Comparisons of Quality-of-Life Scores at Baseline and Follow-Up According to Treatment Status

	Baseline	3 Months	6 Months	12 Months	Time	Group	Time × Group
Parameter	Mean ± Standard Error				P-Value		
Men							
BDI							
Placebo	2.9 ± 0.4	2.0 ± 0.4	1.9 ± 0.4	2.8 ± 0.5	< .001	.26	.85
DHEA	3.4 ± 0.4	2.7 ± 0.4	2.6 ± 0.4	3.2 ± 0.5			
SF-36 Physical							
Placebo	82.4 ± 1.7	82.9 ± 1.7	82.2 ± 1.7	83.2 ± 1.7	.86	.46	.61
DHEA	82.6 ± 1.7	80.8 ± 1.7	80.8 ± 1.7	80.7 ± 1.7			
SF-36 Mental							
Placebo	87.1 ± 1.3	86.6 ± 1.3	87.3 ± 1.4	87.6 ± 1.4	.72	.28	.92
DHEA	86.3 ± 1.3	85.1 ± 1.3	85.2 ± 1.4	85.3 ± 1.4			
Life Satisfaction Index-Z							
Placebo	22.6 ± 0.5	23.1 ± 0.5	23.4 ± 0.5	23.2 ± 0.5	.48	.06	.66
DHEA	21.9 ± 0.5	21.8 ± 0.5	22.1 ± 0.5	22.2 ± 0.5			
Satisfaction with Life Scale							
Placebo	28.2 ± 0.7	27.1 ± 0.7	27.7 ± 0.8	27.5 ± 0.8	.06	.22	.94
DHEA	27.3 ± 0.7	25.9 ± 0.7	27.1 ± 0.7	26.5 ± 0.7			
International Index of Erectile Function							
Placebo	46.3 ± 2.9	48.4 ± 2.9	44.5 ± 2.9	46.5 ± 3.0	.09	.45	.86
DHEA	43.4 ± 2.9	45.3 ± 2.9	43.2 ± 2.9	43.3 ± 2.9			
Women							
BDI							
Placebo	4.3 ± 0.6	3.8 ± 0.6	3.6 ± 0.6	3.5 ± 0.6	.02	.50	.58
DHEA	5.3 ± 0.6	4.1 ± 0.6	3.9 ± 0.6	4.0 ± 0.6			
SF-36 Physical							
Placebo	76.8 ± 2.1	76.1 ± 2.1	75.4 ± 2.1	78.0 ± 2.1	.07	.81	.66
DHEA	78.9 ± 2.0	75.3 ± 2.1	75.9 ± 2.1	78.5 ± 2.1			
SF-36 Mental							
Placebo	82.8 ± 1.7	82.7 ± 1.7	83.4 ± 1.7	83.5 ± 1.7	.08	.62	.25
DHEA	82.1 ± 1.7	80.0 ± 1.7	83.8 ± 1.7	82.4 ± 1.7			
Life Satisfaction Index-Z							
Placebo	21.6 ± 0.6	21.5 ± 0.6	21.7 ± 0.6	22.1 ± 0.6	.43	.60	.80
DHEA	21.0 ± 0.6	21.4 ± 0.6	21.3 ± 0.6	21.6 ± 0.6			
Satisfaction with Life Scale							
Placebo	26.8 ± 0.8	24.5 ± 0.8	26.7 ± 0.8	27.5 ± 0.9	.004	.68	.15
DHEA	26.0 ± 0.8	25.6 ± 0.8	26.3 ± 0.9	26.1 ± 0.9			
Female Sexual Function Index							
Placebo	16.4 ± 1.6	16.8 ± 1.6	16.4 ± 1.6	16.4 ± 1.6	.29	.51	.19
DHEA	13.3 ± 1.6	14.7 ± 1.6	17.2 ± 1.7	15.4 ± 1.7			

BDI = Beck Depression Inventory; DHEA = dehydroepiandrosterone; SF-36 = Medical Outcomes Study 36-item Short Form Survey.

six cognitive function tests (picture memory) in women but not men, it is unclear whether this effect would have persisted over a longer period, whether it was a practice effect or due to multiple comparisons. It is reassuring that, unlike a few previous studies,^{14,19} there were no detrimental effects of DHEA on cognitive function observed in this study.

Men and women in this study showed significant improvement in mood, and women showed improvement on one measure of life satisfaction over time regardless of whether they received DHEA or placebo, but these improvements were small and, although statistically significant, are unlikely to be of clinical significance. Furthermore,

improvements for men and women taking DHEA were no different from those observed for men and women taking placebo, and there were no differences observed between the DHEA and placebo groups on sexual function or the SF-36 measures. Thus, the results of this study do not support a beneficial effect of DHEA supplementation on quality of life.

The lack of an effect of DHEA on quality of life observed in this study, although in accord with some shorter-term studies,^{9,16,17} conflicts with others showing beneficial effects.^{13,18} In one study, women (but not men) showed a nonsignificant trend toward better mood and fewer psychological and physical complaints after 2 weeks of DHEA

supplementation,¹³ but the study sample consisted of only 15 women. It is unclear whether a longer duration of supplementation or use of a larger sample size would have yielded similar results. In a 4-month, double-blind, randomized, placebo-controlled trial with a crossover design, DHEA significantly improved overall well-being and depression and significantly increased sexual interest and satisfaction with sex in 24 women with adrenal insufficiency.¹⁸ Results of the present study suggest that a similar benefit cannot be expected in women (or men) with normal adrenal function.

Several limitations of this study were also considered. By design, this trial assessed the benefits of DHEA supplementation in a healthy sample of men and women. With an average Modified Mini-Mental State Examination score of 96, the participants in this study were limited to those who were not cognitively impaired. Effects of DHEA supplementation may be different for those not cognitively intact or scoring poorly on cognitive function tests at a baseline evaluation. Likewise, levels of depressed mood were low, and life satisfaction scores were fairly high in this cohort. It is unknown whether long-term DHEA supplementation would have an effect in clinically depressed individuals or those with a low quality of life. It is unlikely that the lack of observed effects for DHEA was due to differential adherence; adherence was high in both groups, and changes in DHEA levels in the treatment and placebo groups were consistent with adherence to use. It is also unlikely that the lack of observed effects was due to a lack of statistical power, which was greater than 0.80 for all outcomes.

In conclusion, this study of healthy older men and women who were not selected for endogenous DHEA levels failed to show any benefits from DHEA supplementation for 1 year on cognitive function, mood, quality of life, or sexual function. These results were observed despite restoration of youthful DHEA levels in men and women and enhancement of estrogens and testosterone in women. Although it is unknown whether DHEA supplementation may benefit specific subgroups of men and women, such as those who are clinically depressed or cognitively impaired, the present results suggest that DHEA supplementation should not be recommended for enhancement of cognition or well-being in the general population.

ACKNOWLEDGMENTS

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this manuscript. Funding was received from National Institutes of Aging Grant AG018339 and National Center for Research Resources Grant M01RR 00827.

Author Contributions: DK-S, DvM, and GAL contributed to all aspects of this study and helped conceive of the study and its design, the acquisition of subjects and data, the analysis and interpretation of the data, and edited drafts of the manuscript. RB performed the data analysis, assisted in the interpretation of the data, and edited drafts of the manuscript.

Sponsor's Role: The sponsor had no role in the design, methods, subject recruitment, data collection, analysis, or preparation of the manuscript.

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