JODŁOWSKI, Krzysztof, DUBNIEWICZ, Ewa, MAJEWSKA, Paula, STASZEK, Alicja, ŁOSKOT, Wiktoria, SZWECH, Jan, MATCZAK, Mateusz, JASIŃSKI, Karol, BRODA, Aleksandra and HOKSA, Kacper. Health Implications of Anabolic-Androgenic Steroids: Usage, Risks, and Treatment Approaches - The Literature Review. Quality in Sport. 2025;38:57914. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.38.57914
https://apcz.umk.pl/QS/article/view/57914

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 17.01.2025. Revised: 10.02.2025. Accepted: 11.02.2025 Published: 11.02.2025.

Health Implications of Anabolic-Androgenic Steroids: Usage, Risks, and Treatment Approaches - The Literature Review

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Abstract

Anabolic-androgenic steroids (AAS) are commonly used to enhance athletic performance and physical appearance, but their abuse is linked to a range of serious health consequences, including cardiovascular, liver, and psychological disorders, as well as infertility. Despite the growing concern over AAS misuse, current research is limited by methodological constraints, including a lack of randomized controlled trials and long-term studies. The review explores the health implications of AAS use, highlighting the importance of an interdisciplinary approach to managing AAS-related health issues, emphasizing harm reduction, pharmacological interventions, and fertility preservation techniques. It also underscores the need for improved healthcare support, education, and trust-building to address the challenges associated with AAS abuse effectively.

Furthermore, the review highlights significant gaps in the literature, such as the absence of comprehensive guidelines for harm reduction and the scarcity of longitudinal data on the long-term effects of AAS. The findings suggest a critical need for continued research, better medical management, and societal interventions to mitigate the risks associated with AAS use and provide effective care for affected individuals.

Key words: Anabolic-androgenic steroids; AAS; androgens; hypogonadism; infertility; erectile dysfunction; testicular atrophy; performance enhancing drugs; PED

1. Testosterone: Discovery, Functions, and Misapplications

Testosterone was first identified in 1935. Its discovery quickly gained widespread recognition, and shortly thereafter, this sex hormone began to be used in medicine in various ways, becoming one of the first mass-produced hormones in history.

Testosterone and its derivatives, key male sex hormones, play an essential role in regulating numerous physiological functions. In males, testosterone facilitates the development of secondary sexual characteristics during puberty, including increased muscle mass, body hair growth, vocal cords thickening leading to a deeper voice, and the maturation of reproductive organs. Additionally, testosterone is essential for spermatogenesis and the regulation of libido.

Beyond its role in male physiology, testosterone also exerts significant effects in both men and women. It enhances bone mineral density, contributing to stronger bones, supports erythropoiesis, and influences emotional and psychological well-being[1]. Additionally, testosterone contributes to metabolic regulation by promoting muscle mass preservation and limiting fat tissue accumulation. However, with advancing age, testosterone levels naturally decline, potentially leading to reduced vitality, diminished muscular strength, and lower bone density.

Currently, the use of testosterone can be categorized into three primary applications: medical use, misuse, and abuse [2]. Modern medicine employs testosterone replacement therapy (TRT) to address organic hypogonadism caused by defects in the hypothalamo-pituitary-testicular axis, which remains its only clear medical indication[2].

However, some practitioners misuse testosterone by attempting to treat unrelated male health conditions such as not associated with hypogonadism erectile dysfunction or male

infertility. Testosterone has also been improperly used to address other health issues like obesity, diabetes, osteoporosis, or even non-existent conditions such as "andropause" or "LowT".

The third category, and the focus of this literature review, involves the abuse of testosterone and other anabolic-androgenic steroids (AAS), primarily to enhance sports performance.

2. The evolution of anabolic-androgenic steroids from medical use to widespread doping and controversy in sports

Anabolic steroids or anabolic-androgenic steroids (AAS) are a class of substances whose chemical structure is similar to testosterone and encompass a wide range of substances aimed at improving physical appearance, muscle mass or boosting athletic strength and performance. AAS are predominantly administered either orally or through intramuscular injections. After administration, they undergo metabolism within the body, and their pharmacological effects depend on their ability to bind to androgen receptors in target cells[3].

The history of AAS usage dates back to shortly after the discovery of testosterone. By the 1930s and 1940s, anabolic steroids were already being used to enhance sports performance. The 1950s, 1960s and 1970s saw a surge in their popularity among athletes in strength and endurance sports worldwide[4]. The 1980s marked the peak era of steroid use, often referred to as “the golden age of steroid pharmacology”. During this time, steroids became deeply entrenched in the sports world, particularly amid the Cold War, when countries like the USSR engaged in state-sponsored doping programs to boost athletic performance.

This widespread use occurred in an environment of minimal regulation, sparking significant controversy and ultimately leading to the establishment of stricter anti-doping controls in sports by the late 20th century[5]**.**

3. Profiles, Motivations, and Challenges in AAS Use

The profile of a typical anabolic-androgenic steroid (AAS) user varies significantly across studies. Early research depicted users as young males with low self-esteem, a tendency to

engage in risky behaviors, and a history of substance abuse. However, more recent studies suggest that the average user is an educated professional in their 30s, primarily driven by the desire to enhance physical appearance and muscle strength[6,7]. Additionally, AAS are often purchased by younger individuals, including high school students[8].

Although AAS are prohibited in sports, athletes admit to their ongoing use [9]. Beyond professional sports, anabolic steroids are increasingly popular among amateurs. The most commonly used AAS include testosterone esters, metandienone, and stanozolol[10]. The lifetime risk of using anabolic steroids affects approximately 1-5% of men worldwide[5,11]. However, the true extent of AAS usage remains unclear due to unreliable data and underreporting. Many users are reluctant to disclose the duration or dosages of their AAS use, as such admissions often carry the risk of social stigmatization or legal consequences[5]**.** Motivations for using AAS extend beyond muscle building and include goals such as enhancing libido, improving sexual performance, and counteracting the effects of aging [12].

Researching the side effects of AAS presents significant challenges due to common practices such as "stacking" (combining multiple AAS or other substances), "blast and cruise" (alternating between high and low dosages), and "pyramiding" (gradually increasing and then tapering doses)[13]. These techniques are widely used despite a lack of scientific evidence supporting their efficacy[6,14]. Additionally AAS are often used together with tobacco, alcohol or other illegally obtained substances such as opioids, marihuana and drugs that are intended to counteract the side effects of anabolic steroids[15], or with substances intended to avoid AAS detection such as diuretics[16,17]. The complex and covert nature of AAS usage poses significant challenges to thoroughly studying their effects.

4. Health Risks and Adverse Effects of AAS Use

Despite the general awareness within the population regarding common adverse effects associated with the use of androgenic-anabolic steroids, such as gynecomastia, acne or testicular atrophy, certain side effects that are not directly related to the reproductive system still remain largely unknown to the average user. AAS when used in high doses, increase hemoglobin levels, which can lead to thromboembolism and strokes[9,18]. Prolonged exposure to these substances elevates the risk of arrhythmias, atherosclerosis, hypertension, myocardial hypertrophy, and sudden cardiac death[9,11,19]. AAS also disrupt lipid profiles, leading to increased LDL levels and decreased HDL levels [20].

Beyond their cardiovascular effects, AAS pose risks to liver health. They can cause significant liver damage, including conditions such as peliosis hepatis, and increase the likelihood of hepatocellular carcinoma[3,9,21].

AAS use also has profound effects on mental health. These substances can disrupt sleep patterns, causing insomnia, and contribute to mood disturbances, aggressive behavior, and anger issues[6,9]. Their impact on the brain's limbic system may lead to psychological effects such as heightened aggression, irritability, and even psychotic episodes, including hallucinations and delusions. Long-term use can result in "reverse anorexia," a condition where individuals perceive themselves as weak or underdeveloped despite a muscular appearance. Users may also experience impulsivity, euphoria, depression, and, in some cases, suicidal thoughts[22,23]. The psychological effects of AAS may persist for years even after discontinuation of use [9].

5. Impact of AAS on Male Fertility: Biological and Psychogenic Factors

Anabolic-androgenic steroids (AAS) affect hypothalamic-pituitary-gonadal (HPG) axis by inhibiting luteinizing hormone (LH) and folliculotropic hormone (FSH) release[7,12]. These hormones play a key role in sperm production and in the proper functioning of the reproductive system. Studies indicate that high doses of testosterone suppress the HPG axis in approximately 95–98% of users within six months of use [24]. Prolonged AAS abuse often results in hypogonadotropic hypogonadism, characterized by oligozoospermia or azoospermia, and morphological abnormalities in sperm cells [11] Furthermore, AAS users commonly exhibit significantly reduced sperm motility [12].

Long-term AAS usage may cause destruction or structural damage of Leydig cells resulting in spermatogenesis disorders, including germ cell apoptosis. A frequently observed consequence of AAS abuse, reported by approximately 44% of users, is a noticeable reduction in testicular volume[12,25]. Additionally, research has linked AAS abuse to genetic aberrations in sperm, such as aneuploidy and ultrastructural abnormalities [11].

Psychogenic factors also contribute to fertility decline among AAS users. Although AAS use can enhance sexual performance, patients often report decreased libido and erectile dysfunction following cessation[12] or even during use[25]. Psychological effects, such as frustration caused by reduced athletic performance, muscle mass loss, depression, and

decreased motivation, further diminish self-esteem. These changes negatively affect the frequency and quality of sexual intercourse.

Despite the severity of these effects, cessation of AAS use can often reverse the damage, even after prolonged abuse [11]. Studies reveal that AAS has a contraceptive effect in most previously fertile males within 1–2 years of use. In 95% of cases, sperm parameters return to physiological levels within 12–16 months after discontinuation[26], However, in cases of extended AAS use, recovery may take more than two years [22,27] and in some instances, fertility may not fully return.

The greatest challenge for researchers in this field is the scarcity of longitudinal data. While recovery is possible in many cases, there remains a significant knowledge gap regarding the long-term impact of AAS on fertility.

6. Therapeutic Approaches to Managing AAS-Induced Complications and Infertility

The cornerstone of therapy for complications arising from androgenic-anabolic steroid (AAS) use is the cessation of these substances. In many cases, discontinuation alone is sufficient to resolve adverse effects. However, additional treatment options are often necessary, particularly for more severe or persistent complications. The management of infertility associated with AAS use centers on three primary objectives: harm reduction, pharmacological intervention, and fertility preservation through semen cryopreservation[25]. In certain cases diffrent interventions may also be required, such as surgical intervention of gynecomastia[7].

Harm reduction focuses on educating users and healthcare professionals about the risks and adverse effects of AAS, encouraging dose reduction and motivating users to decrease the frequency of use. Patients should receive tailored support from interdisciplinary teams, with individualized treatment strategies that address varied motivations, consider each patient's specific circumstances, and take their reproductive aspirations into account.

Pharmacological treatments, often forming the basis of post-cycle therapy (PCT), rely on the use of selective estrogen receptor modulators (SERMs, e.g., tamoxifen) to stimulate gonadotropin release, gonadotropins (hCG, FSH) to restore testicular function and prevent atrophy, and aromatase inhibitors (e.g., letrozole) to reduce estrogen levels and counteract

gynecomastia. These therapies aim to restore hormonal balance, reinitiate endogenous testosterone production, and minimize long-term effects of AAS use [28]. However, outcomes remain inconsistent, with studies showing mixed results regarding their efficacy [25].

Testosterone Replacement Therapy (TRT) may be administered to patients who experience significant drops in testosterone levels following the cessation of anabolic androgenic steroids (AAS). This treatment may be suitable for males manifesting severe symptoms of hypogonadism that adversely affect quality of life[29]. When the natural regeneration of the hypothalamic-pituitary-gonadal (HPG) axis is delayed or impaired, TRT can serve as a temporary solution.[7]. However, this approach must be applied cautiously, as it may further suppress endogenous testosterone production by inhibiting gonadotropin secretion, potentially leading to additional complications.

Semen cryopreservation serves as a critical preventative measure against irreversible infertility. It is crucial because of still unpredictable impact of AAS on fertility and the uncertain recovery of reproductive function freezing semen may be the only viable option for some patients to ensure future parenthood. However, a significant challenge is that semen quality parameters rapidly deteriorate during anabolic-androgenic steroid use, making it essential to undertake cryopreservation before initiating a steroid cycle [25].

Current treatment methods often demonstrate limited efficacy, with therapy frequently extending over months or even years. Despite standard treatment protocols, most patients fail to regain full reproductive function within six months of therapy[30]. This highlights the need for continued research and the development of more effective therapeutic strategies.

Summary

The abuse of anabolic-androgenic steroids (AAS) is an increasingly relevant public health issue with significant implications at both individual and societal levels. This literature review highlights the widespread use of AAS for performance enhancement and physical appearance, as well as the significant health risks associated with their misuse. Despite the extensive body of research, several important gaps in our understanding remain, primarily due to methodological limitations in existing studies.

One of the key challenges in studying the effects of AAS is the lack of randomized controlled trials, particularly those involving high doses of AAS. Ethical constraints prevent

the conduct of such trials, limiting the ability to draw definitive conclusions about the long-term effects of AAS at higher doses. Furthermore, longitudinal studies examining the chronic consequences of AAS use are scarce, making it difficult to assess the full extent of their impact on health over extended periods. This lack of long-term data poses significant challenges to both clinicians and researchers working to mitigate the harms associated with AAS abuse.

Another limitation in the field is the widespread occurrence of selection bias in many studies. The heterogeneity of AAS users, including varying motivations, patterns of use, and concurrent substance abuse, means that the findings from existing research often cannot be easily generalized. This variability restricts the ability to form universally applicable recommendations for treatment or harm reduction strategies, further complicating the development of effective public health policies.

The misuse of AAS presents a multifaceted health issue, necessitating an interdisciplinary approach to both prevention and treatment. Given the range of physiological, psychological, and social consequences linked to AAS use, a collaborative effort involving healthcare providers, mental health professionals, and policy makers is critical. In particular, there is an urgent need for better strategies to manage the growing prevalence of AAS abuse, particularly in recreational and non-professional contexts, where usage is often less regulated.

Moreover, the lack of established guidelines for harm reduction remains a significant challenge for healthcare providers. Many AAS users are reluctant to seek medical assistance due to the fear of stigmatization or legal consequences, highlighting the need for a supportive and non-judgmental approach to care. A lack of trust between patients and healthcare professionals further exacerbates the problem, as patients may be unwilling to disclose their AAS use or seek help for associated health issues. Regular health screenings, education about the risks of AAS, and early intervention are critical to reducing the incidence of severe health complications. Additionally, building trust between healthcare providers and AAS users is essential to encourage the discontinuation of steroid use and to foster a more open dialogue about treatment options.

In conclusion, the misuse of AAS remains a significant and complex public health challenge that requires ongoing research and improved medical and societal management strategies. The current evidence base is hindered by methodological flaws, a lack of long-term studies, and challenges in generalizing findings due to selection bias. Addressing the issue of

AAS abuse requires not only enhanced scientific investigation but also comprehensive healthcare interventions that incorporate harm reduction, education, and the development of strategies to foster patient trust and cooperation. Only through a more coordinated and empathetic approach can the health risks associated with AAS abuse be effectively mitigated, leading to better outcomes for those affected.

Disclosure

Authors do not report any disclosures

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All authors have read and agreed with the published version of the manuscript.

Funding statement:

The study did not receive special funding.

Institutional Review Board Statement:

Not applicable.

Informed Consent Statement:

Not applicable.

Data Availability Statement:

Not applicable.

Conflict of Interest Statement:

The authors declare no conflict of interest.

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