

# Self-reported psychological distress associated with steroid therapy for HIV

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**Summary:** Anabolic androgenic steroid (AAS) replacement therapy is standard care for patients with low testosterone, including HIV-related conditions. These medications have been associated with development of aggressiveness, anxiety disorders, and depression, but only in short-term clinical trials. We conducted an anonymous street survey at a gay and lesbian community event and a survey in a clinic-based setting to study the wider prevalence of psychiatric side-effects associated with androgenic steroids. In the street-based survey, almost half of those prescribed AAS reported psychological side-effects, most commonly aggression (29%) followed by depression (21%). In the clinic survey of mostly HIV+ male patients, changes in sex drive were the most commonly reported effect of treatment while impulsive aggression, anxiety and depression were reported at levels similar to those in the street fair survey. These findings suggest that AAS therapy may be more frequently associated with distress than has been reported in the clinical literature.

**Keywords:** anabolic androgenic steroids, low testosterone syndrome, psychological distress, impulsive aggression, depression, sex drive

## INTRODUCTION

Anabolic androgenic steroids (AAS) are derivatives of the male hormone testosterone and are considered standard care for patients with low testosterone levels, a condition often related to HIV and its treatment.<sup>1</sup> Low testosterone levels are found in approximately one-fifth of HIV+ men, and are associated with HIV-induced wasting.<sup>2,3</sup> Along with decreased muscle and bone mass, testosterone deficiency has been reported to cause weakness, fatigue, depression and cognitive impairment.<sup>4</sup> Reduced libido associated with low testosterone levels often is the motivation for a patient to seek testosterone replacement therapy.<sup>5</sup> Serum testosterone levels are not reliable indicators of testosterone deficiency since normal levels can range widely. Thus, clinical symptoms are generally used to establish an optimal treatment dose.<sup>6,7</sup> Other steroids for men who may or may not exhibit low testosterone levels include oxandrolone<sup>8,9</sup> and nandrolone decanoate.<sup>8,10,11</sup>

Most behavioural side-effects of steroid therapy have been described at doses such as those used by competitive athletes or weightlifters.<sup>12</sup> However, a study of intramuscular testosterone for male sexual dysfunction found irritability and uncharacteristic assertiveness in some patients<sup>13</sup> while a second study observed significant increases in hostility and resentment/aggression after six weeks of treatment with testosterone or nandrolone.<sup>14</sup> A meta-analysis of controlled trials of

testosterone for wasting reported scattered adverse effects and no psychological effects.<sup>15,16</sup> However, the longest follow-up period was six months. Few studies have followed patients' long-term or measured side-effects in real-world clinical as opposed to experimental settings.

Studies conducted in animal models have suggested that a GABA<sub>A</sub> receptor-mediated neurotransmission dysfunction plays a major role in causing the behavioural dysfunctions induced by protracted treatment with AAS.<sup>17-20</sup> Long-term exposure to AAS may lead to a downregulation of GABAergic neurotransmission<sup>17</sup> or downregulation of the biosynthesis of neurosteroids such as allopregnanolone.<sup>18,19</sup> This appears to play a role in several psychiatric conditions.<sup>20-23</sup> Decreased GABAergic function mediated by testosterone may lead to impulsive aggression, altered fear, and changes in sexual behaviour.<sup>17-20</sup>

In this study, we employ a street-based survey and a clinic-based survey to explore the prevalence of self-reported psychiatric side-effects associated with steroid therapy. We ask about symptoms of aggression, depression, anxiety, and irrational fear and compare the prevalence of these symptoms among a broad sample of individuals who are taking steroids versus a sample of HIV+ men. We employ an anonymous survey, which may encourage patients to be more forthright in reporting their symptoms.

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## METHODS

The first survey was conducted at an annual street fair heavily attended by gays and lesbians in Chicago. Volunteers from a

gay and lesbian community health centre approached persons at the fair and asked if they wished to complete a 'one minute survey' consisting of a single page. Questions consisted of demographics, whether the respondent had taken steroids (and, if so, whether they were prescribed or not and for what conditions) and whether the respondent who had taken steroids had experienced any of the following: changes in their body or genitals, aggression, feelings of depression, anxiety or fear (see Table 1). The volunteers were trained not to look at the answers and to place completed forms in an envelope.

A second, more detailed, waiting-room survey was conducted at an HIV clinic in Chicago. In the second survey, patients waiting to see the physician could fill out the survey anonymously and place it in a locked box. Along with the questions in the first survey, the second survey included questions on HIV status and on the reason why the respondent had been prescribed steroids: for low testosterone, to build muscle, or for another medical condition. Table 2 shows results from the clinic survey.

## RESULTS

We collected 196 responses from the street fair survey. The response rate was low (<50%) and some persons who might have used AAS at supraphysiological doses (subjectively assessed by the interviewer) declined to respond, likely leading to an underestimate of the use of AAS. Nonetheless, of the 196 responses, 21% reported having used steroids, of which more than two-thirds had been prescribed them (Table 1). In this report, we focus on the 28 persons who reported having been prescribed steroids. (There were no significant side-effect differences between persons who were prescribed versus those who were not prescribed AAS.) About three-quarters were men, almost all reported being gay or bisexual, and most were white. Almost half of those who were prescribed AAS reported psychological distress, most commonly aggression (29%) followed by depression (21%).

Unlike the first survey, the waiting room survey enquired into the medical reason that steroids were prescribed and permitted respondents to respond on a scale rather than yes/no to the side-effects questions (a three-point scale of 'not at all', versus 'a little', versus 'a lot'). Of 139 surveys completed, 61 (44%) had used steroids, almost all by prescription (Table 2).

Table 1 Summary of street fair steroid survey

Total surveys completed	196
Used steroids (total)	41
Prescribed steroids	28
<b>Demographics of those prescribed steroids</b>	
Mean age	38.4
Male	72%
Gay/bisexual	86%
White	82%
<b>Why were you taking steroids?*</b>	
For medical condition	75%
To build muscle	11%
<b>Did you experience any of the following?*</b>	
Changes in body or genitals	14%
Aggression	29%
Feelings of depression	21%
Anxiety or irrational fear	18%
Any side-effect listed above	46%

\*May endorse >1 category

Table 2 HIV clinic survey

Total surveys completed	139	
Used steroids (total)	61	
Prescribed steroids	58	
<b>Demographics of those prescribed steroids</b>		
Mean age	43	
Male	97%	
Gay/bisexual	74%	
White	81%	
HIV status positive	86%	
<b>Why were you taking steroids?*</b>		
For low testosterone	34%	
HIV disease/wasting	19%	
<b>Did you experience any of the following?*</b>		
	<b>'A little'</b>	<b>'A lot'</b>
Changes in body or genitals	34%	20%
Change in sex drive	40%	29%
Aggression	22%	14%
Depression	22%	12%
Anxiety or fear	15%	9%

\*May endorse >1 category

Of these respondents, 86% were HIV+. Changes in sex drive were the most commonly reported effect of treatment, followed by changes in body or genital morphology. Behavioural symptoms were also common, with impulsive aggression the most frequent symptom. A  $\chi^2$  analysis revealed that rates of reporting of aggression, depression and anxiety/fear (collapsing the 'a little'/'a lot' categories) did not differ statistically between the street fair sample and the clinic sample.

## DISCUSSION

These two surveys conducted in very different contexts suggest that psychiatric distress is not an uncommon occurrence among persons prescribed androgenic steroids, despite very little discussion in the clinical literature. While causality cannot be inferred from data from a cross-sectional study, generalized anxiety, fear, aggressiveness and/or depression appear in about half of the subjects who use steroids (Tables 1 and 2). Most respondents in the waiting room sample and probably many in the street fair sample were taking testosterone to normalize low testosterone levels. About 80% of clinic patients taking AAS for low testosterone in the clinic sample were HIV+ homosexual men and about 40% reported increased sex drive (Table 2). Of course, anabolic changes in body volume and increased sex drive may have been the intended purpose of testosterone replacement therapy and hence should not be described as unwanted side-effects. It is significant, however, that many of those in the clinic sample who were prescribed steroids experienced other symptoms of psychological distress. When compared with the lack of reports in the literature, these results suggest that some patients may be more willing to share these symptoms on an anonymous survey than they are with their provider.

While it is not yet fully understood why administration of testosterone may give rise to psychological symptoms, untreated plasma testosterone levels, as mentioned above, vary widely and assessing a person-specific range is difficult. In addition, systemic testosterone administration increases testosterone levels both in peripheral organs and in the brain. While normal endogenous testosterone is unevenly distributed in various brain structures, administration of testosterone results in a global expression of testosterone in the whole

brain. This may give rise to imbalances in some brain structures.<sup>24</sup>

There are several limitations to this study. In both surveys, respondents were not required to specify whether steroid administration occurred prior to the occurrence of symptoms. Moreover, steroid administration may have decreased psychological distress in some patients, since there's no comparison of psychological symptoms to pre- and post-steroid administration. A prospective study is needed that looks at occurrence over time of side-effects in persons taking AAS, one that is not restricted to the short follow-up typical of a clinical trial. We do not know how many of these patients were taking testosterone in higher doses than required to normalize testosterone levels. Finally, we did not survey a comparison group not taking steroids against which to compare the prevalence of these self-reported symptoms. Thus these findings are suggestive only.

Nonetheless, the results of these two surveys suggest that these symptoms should be more closely monitored by health professionals prescribing AAS, and that protocols should include monitoring of psycho-social functioning. Further examination of the behavioural effects of several classes of AAS is needed in HIV therapy and other pathologies characterized by a low testosterone syndrome. Moreover, when clinicians observe increased anxiety, depression, and/or other psychiatric symptoms in patients who are on testosterone replacement therapy, they should consider and evaluate AAS administration as a possible cause. If testosterone administration is linked to psychological distress in future studies, development of alternative treatments is needed that would not produce aggression, depression or anxiety but would ensure anabolic effects together with elevation of cognitive performance and normalization of libido.

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