A Systematic Review of the Literature on the Connection between Anabolic Steroids and Cardiovascular Risk

Abstract

Anabolic Steroids (AS) are synthetic versions of testosterone produced by pharmaceutical companies to mimic the biological effects of natural testosterone. They are widely used to treat various pathological conditions such as anemia and cachexia. Additionally, steroids are commonly prescribed for patients with autoimmune, respiratory, and inflammatory diseases. However, it has been found that athletes, bodybuilders, and weightlifters often misuse these substances to enhance muscle mass and athletic performance.

The misuse of AS, with overdoses ranging from 50 to 1000 times higher than those used for therapeutic purposes, raises significant concerns about the severe side effects associated with drug abuse. Excessive use of AS is significantly linked to cardiovascular complications, including hypertension, arrhythmias, and hypertrophy. Acute Myocardial Infarction (AMI) is one of the most frequently reported consequences of Anabolic Steroid AS. (1,2) use. The causes of AMI can vary, including Vasospasm, Atherosclerosis, and Hypercoagulability. Therefore, these conditions potentially increase morbidity and mortality, especially when AS is combined with thyroid hormones, growth hormones, or insulin.

The primary aim of this study is to conduct a literature review of previous research regarding the combination of different AS mixtures with other substances that are potentially used for athletic and aesthetic purposes. This review seeks to highlight associations with morbidity and mortality. A total of 20 studies from peer-reviewed journals were analyzed following the PRISMA guidelines to provide a comprehensive understanding of the consequences of AS overdose in enhancing sports performance. Data were extracted from each study, and consensus among the studies was synthesized as part of the results and discussion section.

Keywords: Myocardial infarction, Anabolic Steroids, biological effects

1. Introduction

Myocardial infarction (MI) resulting from drug abuse must be recognized, especially in individuals using anabolic steroids to enhance performance. Adverse effects such as hepatic and endocrine dysfunction and cardiovascular issues have been reported (1). Steroids are widely used, ranging from treatments for medical emergencies and other diseases to their abuse by bodybuilders and athletes. While steroids have various applications, their overuse can lead to serious consequences, including cardiac problems linked to coronary artery disease (CAD), coronary spasm, or other unidentified mechanisms (2). However, other risk factors must also be considered, as they are present in more than 50% of CAD cases.

Anabolic Androgenic Steroids (AAS) are synthetic versions of testosterone that athletes abuse and overdose to strengthen their muscles and improve physical performance. The term "anabolic" refers to the increase in male physical characteristics and muscle mass, which enhances athletic performance (3). AAS are human-made substances that act on androgen receptors and are also widely used in the treatment of metabolic and catabolic disorders. In cases of testosterone deficiency, anabolic steroids can be prescribed for treating chronic diseases. Various manufactured forms exist that support and optimize muscle growth without negatively impacting androgen levels (1).

Anabolic steroids attract the interest of young males obsessed with body image and involved in athletics or recreational exercise. However, their abuse and overdose can lead to severe cardiovascular consequences. The doses taken by athletes can be 5 to 15 times higher than those used for medical purposes. Statistics indicate that 18.4% of recreational users and 13.4% of athletes overdose on anabolic steroids, with 6.4% of males and 1.6% of females affected (2). Additionally, steroid use has increased among adolescents, reaching rates as high as 12% (4). Overdosing on steroids can lead to numerous adverse cardiovascular events, with myocardial infarction and stroke being the most obvious results. Predictors such as ventricular hypertrophy and hypertension are associated with increased mortality and morbidity.

Estimating the true damage caused by steroid overdose is challenging due to ethical restrictions, lack of information, and polypharmacy. Nevertheless, the adverse effects of anabolic steroids are scientifically documented in the literature. For example, anabolic steroids are significantly associated with acute myocardial infarction (1, 4), and several cases of mortality have been reported due to excessive use (6). Literature also confirms a significant correlation between steroid abuse and aggressive behaviors among athletes and bodybuilders. While steroids are widely used for therapeutic treatment, long-term use can lead to toxicity affecting various organs, exposing individuals to symptoms associated with hypertension, liver failure, coronary complications, and prostate cancer (2).

The reasons for abusing AAS can be attributed to a lack of awareness among athletes regarding the physiological risks of overdosing. AAS overdosing can be as high as 50 to 1000 times the therapeutic dosage. Additionally, AAS are often used in combination with other substances, such as testosterone, boldenone, nandrolone, and insulin (4).

Androgen receptors are the main catalysts of the anabolic androgenic effect. These receptors are linked to body tissues and organs through three primary mechanisms: a) direct linkage to the receptor, b) action via estrogen receptors through 5-alpha-reductase, and c) action via dihydrotestosterone produced by the action of 5-alpha-reductase (5). AAS are chemical and pharmacological derivatives of the male hormone testosterone, used to enhance athletic performance. AAS can impair testosterone biosynthesis in the body when taken in supra-physiological doses (3). They are significantly associated with activating androgen receptor signaling in various body tissues.

There are multiple mechanisms describing how AAS work in the body, but the most common involves the administration of testosterone and its synthetic derivatives (6). Under normal physiological levels of testosterone, androgen receptors reach saturation, while AAS can stimulate mechanisms beyond simple receptor activation. Elevated testosterone levels can antagonize glucose synthesis and protein catabolism. Overdoses of AAS can displace glucocorticoids from their receptors (5), which decreases muscle protein, thereby increasing the potential for muscle growth.

AAS usage can be categorized into two directions: supervised and unsupervised. AAS use under medical supervision is familiar within restricted medical practices. However, many athletes not only overdose on AAS but also combine them with other drugs such as alcohol, opioids, cocaine, gamma-

hydroxybutyrate, and marijuana. This combination complicates the accurate identification of side effects associated with overdosing on specific drugs (2).

1.2 Autopsy findings

Literature has reported a variety of consequences associated with anabolic steroid overdose, including sudden cardiac death and coronary artery disease. There is also evidence of extensive myocardial damage due to hypertrophy and small vessel disease. Toxicological investigations, utilizing various screening methods and data analyses of blood, hair, and urine samples, detected stanozolol in hair and nandrolone in blood (5). The predisposition to specific myocardial patterns can lead to sudden cardiac death. An analysis of autopsy cases involving sudden death revealed associations between anabolic steroid use and symptoms such as testicular atrophy, muscle hypertrophy, and gynecomastia. While steroids are widely used for therapeutic purposes, long-term use can result in toxicity affecting several organs, manifesting symptoms such as hypertension, liver failure, coronary complications, and prostate cancer (2).

This study aims to explore the extent to which AASs have been investigated, highlighting conditions across various cases and medical treatments. Analyzing different cases diagnosed with steroid abuse based on a range of symptoms can enhance understanding of the physical and psychological consequences involved.

2. Methodology

Data were collected from eleven different medical studies published in peer-reviewed journals (Table 1). The included scholarly articles focus on steroid overdosing by athletes, bodybuilders, and weightlifters to enhance muscle mass and performance. Data analysis involved both descriptive and contextual approaches, reaching a consensus among the studies. Thematic analysis was also employed to identify key themes and patterns in the text. The PRISMA guidelines are detailed in the following paragraphs.

2.1 Searching strategy

2.1.1 Keywords

A systematic literature review was conducted following PRISMA guidelines (7). In the initial phase of secondary data collection, a number of keywords were identified, including “anabolic steroids,” “myocardial infarction,” “steroids,” “bodybuilder,” “athletics,” “heart disease,” and “cardiovascular.”

Boolean operators were used to combine these keywords, enhancing the search strategy. A total of 215 studies were identified, of which 11 relevant studies were ultimately included.

2.1.2 Databases

The academic databases "PubMed," "Google Scholar," and "Web of Science" were utilized to locate research papers from peer-reviewed journals indexed in Q1 and Q2. These databases were selected for their relevance to medical research and steroid studies. Google Scholar was included to access well-cited research papers in the medical field.

2.2 Selection criteria

Research papers written in English were selected. Inclusion criteria included full-text papers published in peer-reviewed journals. Papers available only as abstracts were excluded, as were those written in languages other than English. Only original research papers were included; communication pieces, reviews, and technical reports were excluded.

2.3 Research quality

All selected papers were reviewed against established quality standards. Sufficient and systematic data collection is considered a high priority for reputable research papers. To maintain overall research quality, only papers published in Q1 and Q2 journals were included in the final list.

Table 1. Studies overviews

Author	**Region**	**Aims**	**Method**	**Results**	**Themes**
Sivalokanathan et al., (2021)	UK	To what extent performance-enhancing drugs mainly caffeine and steroid impact cardiovascular activities.	Literature review	Caffeine has no direct impact on Cardiovascular system. However, Anabolic Steroid failed to negate the adverse consequences that associated it with cardiovascular illnesses.	Caffein and steroid on cardiovascular consequences
Jain and Goel, (2020)	India	Talking a case report of a younger man that struggle out of sever lifted side chase due to overdosing anabolic steroid. CAD disease seems to be for elderly group of population. However, new upward trend of body builder	Case report	There is a significant association between abusing steroid and perceiving cardiovascular consequences. avoidance of taking steroid reduce the risk of Coronary artery diseases CAD.	Steroid on coronary artery diseases.

		increases the possibility of taking proteins, amino acids and steroid to fasten the process of muscles building.			
Johnson et al. (2023)	USA	The abuse of using Anabolic androgenic steroid for better body muscles, physical appearance and sexual function. This report aims to investigate ischemic stroke in a young individual who abuse taking stanozolol and clenbuterol for body builder context.	Case report	By investigating the patient was found that he was consuming testosterone and stanozolol for a number of weeks which leads to left sided weaknesses, ringing in the ear and slurred speech resulting failing in bathroom. Anticoagulant therapy was conducted by giving a heparin drip per cardiac protocol.	Steroid on ischemic stroke
Hernández-Guerra *et al*.(2019)	Spain	Investigating the abuse of Anabolic for a number of 6 months Steroid on a young athlete in a sudden death cases after coming back from a party	Case report	After receiving cardiorespiratory arrest, the forensic autopsy was conducted and the body show the following observations: a) external examination of the body show hypertrophy of muscles, while b) internal examination show cardiomegaly with sever coronary atherosclerosis. B) at histology acute myocardial faction was observed while blood results show existence of ethanol, stanozolol, nandrolone, and testosterone	Impact of Anabolic Android on cardiovascular activities
Heydari et al., (2020)	Iran	Aorta dissection is one of injury caused by having supra physiologic doses of steroid. This happens by weakening the connective tissue. The case of bodybuilder was investigated and all examinations of laboratory exams were conducted	Case report	Findings show that abusing steroid is significantly associated with determinate effect on myocardium. Results also reveal that overdosing steroid for exercising people may lead to aortic dissection.	Steroid on aortic dissection

Gagliano-Jucá and Basaria, (2019)	USA	Investigating the mechanism behind the ergogenic effect of Anabolic Asteroid as using it abusively amongst athletes and those who seeking for improving their body image.	Review	Investigating and reviewing in details endogenic drugs and its testosterone. It is also. Investigating its ability to exert tissue androgenic effects as it binds to androgen receptor. Finding out the verse impact of using AAS on vascular system and overall body health status.	Steroid and its impact on myocardial condition.
Tan *et al.* (2020)	USA	Investigating the overdosing of Anabolic steroid on the young man 25	Case report		
Seara et al. (2020)	Brazil	The aim of this study is to investigate the impact of overdosing Anabolic Steroid on myocardial infarction.	Review	Overdosing AS can have a negative consequence on cardiovascular system including, hypertension, hypertrophy, and arrhythmias. The challenge of reaching the cause of symptom can be due to the combination between steroid and other growth hormones but also taking insulin.	Review on the impact of AS on cardiovascular system.
Favretto et al. (2022)	Italy	To identify the cause of the death for a body builder person who found dead in hotel room	Death cause examination: toxicological investigation/ forensic medical investigation	Abusing steroid leads to death. The measurement of hair analysis leads to better identify the overdosing Anabolic steroid.	overdosing AS
Fadah et al. (2023).	USA	Investigation the supra physiological uses of ASS on cardiomyopathy	Review		
Liu et al. (2019)	China	This study aims to investigate the correlation between abusing AAS and its direct effect on cardiovascular system risks.	Data was collected within a literature review by selecting peer reviewed articles from well-established databases such as PubMed & biotechnology information databases.	There is an association between overdosing AAS and having adverse effects on cardiovascular system. There was consensus amongst studies that cause-effect relationship can be found for those who abuse AAS and developing relevant diseases.	Review on the impact of AS on cardiovascular system.

3. Results

Data were analyzed at two different levels: descriptive data analysis, which includes bibliometric research, and contextual data analysis to reach consensus among the included studies.

3.1 description data analysis

This section presents bibliometric research concerning the years of publication, methodologies, and data collection. The regions where studies were conducted are also highlighted.

3.1.1 country of studies

Based on our inclusion criteria, the UK shows a higher interest in investigating steroid abuse cases (36%), while cases in the USA, Spain, Iran, India, Italy, and China are less frequently studied. These findings indicate that steroid abuse is a significant area for medical research, as many athletes use steroids to enhance performance and for display purposes.

3.1.3 Research year of publication

Academicians and researchers have shown increasing interest in steroids over the last century, and this trend continues recently. The included studies were published within the last five years, reflecting the ongoing issue of steroid overdosing among bodybuilders and athletes. This situation underscores the confirmed negative medical consequences and mortality rates associated with steroid abuse, adding further responsibilities for healthcare services to investigate and provide abusers with appropriate guidelines.

3.1.4 Research methods for selected study

Research on steroid abuse typically follows a specific structure concerning data collection. It was found that studies often identify specific case reports, providing detailed information on symptoms and medical treatment. Analyzing individual cases facilitates a deeper understanding of each situation, allowing for comparisons of similarities and differences, which can help develop standardized medical guidelines for treatment. Additionally, some research gathered data through literature reviews. A combination of case reports and literature reviews was also noted as a common research design in steroid studies.

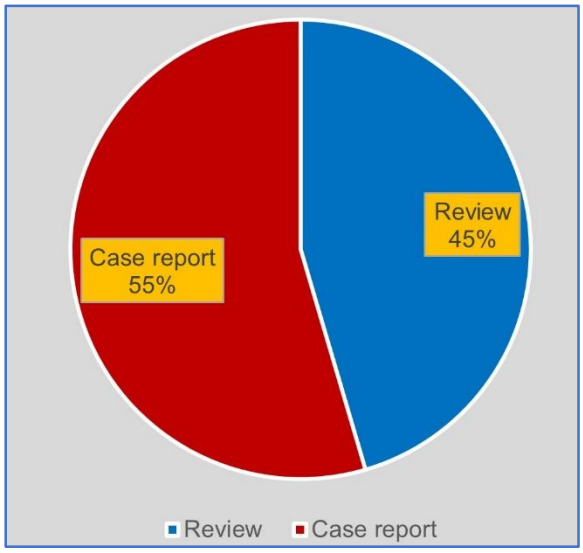

Fig1. Research methods and data collection (n=11)

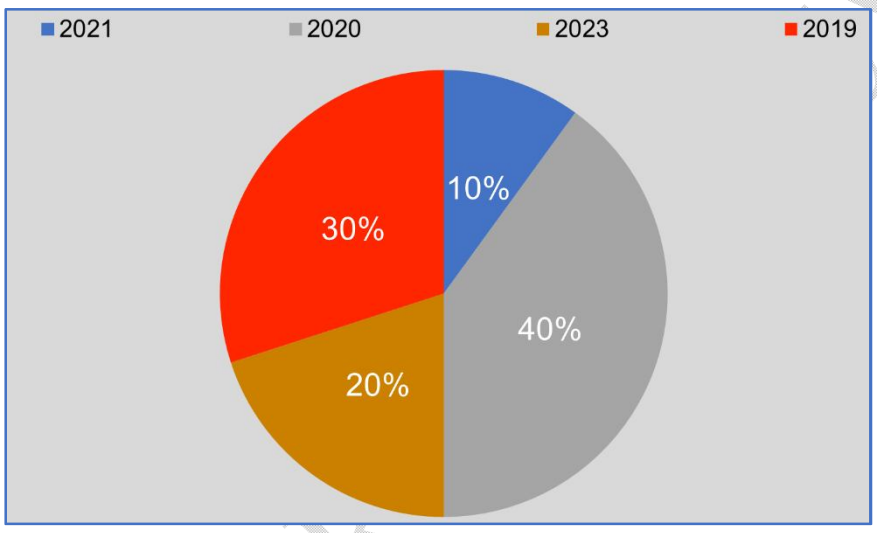

Fig2. Studies by published year (N=11)

3.2 Contextual data analysis

Studies provide numerous insights into the adverse consequences of anabolic steroid overdosing, as well as various medical treatments.

3.2.1 UK context

In a comparative study examining the impact of steroids and caffeine on cardiovascular disease and sudden death due to overdosing (8), it was found that while caffeine does not alter myocardial structure, steroids cause significant changes. Cardiovascular alterations include elevated blood pressure and myocardial toxicity, which are associated with impaired ventricular function and arterial thrombosis.

While caffeine has no direct impact on the cardiovascular system, anabolic steroids fail to mitigate the adverse consequences linked to cardiovascular illnesses.

3.2.3 India context

Regarding steroids and coronary artery disease, a case report highlighted a young man who experienced severe left-sided chest pain due to anabolic steroid overdosing. Coronary artery disease (CAD) is typically associated with older populations; however, the rising trend among bodybuilders increases the likelihood of using proteins, amino acids, and steroids to expedite muscle building. There is a significant association between steroid abuse and cardiovascular consequences, and avoiding steroid use can reduce the risk of CAD (9).

3.2.4 USA context

In another case report from the USA, a young individual presented with severe left-sided chest pain and was admitted to the emergency unit for 20 minutes. His medical history revealed the abuse of anabolic steroids. This trend among young people to enhance body image leads to the unsupervised use of anabolic steroids and various synthetic supplements (14). In a related investigation linking steroids to ischemic stroke, the report focused on a young individual who abused stanozolol and clenbuterol. After several weeks of consuming testosterone and stanozolol, he exhibited left-sided weakness, tinnitus, and slurred speech (10).

Research into the mechanisms behind the ergogenic effects of anabolic steroids has examined how their abusive use among athletes impacts body image. Studies have explored endogenous drugs and their testosterone-like effects, highlighting the significant impact of anabolic steroids on the vascular system and overall health (13, 15).

3.2.5 Spain context

Investigating the impact of anabolic steroids on cardiovascular health, a case study reported on a young athlete who suffered sudden death after returning from a party following six months of steroid abuse. After experiencing cardiorespiratory arrest, a forensic autopsy revealed: a) external examination showing muscle hypertrophy, and b) internal examination indicating cardiomegaly with severe coronary atherosclerosis. Histological analysis confirmed acute myocardial infarction, while blood tests indicated the presence of ethanol, stanozolol, nandrolone, and testosterone (11).

3.2.6 Iran context

Aortic dissection can result from the use of supra-physiological doses of steroids, which weaken connective tissue. A case involving a bodybuilder was investigated, and laboratory examinations revealed significant associations between steroid abuse and detrimental effects on the myocardium. Results indicated that steroid overdosing in athletes may lead to aortic dissection, with symptoms including retrosternal pain lasting more than 30 minutes, anxiety, cold sweats, and delirium. Treatment involved administering nitroglycerin for angina relief, performing sternotomy, and removing a large hematoma. Post-operation, the patient was weaned off inotropic drugs. The concurrent use of steroids, growth hormones, and testosterone for bodybuilding purposes was noted (12).

3.2.7 Brazil context

A review investigating the impact of anabolic steroids on the cardiovascular system aimed to assess the consequences of overdosing on myocardial infarction. The findings indicated that steroid overdosing can lead to negative cardiovascular outcomes, including hypertension, hypertrophy, and arrhythmias. The challenge in identifying the root causes of symptoms may stem from the combination of steroids with other growth hormones and insulin (4).

3.2.8 Italy context

In an investigation to determine the cause of death of a bodybuilder found dead in a hotel room, steroid abuse was identified as a contributing factor. Hair analysis provided insights into the overdosing of anabolic steroids, revealing the presence of clenbuterol (a long-acting selective beta-2 agonist) with levels of 1 ng/ml in blood, 1 ng/ml in urine, and 25 pg/mg in hair. Laboratory tests conducted on urine, blood, and hair included gas chromatography-mass spectrometry (GC-MS), liquid chromatography-high-resolution mass spectrometry (LC-HRMS), and liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). Results showed steroid levels of 202 ng/ml in urine and a positive testosterone result (T/E = 11) (2).

3.2.9 China context

This study aims to investigate the correlation between anabolic androgenic steroid (AAS) abuse and its direct effects on cardiovascular risk. Data were collected through a literature review of peer-reviewed articles from established databases such as PubMed and biotechnology information databases. There is a consensus among studies that a cause-and-effect relationship exists between AAS abuse and the development of relevant diseases (16).

4.Discussion

The results reveal several adverse cardiovascular events caused by anabolic steroid overdosing. These consequences include hypertension, left ventricular hypertrophy, and cardiomegaly. Such changes and remodeling of the cardiovascular system can be observed through various indicators, such as alterations in lipid profiles, myocardial toxicity, venous thrombosis, and reductions in ventricular function (14). Arrhythmias are another significant consequence of anabolic steroid abuse. Reporting these results in a broad study is challenging due to issues of standardization and variations in study conditions. Studies have indicated that the direct impacts of steroids include fibrosis and left ventricular hypertrophy (3, 9). Additionally, it is challenging to measure the sole effects of steroids versus their combination with other illicit drugs. One major challenge in investigating the athlete's heart is determining whether reduced left ventricular function is due to exercise or anabolic steroid overdosing. Moreover, risk factors for not taking steroids, such as hypogonadism and depression, can drive steroid addiction. However, addiction to steroids increases the risks of hypertension and insulin resistance (16).

Abusing anabolic androgenic steroids can adversely affect various body organs and systems, including musculoskeletal, cardiovascular, hepatic, neuroendocrine, and dermatologic systems. In terms of the musculoskeletal system, it has been reported that steroid abuse can lead to a nine-fold enlargement of body tendons, as well as increased skeletal muscle mass and strength. Androgen receptors directly impact the myocardium and vascular muscles. The safety of cardiovascular physiology under physiological testosterone levels remains controversial (4, 17, 18). Adverse cardiovascular effects include a higher risk of arrhythmias, hypertension, myocardial dysfunction, and impaired systolic and diastolic function. Regarding hepatic health, supra-physiological doses of steroids have been shown to elevate hepatic enzymes. The duration of 17α-alkylated AAS can lead to hepatotoxicity. Neuropsychiatric effects include increased aggressive behavior associated with androgen withdrawal, with reports of suicidal attempts as a consequence. Additionally, dermatological symptoms such as acne vulgaris and folliculitis are commonly observed in those who overdose on steroids (16, 18, 19, 20).

Several arguments and questions remain open in the majority of the analyzed studies that should inform future research. For instance, most studies on steroid abuse have been conducted as case reports rather than formal epidemiological research, raising concerns about the accuracy and integrity of the results. Individuals who overdose on steroids often consume various other substances, making it challenging to attribute adverse consequences or deaths solely to steroid abuse (2). Supra-physiological

doses of AAS have been confirmed to significantly associate with left ventricular failure; however, studies examining the impact of AAS on the right ventricle remain limited (2, 12, 14).

Research indicates several risk factors associated with anabolic steroid overdosing. AAS toxicity can significantly exceed therapeutic levels, increasing the risk of complications from taking multiple steroids in cycles. Blood pressure elevation is another risk reported in studies. Abusing AAS can lead to elevated blood pressure, known as hypertension, due to sodium and water retention, along with the development of angiotensin in blood vessels. Elevated blood pressure places physical strain on the heart and arteries (13, 16, 21), increasing the likelihood of heart attack and cardiovascular diseases. Dyslipidemia is another well-recognized adverse effect of steroid overdosing, characterized by changes in lipid profiles and increased levels of low-density lipoprotein (LDL) cholesterol, potentially leading to coronary artery disease. Additionally, heart rhythm disturbances are risks associated with injecting steroids from unreliable sources (4). Metabolic effects are significantly linked to cardiovascular diseases, highlighting the need for AAS use to be under medical supervision with the lowest effective doses. For individuals who have previously used steroids, a personalized cardiovascular disease prevention plan must be considered.

5.Conclusion

Overdosing on steroids among bodybuilders and athletes poses significant risks for cardiovascular diseases. The misuse of steroids can lead to serious adverse effects, including increased blood pressure, heart rhythm disturbances, cholesterol imbalances, and overall cardiovascular diseases. The literature reveals a variety of symptoms treated through uncommon medical interventions. Ongoing debates surround steroid use for improving athletic performance, particularly regarding dosage, source, duration, developed symptoms, and whether these symptoms arise from pure steroid use or from combinations with other substances. Future research should conduct longitudinal studies across different generations to observe changes in steroid consumption, associated needs, behaviors, and psychological circumstances.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

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