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Prolonged Hypogonadism in Males Following Withdrawal from Anabolic-Androgenic Steroids: an Underrecognized Problem

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Abstract

Aims—To assess the frequency and severity of hypogonadal symptoms in male long-term anabolic-androgenic steroid (AAS) misusers who have discontinued AAS use.

Design—Cross-sectional, naturalistic.

Setting—Outpatient facility.

Participants—Twenty-four male former long-term AAS users and 36 non-AAS-using weightlifters, recruited by advertisement in Massachusetts, USA. Five of the former users were currently receiving treatment with physiologic testosterone replacement, leaving 19 untreated users for the numerical comparisons below.

Measurements—The Structured Clinical Interview for DSM-IV, questions regarding history of AAS use, physical examination, serum hormone determinations, and the International Index of Erectile Function (IIEF).

Findings—Compared with the 36 non-AAS-using weightlifters, the 19 untreated former AAS users displayed significantly smaller testicular volumes (estimated difference [95% confidence interval (CI)]: 2.3 [0.1, 4.5] ml; p = 0.042) and lower serum testosterone levels (estimated difference: 131 [25, 227] dL; p = 0.009), with five users showing testosterone levels below 200 ng/dL despite abstinence from AAS for 3–26 months. Untreated former users also displayed

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Declaration of interests

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significantly lower scores on the IIEF Sexual Desire subscale (estimated difference: 2.4 [1.3, 3.5] points on a 10-point scale; $p < 0.001$). In the overall group of 24 treated plus untreated former users, 7 (29%) had experienced major depressive episodes during AAS withdrawal; 4 of these had not experienced major depressive episodes at any other time. Two men (8%) had failed to regain normal libidinal or erectile function despite adequate replacement testosterone treatment.

Conclusions—Among long-term anabolic-androgenic steroid misusers, anabolic-androgenic steroid-withdrawal hypogonadism appears to be common, frequently prolonged, and associated with substantial morbidity.

Keywords

Anabolic-androgenic steroids; testosterone; hypogonadism; drug withdrawal; libido; erectile function; men

INTRODUCTION

It is well known that administration of exogenous anabolic-androgenic steroids (AAS) leads to suppression of the male hypothalamic-pituitary-testicular (HPT) axis via negative feedback. Thus men who misuse AAS for athletic purposes or for personal appearance are at risk for developing AAS-induced hypogonadism, especially if they have ingested AAS for prolonged periods (1–5). Symptoms of AAS-induced hypogonadism typically appear during the withdrawal phase after completing a course of AAS use, and are usually characterized by decreased or absent libido, impaired erectile function, and sometimes by symptoms of depression. Depressive symptoms may occasionally become severe (6, 7), even leading to suicide attempts or successful suicide in rare cases (8–10). The frequency and mechanism of these major depressive episodes is unclear, but clinical studies suggest that the predisposition to depression is idiosyncratic, with a majority of hypogonadal men showing few depressive symptoms, while a minority shows severe symptoms (11–13). Moreover, even among men who do not develop outright depression during AAS withdrawal, the symptoms of impaired sexual desire and function may be sufficient to prompt them to resume AAS use as a method to self-treat hypogonadal symptoms (14). Thus hypogonadism may perpetuate repeated AAS use, leading eventually to AAS dependence – a “hooked-on-hormones” syndrome first proposed 25 years ago (15) and noted by several subsequent investigators (16–18).

Unfortunately, however, the problem of AAS-induced hypogonadism has rarely been discussed in the psychiatric or substance-abuse literature, and most of the available studies have come from urologists and endocrinologists. These studies have suggested that AAS-induced hypogonadism may be more common and more persistent than is generally recognized. For example, in one recent series of consecutive hypogonadal men encountered in an academic-based urology practice, AAS-induced hypogonadism accounted for 42 (43%) of 97 cases of profound hypogonadism (total testosterone levels of 50 ng/dL or less, where the normal range is typically quoted at about 300–1000 ng/dL) (4).

Early studies of AAS users have generally suggested that hypogonadism will gradually resolve after AAS use is discontinued, with eventual restoration of normal HPT function

within a few weeks to a few months of AAS abstinence (19). However, a growing literature of case reports and small case series has now suggested that some AAS users exhibit HPT suppression that persists for many months after AAS are discontinued (20–27), with at least eight reports describing cases of hypogonadism and/or azoospermia persisting more than a year after last AAS use (Table 1) (28–35).

In two ongoing studies of long-term AAS users, described below, we have encountered numerous men exhibiting marked features of hypogonadism, including erectile dysfunction, loss of libido, and episodes of major depression, following AAS withdrawal. To better delineate these syndromes, we report data from psychiatric interviews, endocrine measures, and assessments of erectile and libidinal function in all of the former AAS users evaluated in our ongoing studies through January 2014, as compared to consecutive male weightlifters reporting no lifetime history of AAS use, evaluated in the same studies over the same time interval.

METHODS

Design

Participants for the present report were drawn from two ongoing studies whose primary aims are to examine 1) the cardiovascular effects and 2) the neurocognitive effects of long-term AAS use. These studies were designed with a secondary aim to assess features of hypogonadism among study participants, since this represents a recognized potential adverse effect of AAS. In both studies, we are comparing groups of male weightlifters age 35–55: men reporting at least two years of cumulative lifetime AAS use and men reporting no lifetime AAS exposure. Participants for both studies are recruited by advertising in local gymnasiums in the vicinity of Boston, USA, using recruitment methods developed in earlier studies and detailed in previous publications (36; 37). Briefly, we advertise for men who “could bench-press 275 pounds for at least one repetition, currently or in the past, for a psychiatric and medical evaluation.” As explained in previous publications (36, 37), the bench-press requirement is simply a device to generate an unselected group of experienced weightlifters. Importantly, advertisement respondents are recruited and screened by telephone without inquiring about their AAS status or disclosing the study’s focus on AAS, thus minimizing possible selection bias that might arise from respondents’ advance knowledge of the exposure variable of interest.

For both studies, individuals qualifying on telephone screen are then evaluated at a screening interview where they receive 1) demographic questions; 2) the Structured Clinical Interview for DSM-IV (SCID) (38) to assess lifetime psychiatric and substance-use diagnoses; 3) detailed questions about lifetime use of AAS and other performance-enhancing drugs, if any, including questions about specific drugs used, dosages, and lifetime duration of exposure; 4) the self-reported International Index of Erectile Function (IIEF) (39); 5) measurements of height, weight, and body fat; and 6) collection of hair and urine samples. Urine samples are tested for AAS, using methods previously described (40, 41). Urine samples are also tested for opiates, amphetamines, cannabis, cocaine, and phencyclidine, and for the performance-enhancing drug clenbuterol. Hair samples are analyzed for residues of opiates, cannabis, phencyclidine, amphetamines, and cocaine from

the last 90 days (Psychemedics, Culver City, California). Participants are excluded from analysis if they display urine or hair findings inconsistent with their self-reports of AAS or other substance use. As a further check on the validity of self-reports, we use participants' height, weight, and body fat to calculate their fat-free mass index (FFMI), an index of muscularity that we have developed and described previously (42). Participants are excluded from analysis if they deny AAS use, but exhibit a fat-free mass index greater than 25.5 kg/m^2 while displaying less than 10% body fat – because a combination of leanness and muscularity beyond this threshold strongly suggests surreptitious AAS use (42).

Participants fully qualifying on screening evaluation as long-term AAS users or as AAS nonusers then receive an evaluation of cardiovascular function (study #1) or an evaluation of cognitive function together with magnetic resonance imaging of the brain (study #2). Preliminary findings from the cardiovascular study have been reported (43, 44); findings from the neurocognitive study are still being analyzed.

In the course of these evaluations, participants in both studies receive a physical examination, which includes estimation of testicular volume by orchidometry. Participants also receive a battery of laboratory tests including a chemistry and hematology panel, together with determination of serum hormone levels. Serum total testosterone is measured using a liquid chromatography tandem mass spectrometry assay, previously described, and certified by the Hormone Assay Standardization Program for Testosterone (HoST) of the Centers for Disease Control (45). Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels are measured on serum from two pooled samples, drawn at least 30 minutes apart. These determinations use two site-directed immunoflurometric assays, also previously described (46, 47). It should be noted that one of the participants reported below received these hormone determinations via commercial immunoassay, rather than the above methods.

All of the above procedures in both studies have been approved by the institutional review boards of our institutions, and all participants have provided written informed consent before study procedures were undertaken. If any participants report or display conditions for which they desire medical or psychiatric treatment, the study physicians attempt to provide suitable referrals for follow-up.

Participants

We identified all men evaluated in the above two studies from February, 2011 (the inception of the first study) through January, 2014 who 1) reported at least two years of cumulative lifetime AAS use; 2) had discontinued use of supraphysiologic doses of AAS at least three months before the time of medical evaluation (mean [SD]: 58.9 [79.0] months; range 3–253 months); and for whom we possessed complete data including 3) serum total testosterone, LH, and FSH levels; 4) lifetime psychiatric diagnoses from the SCID and 5) IIEF scores. (Note that the SCID and IIEF were typically performed about 1–2 months prior to the date of the medical and laboratory evaluations, so that the mean abstinence interval since last AAS use was slightly shorter at the time that these instruments were administered.) We found 24 men who met these criteria. At the time of evaluation, five (21%) of these men were receiving testosterone replacement at physiologic doses (physician-prescribed in 4

cases; illicit in one case) to treat hypogonadal symptoms, leaving 19 untreated cases. We compared these 19 untreated men with 36 consecutive non-AAS-using weightlifters recruited through the same studies during the same time interval of 2011–2014.

Statistical analysis

We quantitated participants' level of education on an eight-point scale as used in the SCID (38). Annual income was quantitated on a five-point scale used previously (37). Total lifetime dose of AAS was calculated as milligrams of testosterone equivalent as described previously (36, 37).

For comparisons between the two groups, we used linear regression for continuous variables, a nonparametric trend test for ordered categories, and Fisher's exact test for non-ordered categories. Analyses for the outcomes of interest (see Table 3) were performed with adjustment for age, race (African-American versus White or Asian), level of education, and annual income with the exception of strata of testosterone levels, which were assessed by an unadjusted nonparametric trend test. Alpha was set at 0.05, two-tailed. Since the IIEF contains 15 questions and generates five subscale scores, we set alpha at 0.005 for comparisons using this instrument in order to adjust for multiple testing. The analyses were performed using Stata 9.2 software (Stata Corp., College Station, TX).

Note that the sample size in the present study was not determined in advance, since the two parent studies were powered to detect their respective primary outcome variables, and hypogonadal symptoms represented a secondary outcome of interest.

Results

The 19 untreated former AAS users resembled the 36 non-users in demographic features, including lifetime duration of regular weightlifting (Table 2). However, the former users displayed significantly smaller testicular volumes and lower total testosterone levels than non-users (Table 3), with 5 (26%) of the 19 users displaying levels below 200 ng/dL (176, 147, 101, 63, and 30 ng/dL, despite abstinence from AAS for 7, 3, 16, 26 and 8 months, respectively). The former users also scored markedly lower on the IIEF "Sexual Desire" subscale, with 7 (37%) men scoring 4 or less (indicating moderate to severe dysfunction (39)) despite abstinence from AAS for 2, 2.5, 4, 7, 10, 15, and 26 months, respectively, at the time of IIEF administration.

We considered the possibility that the above results might be influenced by the fact that 4 of the 19 untreated users had been abstinent for only 3–6 months at the time of their medical and laboratory evaluations (see Table 2). These same 4 individuals had been abstinent only 2–4 months at the time of their initial SCID and IIEF evaluations. Therefore, we performed a sensitivity analysis excluding these 4 individuals and restricting consideration to the 15 users who had been abstinent for 7 months or longer at the time of their medical evaluation. Even with this restriction, however, the results remained largely unchanged: for testosterone levels, the estimated mean difference between groups was 127 [20, 235] ng/dL; for testicular volume, the difference was 2.6 [−0.1, 5.0]; for Sexual Desire, it was 1.8 [0.8, 2.9]. Thus the results did not appear to be driven by the inclusion of individuals with briefer abstinence.

In exploratory analyses, we also examined the association between the above outcome variables and 1) years of cumulative lifetime AAS use and 2) the percentage of time that users were actually taking AAS (i.e., were "on-cycle") over their AAS-use career. None of these analyses revealed significant associations, save for an inverse association between years of AAS use and testicular volume, after adjustment for duration of abstinence from AAS (estimated change in testicular volume per year of AAS use: −0.5 [−0.1, −0.9] ml; p = 0.029).

On the SCID, 5 (26%) of the 19 untreated former users reported a history of major depressive disorder, in one case associated with suicidal ideation, arising during AAS withdrawal. Of these 5 men, 2 displayed a lifetime history of bipolar II disorder, and both had experienced additional major depressive episodes at times other than during AAS withdrawal. One of these 2 men was the individual who reported suicidal ideation during AAS withdrawal. The remaining 3 men had experienced major depressive episodes only during AAS withdrawal. Among the 5 additional users receiving testosterone replacement, 2 had displayed major depressive episodes during AAS withdrawal. Of these, one had experienced an additional major depressive episode at a time unrelated to AAS withdrawal, and the other had experienced a major episode only during AAS withdrawal. Thus, in the overall group of AAS users, the lifetime prevalence of major depressive disorder occurring at times *other* than AAS withdrawal was 3 (13%) among 24 men – a prevalence closely comparable to the rate of 5 (14%) among the 36 non-users (p = 1.0 by Fisher's exact test, two-tailed).

Notably, among the 5 users receiving testosterone replacement, one reported an IIEF Sexual Desire score of 2 (the lowest possible score) despite having received three months of transdermal testosterone therapy at the time of evaluation, and despite a current testosterone level of 931 ng/dL. Also of note, one of the 19 former users described in the paragraph above had previously received replacement therapy with testosterone cypionate, 200 mg every 10 days – an ample dose to restore physiologic levels of testosterone – but also had noticed no improvement in libido or erectile function after six weeks, and had abandoned the treatment.

The participants' physical examinations and laboratory tests showed little evidence of medical abnormalities that might account for sexual dysfunction or psychiatric conditions. In particular, none of the participants exhibited a diastolic blood pressure greater than 95 mm Hg, all exhibited creatinine clearance of at least 55 mL/min/1.73m^2, none exhibited a total cholesterol/HDL cholesterol ratio greater than 7.1, and only one (a non-user) showed hepatic transaminase levels greater than twice the upper limit of normal in our laboratory. No participant reported a history of peripheral vascular disease or diabetes. Four participants (two users and two nonusers) showed fasting glucose levels greater than 110 mg/dL, but three of these individuals admitted that they had failed to follow instructions for fasting, and the fourth only slightly exceeded the normal range for fasting glucose at 113 mg/dL. Thus, our findings appear unlikely to be attributable to hypertension, dyslipidemia, peripheral vascular disease, renal disease, hepatic disease, or diabetes.

Overall, 13 (54%) of the 24 men demonstrated pronounced symptoms of AAS-withdrawal hypogonadism, as evidenced by Sexual Desire scores of 4 or less, and/or a history of major depressive episodes associated with AAS withdrawal.

4. Discussion

The illicit use of anabolic-androgenic steroids (AAS) has recently emerged as a major form of substance abuse worldwide (48), with 2.9–4.0 million men in the United States alone estimated to have used these drugs at some time in their lives (49). Chronic AAS use suppresses the function of the hypothalamic-pituitary-testicular (HPT) axis, which may lead to symptoms of hypogonadism following AAS withdrawal (2). Over the last 25 years, several case reports and small case series have described individuals with AAS-induced hypogonadism, sometimes persisting for more than a year after stopping AAS use. However, most of these case reports have appeared in urological or endocrinological journals, rather than in the substance-abuse literature.

In this report, we present our experience with illicit AAS users age 35–55, encountered in the course of two ongoing studies, in whom we found that AAS-induced hypogonadism was common, frequently prolonged, and often associated with marked morbidity in the form of decreased or absent libido, impaired erectile function, and episodes of major depressive disorder. Our findings suggest that these symptoms may persist for more than a year after the last AAS use, and possibly much longer.

The mechanisms of AAS-induced hypogonadism are incompletely understood. It seems likely that several different mechanisms may be operative in various subsets of individuals. One subset of individuals appears to display incomplete recovery of gonadotrope function and has hypogonadotropic hypogonadism. Some reports have described successful restoration of HPT function in AAS users following administration of gonadotropin releasing hormone agonists, such as triptorelin (21), selective estrogen receptor modulators such as clomiphene citrate (25), or agents mimicking pituitary LH and FSH, such as human chorionic gonadotropin or human menopausal gonadotropin (2, 29, 32). However, such strategies are not always successful (27, 29). In particular, some patients may respond to clomiphene, but in spite of elevated LH and FSH levels, do not normalize testosterone levels, suggesting possibly irreversible damage to Leydig cells (20). More interestingly, still another subset appears to show continued loss of sexual desire and erectile dysfunction even when normal testosterone levels are restored, as illustrated in the two cases described above. Such cases may possibly represent end organ resistance – reflecting a possibly irreversible down-regulation of androgen receptors or androgen receptor signaling mechanisms.

Our findings are subject to several limitations. First, our sample may not be representative of the overall population of illicit AAS users. In particular, we recruited men age 35–55 who reported at least two years of cumulative lifetime AAS exposure. It seems likely that younger men, and men with briefer lifetime AAS exposure, might show a lower prevalence of hypogonadal symptoms than seen in our sample. More generally, since participants were self-selected, we cannot exclude the possibility of selection bias. Second, our participants reported varying durations of abstinence from AAS at the time of evaluation. Although our

sensitivity analysis above found consistent results even with exclusion of the 4 participants reporting less than 7 months of abstinence, we cannot be sure that the results would have remained consistent if all participants had been evaluated after the same abstinence interval. Third, we relied on participants' self-reports to obtain a history of AAS and other drug use. Although we obtained some objective data from our urine and hair tests for drugs of abuse, together with measurements of fat-free mass index as described above, most of our information was based on participants' retrospective accounts of using illicit drugs of uncertain potency or authenticity. Thus, the nature, dosage, and chronology of AAS use in each case may have been imprecise. Also, we cannot exclude the possibility that one or more of the non-AAS-using weightlifters might have surreptitiously used AAS in the past, but denied this on interview, and also escaped detection with our hair, urine, and FFMI screening methods. However, if such misclassification did occur, it would likely have only narrowed the difference between the two groups and rendered our findings more conservative. All of these various limitations are inherent to most field studies of illicit drug users, and are difficult to avoid when studying phenomena that cannot ethically be duplicated under laboratory conditions. Finally, we acknowledge that possible unrecognized confounding variables (e.g. medical disorders or use of other drugs) may have contributed to the clinical findings reported here. For example, one study has reported that AAS users identified themselves as being driven and motivated, with a focus on goal achievement (50) – a trait that plausibly might make them more vulnerable to depression when experiencing hypogonadal symptoms. Since we did not assess these or other personality traits among participants, we cannot determine the possible contribution of personality traits to the findings. Similarly, we did not formally assess possible stressors that might have contributed to depressive episodes among the participants.

The present observations, despite their limitations, suggest that AAS-induced hypogonadism likely represents an emerging issue in the growing world population of AAS users – an issue still apparently underrecognized in the scientific literature. Hypogonadal symptoms are of particular concern because they may induce individuals to quickly resume AAS use after stopping a prior course of these drugs, in an attempt to self-treat dysphoric sexual and mood symptoms (15). Repeated cycles of AAS re-use may then lead to AAS dependence, a disorder that appears to develop in as many as 30% of illicit AAS users (16–18, 51). To prevent AAS dependence, and to reduce the risk of prolonged hypogonadal syndromes, hypogonadal patients will likely require endocrinological treatment to restore normal HPT function, possible antidepressant treatment (if depressive symptoms are pronounced), and substance-dependence treatment to reduce the risk of relapse into AAS use (14). Future clinical and research work in this area will likely require increasing collaboration among substance-abuse professionals, sports-medicine clinicians, endocrinologists, and urologists.

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Table 1

Reports of AAS-withdrawal Hypogonadism With Signs Persisting > 1 Year After Last AAS Exposure

Study	Location	No. of cases	Age, yrs	Duration of AAS use, yrs	Follow-up, mo	Status
Jarow & Lipshultz, 1990 (27)	United States	2	36, 39	2, NS	12–36	The two men displayed a blunted pituitary response to GnRH stimulation at 12 mo and 36 mo after AAS discontinuation, respectively.
Turek et al., 1995 (28)	United States	1	34	2.5	60	T remained below normal 3 yrs after stopping AAS; the patient failed to respond to HCG at 3 yrs but did respond to a second trial of HCG at 5 yrs
Lloyd et al., 1996 (29)	United Kingdom	5	28–35	NS	Up to 16	Four men apparently recovered within ≤ 1 yr, but one still displayed decreased sperm count at 16 months
Gazvani et al., 1997 (30)	United Kingdom	4	27–33	NS	8–20	Three men largely recovered within one year, but one showed persistently low T at 18 months despite normal FSH & LH
Menon, 2003 (31)	Malaysia	1	37	NS	15	At 12 mo, FSH, LH, and T all below normal; the patient subsequently responded to HCG + HMG with normalization of all hormones after 1 mo
Urhausen et al., 2003 (32)	Germany	2	Mean 38.0	Mean 4.5	≥ 12	Two (13%) of 15 former AAS users displayed T below normal at least 12 months after discontinuing AAS.
Garevik et al., 2011 (33)	Sweden	NS	18–57	0.5–17	Up to 12	Study of 39 subjects; individual data not provided, but “some individuals had a sustained suppression of LH and FSH for a period of one year.”
Boregowda et al., 2011 (34)	United Kingdom	1	40	10	36	At 18 months, FSH & LH normalized, but T remained below normal even at 36 months despite supranormal FSH and LH

Abbreviations: NS = Not specified; T = testosterone; LH = luteinizing hormone; FSH = follicle-stimulating hormone; HCG = human chorionic gonadotropin; HMG = human menopausal gonadotropin.

Table 2

Demographic Features of Former AAS Users versus Non-AAS-Using Weightlifters

Attribute[a]	Former AAS users N = 19	AAS Non-users N = 36	*p*
Age, yrs.	42.7 (3.8)	42.9 (5.8)	0.89
Self-reported race/ethnicity			
Non-Hispanic White	15 (79)	24 (67)	
Non-Hispanic African-American	3 (16)	9 (25)	
Hispanic White	1 (5)	1 (3)	0.81
Hispanic African-American	0	1 (3)	
Asian	0	1 (3)	
College graduate, N (%)	7 (37)	22 (61)	0.10
Annual income > $50,000, N (%)	9 (47)	21 (58)	0.57
Years of regular weightlifting	22.2 (6.1)	19.2 (10.3)	0.25
Age at first AAS use, yrs	22.3 (4.6)	-	
Cumulative lifetime AAS use, yrs	6.9 (4.5)	-	
Cumulative lifetime AAS dose, mg	353,000 (300,000)	-	
Time since last AAS use:			
3–6 months	4 (21)	-	
7–12 months	3 (16)	-	
13–24 months	4 (21)	-	
25–120 months	4 (21)	-	
> 120 months	4 (21)	-	

[a] Attributes shown as mean (SD) for continuous variables and N (%) for ordinal variables.

Table 3

Features of Former AAS Users versus Non-AAS-Using Weightlifters

Attribute[a]	Former AAS users N = 19	AAS Non-users N = 36	Estimated Difference (95% confidence interval)	p[b]
Total testosterone level, ng/dL	319 (163)	449 (153)	131 (25, 227)	0.009
Range of total testosterone levels:				
Testosterone < 200 ng/dl, N (%)	5 (26)	1 (3)		0.011
Testosterone 200 – 348 ng/dl, N (%)[c]	5 (26)	7 (19)		
Testosterone > 348 ng/dl, N (%)[c]	9 (47)	28 (78)		
Free testosterone, pg/mL[d]	107 (51)	132 (49)	29 (−2, 61)	0.065
Luteinizing hormone, mIU/mL	3.9 (2.5)	4.6 (2.1)	0.9 (−0.5, 2.2)	0.19
Follicle-stimulating hormone, mIU/mL	4.7 (4.6)	5.2 (4.1)	0.9 (−1.6, 3.5)	0.46
Testicular volume, ml	19.9 (4.0)	22.2 (3.4)	2.3 (0.1, 4.5)	0.042
International Index of Erectile Function:[e]				
Erectile Function	26.3 (6.1)	27.6 (4.3)	1.6 (−1.5, 4.6)	0.31
Orgasmic Function	9.3 (1.4)	9.5 (0.9)	0.2 (−0.5, 0.9)	0.55
Sexual Desire	5.6 (2.5)	7.8 (1.4)	2.4 (1.3, 3.4)	< 0.001
Intercourse Satisfaction	11.6 (1.8)	11.5 (2.9)	0.1 (−2.0, 1.7)	0.91
Overall Satisfaction	6.3 (3.1)	7.2 (2.1)	1.0 (0.5, 2.5)	0.17
Total	60.8 (10.8)	64.3 (8.6)	4.1 (−2.1, 10.3)	0.19

SI conversion factors: To convert testosterone to nmol/L, multiply values by 0.0347

[a] Attributes shown as mean (SD) for continuous variables and N (%) for ordinal variables.

[b] By linear regression with adjustment for age and race, with the exception of strata of testosterone levels, which were tested by an unadjusted nonparametric trend test.

[c] The cutoff of 348 ng/dL represents the lower limit of the reference range for normal testosterone levels, based on data from the Framingham Heart Study (see Bhasin S, Pencina M, Jasuja G, et al, J Clin Endo Metab. 2011; 96: 2430–2439.).

[d] N = 18 for AAS users because of missing data

[e] Scores on Erectile Function, Orgasmic Function, and Intercourse Satisfaction, as well as Total Score, are restricted to men reporting at least one sexual partner in the past month (N = 15 former AAS users and 32 non-users).