DET PSYKOLOGISKE FAKULTET

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Lifetime Prevalence, Correlates, and Sequelae of Anabolic-Androgenic Steroid Dependence: A Meta-Analysis, Meta-Regression Analysis, and Meta-Synthesis

Hovedoppgave
Profesjonsstudiet i psykologi

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Vår 2023

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Acknowledgements

First and foremost, I would like to take this opportunity to express my gratitude to my supervisor, Dominic Sagoe. I could not have asked for a more dedicated, supportive, and encouraging person to open my eyes for this important subject and guide me through this process. I would also like to thank my parents, always encouraging me to make my own path in life, while at the same time being a phone call away and showing interest in the things I do. Additionally, I want to express my appreciation for my hometown girls, Matilde, Vilde and Maria, for being there through all these years and making life brighter. To Pia, Cecilie and Anita, thank you for being my go-to partners in what has felt like an endless amount of group work assignments, and making these past six years the best they could be. To Elise, for being my much beloved housemate, offering endless amounts of laughter, comfort and always matching my mood. Finally, a special thanks to Anita, for all your authenticity, exceptional humor, and love.

Sammendrag

Tidligere litteratur på forekomst av avhengighet til anabole androgene steroider (AAS) har vært usystematiske og mangler generaliserbarhet. Denne studien retter seg mot å undersøke global livstidsprevalens, korrelater og sekvele av AAS-avhengighet gjennom å utføre en meta-analyse, en metaregresjonsanalyse, og en metasyntese basert på et systematisk litteratursøk i Google Scholar, ISO Web of science, PsycNET og PubMed. Tjuefem studier ble inkludert i litteraturgjennomgangen og sytten studier i metaanalysen. Cochrans Q og I^2 statistikk ble brukt for å vurdere heterogenitet. I meta-analysen av helhetlig forekomst av avhengighet ble en random-effekt-modell brukt, og publikasjonsbias ble analysert ved bruk av Eggers test. Resultatene viste en helhetlig livstidsprevalens av avhengighet på 36.0% (95% CI: 29.1–43.4, $Q = 102.6$, $I^2 = 84.4$, $p < .001$). Det ble ikke funnet publikasjonsbias. Nord-Amerika og Oceania var assosiert med lavere prevalens sammenlignet med Europa, avhengighetsmål som brukte intervjuer var assosiert med høyere prevalens sammenlignet med spørreskjema, og publikasjoner fra 1990–1999 var assosiert med høyere forekomst sammenlignet med de fra 2000–2009 og 2010–2023. AAS-avhengige var assosiert med flere demografiske, biofysiologiske, kognitive, emosjonelle og psykososiale problemer sammenlignet med ikke-avhengige og personer som ikke bruker AAS, som understreker at dette er en neglisjert global helseutfordring som fordrer målrettede tiltak.

Nøkkelord: anabole-androgene steroider; avhengighet; meta-analyse; prevalens; sekvele

Abstract

Previous estimation literature reviews on AAS dependence are unsystematic and lack generalizability. The present study investigates the global lifetime prevalence, correlates, and sequelae of AAS dependence. A meta-analysis, meta-regression analysis, and a meta-synthesis were conducted based on a systematic literature search in Google Scholar, ISO Web of science, PsycNET, and PubMed. Twenty-five studies were included in the review and 17 in the meta-analysis. Cochran's Q and the I^2 statistic were used to assess heterogeneity. A random-effects model was used in the dependence prevalence meta-analysis, and publication bias was tested using Egger's test. Results show an overall lifetime AAS dependence prevalence of 36.0% (95% CI: 29.1–43.4, $Q = 102.6$, $I^2 = 84.4$, $p < .001$). There was no publication bias. North America and Oceania were associated with lower dependence prevalence compared to Europe, interview-based assessment was associated with higher prevalence compared to questionnaires, and 1990–1999 publications were associated with a higher prevalence compared to 2000–2009 and 2010–2023 publications. Dependents were associated with a wide array of demographic issues, and biophysical, cognitive, emotional, and psychosocial problems compared to nonusers and nondependents. AAS use and dependence should be considered a serious public health issue requiring targeted health interventions.

Keywords: anabolic-androgenic steroids; dependence; meta-analysis; prevalence; sequelae

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Anabolic-androgenic steroids

Anabolic-androgenic steroids (AAS) are a group of hormones synthetically derived from the natural male hormone testosterone, producing similar effects on the body. They involve anabolic effects referring to muscle-building, and androgenic effects known as masculinizing (Bond et al., 2022). By stimulating protein synthesis, AAS facilitate muscle-building and muscularity. AAS were initially developed for clinical purposes, primarily to treat hypogonadism, a condition involving insufficient production of testosterone, affecting development and sexual functioning among other bodily functions. They have since been used to treat other conditions, such as breast cancer and anaemia (Barceloux & Palmer, 2013). The masculinizing and muscle-building properties of AAS have led to the use of these drugs for non-medical purposes. From the 1960s, they became widely used non-medically, as is the focus of the present study, for performance enhancement in sports, and their use among elite athletic and bodybuilding communities has received research and media attention for decades (Cohen et al., 2007).

AAS can be administered orally, by intramuscular injections or through transdermal patches or creams, possibly reaching physiological androgen concentrations of 100 times the natural levels for adult males (Wood, 2004). Furthermore, it is common for users to combine several steroids, a practice called “stacking”. Typically, users self-administer AAS in “cycles” involving administering for 8–16 weeks followed by time intervals without using. Administering AAS in a cycle where the dosage increases and decreases, so-called pyramiding, is intended to help the user avoid developing tolerance and possible adverse side-effects and restore natural testosterone production (Kanayama et al., 2009).

Prevalence and correlates of AAS use

The use of drugs as a method of enhancing performance is not new, with records reaching at least back to the ancient Greeks and Roman gladiators (Barceloux & Palmer,

2013). Despite potential risks and AAS being illegal in several countries, a global meta-analysis and meta-regression study conducted by Sagoe et al. (2014b) found an estimated global lifetime prevalence of 3.3%. They also found a significant gender gap in the study, with an overall lifetime prevalence rate for men being 6.4% compared to 1.6% for women. The study found that the largest group of users are people involved in recreational sports and athletes. Thus, over the last four decades, the general public, more specifically the recreational exercisers and athletes, appear to represent the majority of users. Furthermore, the trend seems to involve AAS use for muscle-building and cosmetic purposes in contrast to performance enhancement (Barceloux & Palmer, 2013; Cohen et al., 2007; Ip et al., 2011; Kanayama et al., 2009; Sagoe et al., 2014b).

The literature has described common features among AAS users based on the accumulated research. A systematic review and synthesis of qualitative research by Sagoe et al. (2014a) found that AAS users usually initiate use before the age of 30 and commonly have a history of mental illness, such as affective disorders, and previous body image issues. Furthermore, they found specifically power sports such as weightlifting and bodybuilding to be common preceding initial use, along with other sports, and that a majority of users obtained their initial AAS dosage from the illicit market and their surrounding social network (Sagoe et al., 2014a). Moreover, Sagoe et al. (2014a) investigated the reported motives for the initial use, finding that enhancing appearance, muscle mass or strength and performance were the motivational factors of most prominence.

Harmful effects of AAS use

AAS use, especially long-term use, has been associated with several health-related risks of various degrees of severity, ranging from skin conditions to heightened cardiovascular morbidity and heightened mortality rate (Bond et al., 2022). Many of the known negative medical effects associated with AAS use are temporary, associated with

ongoing use, and often not of a severity putting users off the drugs (Pope & Kanayama, 2012). Some examples of such conditions are gynecomastia, acne and hypertension.

There are however, known adverse medical effects of more severe kinds, leading to long-term issues for some individuals. There have been found rare cases of hepatotoxicity caused by orally ingested AAS, which in serious cases can include liver cancer (Hardt et al., 2012; Stoot et al., 2010; Woodward et al., 2019). Some long-term AAS users experience chronic hypogonadism after they have stopped using, which can be both physically and psychologically straining (Albano et al., 2021; Rahnema et al., 2014). Furthermore, AAS use could be involved in developing permanent kidney disease for some users (El-Reshaid et al, 2018; Herlitz et al., 2010). The most prominent long-term risk in the accumulated literature, however, is the possible adverse effects on the cardiovascular system, which has been linked to conditions such as fibrosis, dyslipidaemia, myocardial damage, increased risk of thrombosis and myocardial infarctions (Albano et al., 2021; Kanayama et al., 2020; Pope & Kanayama, 2012).

The literature also describes negative psychological effects linked to AAS use. The common findings are mood-related conditions, such as depressive symptoms experienced when off the AAS, and manic symptoms when administering the drugs (Kanayama et al., 2020). Other types of psychological effects that has been associated with AAS is behavioural problems related to aggression and violence, AAS dependence, body image issues and developing new kinds of substance misuse (Chegeni et al., 2021a, 2021b; Hauger et al., 2021; Kanayama et al., 2020; Pope & Kanayama, 2012).

AAS dependence

Previously, the concept of addiction was commonly associated with drugs, where the specific drug induces a ‘high’ or experience of wellbeing when administered, which the user will crave and build a tolerance for, and then experience physiological withdrawal symptoms

when the effect wears off, creating a vicious cycle. However, a growing amount of literature has added to such narrow biological definitions and a growing number of behaviours are now included in what is viewed as potentially addictive within a biopsychosocial framework (Becona, 2018; Chamberlain et al., 2016; Griffiths, 2005). The definition of dependence has been the subject of debate for a long time, and how it is conceptualized has implications for the attention and research a substance or behaviour will receive. Adding the construct of behavioural addictions to research and to the diagnostic manual, such as gambling addiction in the DSM-V, has contributed to the development of further treatment options for previously overlooked addictions (Chamberlain et al., 2016). Thus, how addiction is conceptualized can determine who receives research and clinical attention, which is of great consequence for individual groups, including people struggling with addiction and their loved ones, health care workers, researchers and in consideration of a public health perspective in prevention work and treatment (Griffiths, 2005).

It is common for users of AAS to administer a small number of cycles during a lifetime. However, some of them develop a pattern of use over time where they administer the drugs almost continuously, despite experiencing negative social, physical, and psychological effects (Kanayama et al. 2009). These kinds of cases started showing up in the literature during the 1980's, which led researchers to investigate if AAS dependence could be in line with the criteria for a diagnosis of substance dependence according to the definitions of the Diagnostic and Statistical Manual(s) of Mental Disorders (DSM-III and DSM-IV) at the time (Kanayama et al., 2009; Kirkwood, 2017). In a review of the AAS literature, Kirkwood (2017, p. 2) denotes and discusses the validity of dependence according to elements typical for people experiencing drug addiction: "1) Compulsive engagement with the behaviour, a preoccupation with it; 2) Impaired control over the behaviour; 3) Persistence

or relapse despite evidence of harm and; 4) Dissatisfaction, irritability or intense craving when the object – be it a drug, activity or other goal – is not immediately available".

In his review, Kirkwood (2017) posits that AAS users show patterns in line with the elements mentioned above. Some of the relevant features are increased use with less control in relation to cycling, the lack of willingness to stop using despite negative effects and risk of punishment, and craving intensity experience similar to people addicted to substances known to be mildly reinforcing, however known to be difficult to quit, like nicotine (Kirkwood, 2017; Wood, 2004). Moreover, Kirkwood (2017) summarizes that the literature has found that users describe a subjective feeling of pleasure when using after long-term use, which indicates a positive reinforcement present. Furthermore, former AAS users report withdrawal symptoms like depression and experiencing cravings to use again when quitting. The experience of losing the muscle mass and gain bodyfat also appear to prevent willingness to quit (Kirkwood, 2017).

Animal studies have also given support to the potential of developing AAS dependence. Hamsters have been shown to self-administer testosterone in fatal amounts, and they also show symptoms following testosterone intoxication similar to features normally associated with opioids (Kanayama et al., 2009; Wood, 2006). Moreover, rats and mice have been demonstrated experiencing AAS as rewarding also when it's not in combination with exercise and fitness, finding that they will prefer to spend time in the same surroundings where they have been administered AAS (Alexander et al., 1994; Arnedo et al., 2000;). It's important to note that findings have not been found consistent across different species of animals (Kanayama et al., 2009).

AAS dependence has until more recently been proven difficult to structurally assess and diagnose, especially considering how the standard criteria for substance dependence according to DSM-IV-TR were developed for substances with more intoxicating and

immediately rewarding effects, such as stimulants and hallucinogens, which has been less prominent with AAS use (Piacentino et al., 2015). Furthermore, AAS users can usually keep up a reasonable daily functioning compared to more typical substances associated with addiction (Kanayama et al., 2009; Piacentino et al., 2015).

However, the literature indicates that a subgroup of AAS-users report experiencing several symptoms usually associated with dependence, which has led researchers to conduct studies during the past couple decades where they have applied criteria or modifications of the criteria according to DSM-III and DSM-IV to investigate AAS dependence. A set of diagnostic criteria for AAS dependence specifically has been proposed, which is modified and adapted to AAS use, but based on the DSM-IV substance-dependence criteria, and a structured interview module based on these criteria called AAS Interview Module has been developed (Pope et al., 2010).

DSM-V recommends applying the code for "other substance use disorder" when diagnosing AAS dependence (American Psychiatric association [APA], 2013), which describes a psychological disorder where use of a substance continues, despite the user being aware that it's causing harm. The user has to experience at least two of the criteria for minimum a period of 12 months, to meet the criteria for a diagnosis (Piacentino et al., 2015). The ICD-10 codes AAS and hormone use in the "Abuse of non-psychoactive substances" section and argues that there is a lack of dependence or withdrawal symptoms in comparison to those found in users of psychoactive substances (World Health Organization, 1993).

In summarizing seven studies conducted between 1991 and 2005, Kanayama et al. (2009) estimated a prevalence of about 30% of dependence among AAS users. Furthermore, a study investigated the prevalence of AAS dependence in the United States, using the data from studies applying DSM-III-R or DSM-IV criteria to diagnose AAS dependence (Pope et al., 2014). Collectively, the pooled studies included 1,247 AAS users, and the authors

estimated a 30% lifetime prevalence of AAS dependence. It is noteworthy that both studies (Kanayama et al., 2009; Pope et al., 2014) are characterized by a lack of systematic literature search and selection process, whereas the study by Pope et al. (2014) included only American samples.

Theories of AAS dependence

A components model of AAS dependence

Griffiths (2005) suggests that there are specific components common for all addictions, and that all these must be present to define a behaviour as such. This is specifically to ensure differentiating between healthy enthusiasm that might be quite preoccupying, but without causing any significant damage, compared to a behaviour that negatively affects the individual's quality of life and/or their surroundings. The five components are salience, mood modification, tolerance, withdrawal symptoms, conflict, and relapse.

First, there is the component of 'salience' which typically involves the individual becoming preoccupied with AAS. Some kinds of behaviours or substances are available most of the time, and the salience might not be as prominent until its unavailable. Users might be preoccupied with how to afford, get hold of the drugs or organizing their life to fit in with their use, but might not be constantly thinking about using or the experience of using unless they for some reason have to cut back.

Second, there is 'mood modification' which consists of what the individual experiences acutely associated with the behaviour or a substance, for example feeling relaxed or a 'high'. The lack of these kinds of experiences associated with AAS use has been used as an argument for considering AAS to be less addictive than other substances of abuse Kirkwood, 2017). However, as previously mentioned, some long-term users experience feelings of well-being when administering the AAS. Furthermore, the experience of positive

expectations considering the purpose of using (e.g., increase muscle mass) could give a positive and reinforcing experience associated with using.

A third component is that of 'tolerance' meaning that the person experiences a need to increase the drug dosage or amount of behaviour to experience the initial effects. Behaviourally, this could also involve increasing risk. In AAS users this seems to involve continuous use despite adverse side effects, with less off-cycles, seeking increased results, and by doing so increasing the risk of further and more serious negative side effects.

The fourth component of AAS dependence, in terms of the components model, is 'withdrawal symptoms', involving negative effects following discontinuing or reducing the use. Withdrawal symptoms can be physiological, such as feeling nauseated, insomnia or excessive sweating, or they can be psychological, for instance experiencing irritability or mood changes. Withdrawal symptoms reported in relation to long-term use of AAS are for instance depressed mood, headaches, nausea, hypogonadism and decreased libido (Albano et al., 2021; Kanayama et al., 2020; Sharma et al., 2022).

The fifth component, 'conflict', which can refer to interpersonal conflict between the person struggling with the AAS dependence and people in their surroundings, or it can refer to an intrapsychic conflict, which is an internal conflict within the person related to the use. Experiences of increased aggression with ongoing use or irritability when discontinuing use could contribute to such conflicts. Furthermore, there is commonly an experience of stigma related to AAS use (Harvey et al., 2019). This could contribute to intrapsychic conflicts.

The sixth, and final, component is 'relapse', referring to how people suffering from addiction tend to repeatedly fall back to their previous behaviour patterns, and often quickly restore the use or behaviour amount of their most extreme point of addiction, even after years of perceived control. In relation to AAS use, it is reasonable that the distressing withdrawal symptoms delineated in the fourth component sometimes triggers relapse. In a recent study of

health professionals treating AAS-using patients, most respondents expected AAS use relapse in 60–90% of patients (Al Hashimi et al., 2023).

A body image model of AAS dependence

Considering the common characteristics of AAS users and the accumulated research on motivation for initial use mostly being related to physical attractiveness and strength, it is reasonable that AAS is tempting in a societal context where people experience physical fitness and a muscular appearance to be of great social importance (Sagoe, 2014). This makes AAS dependence quite different from other kinds of substance misuse, and it has been suggested that AAS are primary reinforcing because of the muscle-active effects, as opposed to acute rewarding psychoactive effects (Brower, 2002).

The use of AAS has been hypothesized to be linked to psychological disorders relating to body image, such as muscle dysmorphia. This is a disorder where the individual will have a subjective experience of being smaller and weaker than they actually are, sometimes referred to as “reverse anorexia nervosa” (Kanayama et al., 2010). Considering the accumulated amount of research finding that common motivational factors of initial use is enhancement of physical appearance and strength, body image issues seem to be implicated as an important factor. This also appears to be supported by the fact that the male gender is particularly at risk for AAS use and dependence, whereas it is unusual for women to seek to attain the body type associated with use and the corresponding masculinizing effects (Kanayama et al., 2018; Sagoe et al., 2014a). Furthermore, qualitative research has found situational contexts, commonly the gym, to be one of the situations where young men experience both positive experiences and discomfort relating to their body due to comparison to others and the corresponding thoughts about their appearance (Lamarche et al., 2018). Considering the common engagement of recreational sport, and more specifically power

sports, within the AAS user group, the impact of the cultural context of the gym could be a significant factor involved in initial use and self-evaluation.

The literature and research indeed provide support for this hypothesis, by reporting that a negative body image and/or symptoms of muscle dysmorphia often precede initial AAS use and are common among users (Kanayama et al., 2018; Piacentino et al., 2015; Pope et al., 2012; Sagoe et al., 2014a). Considering the mechanism of a subjective assessment and experience of being less muscular in the context of muscle dysmorphia, it is unlikely that the symptoms of the disorder automatically will be reduced after achieving effects from AAS, which could be involved in the development of AAS dependence where users show increased and continuous use despite the associated adverse consequences and risks. The observations of motivation for initial AAS use being for the musclebuilding and body enhancing properties led to attempts to describe the effect AAS has on muscle mass and on a neurological level and how this relates to why some individuals experience dependence (Brower, 2002).

To attain a large muscle mass, the individual is required to be dedicated to frequent and intensive exercise, usually weightlifting, and they also usually have to be excessively mindful of their diets. When this lifestyle is combined with AAS, the users will still maintain structured and goal-directed, which usually differs from people with other kinds of substance dependencies. At this stage, the user will be preoccupied with AAS mostly because of the effects they have on physical fitness, and the use is characterized by compulsive patterns corresponding with intensive exercise and corresponding lifestyle (Brower, 2002). For some users, the AAS journey ends here, for example if the body goal is no longer relevant, such as retiring from body building, seeking other interests or a change in priorities.

However, as mentioned initially, some individuals continue the use, increasing the dosage and decrease the time off the drugs. Chronic high-dosage use increases the risk for several adverse side-effects, but also the possibility for psychoactive effects which could be a

reinforcing factor for use (Brower, 2002; Cafri et al., 2005; Kirkwood, 2017). Animal studies have indeed provided some support for the hypothesis that AAS, administered as supraphysiological doses, affect the reward systems in the central nervous system (Alexander et al., 1995; Arnedo et al., 2000; Kanayama et al., 2009; Wood, 2006), and as previously mentioned, long-term users have reported experiencing rewarding sensations when administering the drugs.

The observation of these two stages in a subgroup of AAS users, led to a two-stage model of AAS dependence, where stage 1 involves the user administering supraphysiological dosages of AAS predominately to gain muscle mass in combination with a regimen of intense exercise and strict dieting. Even though this stage is commonly strict and structured, the lifestyle is time consuming and although the individual experiences physical, psychological and/or social problems, the AAS use will continue. If the use is discontinued, in the second stage, the user can experience symptoms of withdrawal such as depressed mood and crave to start using again, especially if they experience losing the muscle mass they've gained (Albano et al., 2021; Brower et al., 2002; Kanayama et al., 2020; Sharma et al., 2022).

Allostatic model of AAS dependence

Allostasis is the body's process to maintain homeostasis, engaging the necessary physiologic systems to adapt to environmental stress (Romero et al., 2009). The consequence of engaging these systems to maintain this state over time is called allostatic load (Hildebrandt et al., 2011). When the body must keep adapting for long periods of time, the allostatic load will increase in a cumulative fashion, and so will the risk for allostatic overload, possibly leading to adverse physiological and/or psychological effects. This could lead to a failure to adapt to the environment and maintain a homeostatic state and has been linked to conditions such as post-traumatic stress disorder (George et al., 2012). Summarized, these processes can account for the effects of long-term stress, and they have been applied

when understanding how the body adapts physiologically in the context of substance addiction in relation to the motivation-reward system within the central nervous system (George et al., 2012; Hildebrandt et al., 2011; Koob & Le Moal, 2001; McEwen & Wingfield, 2003).

In the context of traditional drug use, allostasis is associated with maintaining stability in the motivation-reward system based on the opponent-process theory of motivation (George et al., 2012; Solomon & Corbit, 1974). This model describes that with repeated experiences of opposing hedonic states, meaning aversive or pleasant states, the central nervous system will adapt to reduce said hedonic state. In relation to typical drug use, there will be an experience of immediate pleasure which will produce a biological response, but then an opposing process with further repeated exposure to the substance will happen, producing a state similar to withdrawal, which reduces the acute effects, and a drug tolerance develops (George et al., 2012; Hildebrandt et al., 2011).

The nucleus acumbens is known to be involved in experiences of reward and motivation and plays a role in mediating the experience of reward in relation to both natural behaviors and behavior related to drug use and addiction (Carlezon & Thomas, 2009). Animal studies suggest that changes in opiate peptides or increased extracellular dopamine in the ventral tegmental area or nucleus acumbens could be involved in the reinforcing effects of typical drugs of abuse, and that the same neurotransmitters and others involved in the positive reinforcement will decrease during withdrawal in abstinence leading to adverse experiences, such as anxiety and dysphoria, and involves a physiological stress response associated with changes in related neurotransmitters such as norepinephrine (Hildebrandt et al., 2011; Koob, 1992).

It is during this withdrawal process where the antireward process is introduced, which involves the hypothalamic-pituitary-andrenal (HPA) axis engaging to reduce the hedonic

state, lowering the set point of reward and thus the ability to experience pleasure, leading to less pleasurable effects from the drugs, and increased discomfort associated with abstinence from them (Hildebrandt et al., 2011; Koob & Le Moal, 1997). The person will then develop increasing preoccupation with the drug and experience an addiction because of the change in set point of reward, which involves increased substance use, tolerance and stronger withdrawal symptoms, and eventually to a pattern of use driven by negative reinforcement. This process is also influenced by individual factors such as the environment and genetic predisposition, and the type of drug used (Le Moal, 2009). Summarized, the allostatic model insinuates that addiction involves a change in motivations for use, moving from positive reinforcement, where the person is seeking the immediate rewards of the drug, to negative enforcement, where the user is avoiding or relieving adverse effects of abstinence.

AAS however, are not used for the typical acute effects associated with traditional drug use. Rather, the users appear to seek the effect they have on the hypothalamic-pituitary axis and the musculoskeletal system (Sagoe et al., 2014a), while the effects on the motivation-reward system seems to be of secondary value. In this context, allostasis could be best defined as the process in which physiological systems are engaged to maintain adaptive stability in the hypothalamic-pituitary-gonadal (HPG) and HPA axes (Hildebrandt et al., 2011). The allostatic process in AAS use is based on exercise and drug administration in an attempt to improve appearance and strength. For this reason, it is argued that AAS use starts off as an attempt to affect mood states related to body satisfaction, or more specifically a lack thereof. AAS users usually have an intense exercise regimen preceding initial use, and it has been proposed that AAS use has increased in connection to increasing body image issues among males (Goldman et al., 2019). This could imply that the individuals initiating AAS have a low hedonic state preceding use (Hildebrandt et al., 2011). Simultaneously, exercise is associated with positive mood (Helfer et al., 2015), and therefore heightened hedonic states,

which could contradict this hypothesis. The allostatic model, however, gives an account for how the physiology of these behaviors are connected.

Exercise is, as mentioned previously, associated with positive effects. Physiologically it is a form of functional stress giving adaptive neuroendocrine and hormonal effects which can serve as protecting factors from aversive consequences associated with chronic stress (Tsatsoulis & Fountoulakis, 2006). The opponent-process model relevant to exercise describes the initial increase in stress hormones to mobilize energy, which is associated with discomfort and dysphoria, and the opposing response where androgens are secreted, such as testosterone, and endorphins, which has the purpose of reducing the sensation of pain and to stimulate recovery, and thus can give an experience of wellbeing which makes the behavior enjoyable. The allostatic adaptation made through the HPG and HPA axes is encouraged by repeating the behavior, and if this process is successful, exercise will reduce reactivity in the HPA axis to other stressors and contribute to the positive effects associated with exercise. For instance, it can lead to an increase of neurotransmitters known to facilitate mood-enhancement, such as dopamine, serotonin, and noradrenalin (Helfer et al., 2015; Hildebrandt et al., 2011; Ma, 2008).

However, the consequence of excessive exercise can lead to the “overtraining syndrome” characterized by HPA axis hypoactivation and related depressed mood, fatigue and can lead to decreased performance (Cadegiani & Kater, 2017). The allostatic response will aim to adapt to the change in the exercise tolerance through the HPA and HPG axis through an increase in repair processes and enhancement of the relevant muscles, which will allow the body to adapt to increased exercise behavior and intensity (Morton et al., 2009). The allostatic response involved in this process require androgenic hormone-dependent processes (Aizawa et al., 2010).

The consequences of the allostatic overload as described in overtraining syndrome, is the suppression of the androgenic processes and relating HPA and HPG axial functions. When the muscles are under too much stress, an inflammatory response will be initiated, which can lead to increased cortisol and decreased testosterone levels. AAS protect users against this allostatic response by stimulating the effect androgens have on muscles subjected to an overload of stress (Hildebrandt et al., 2011). AAS use can in this way prevent allostatic overload in the musculoskeletal system by improving the allostatic response, and the user will be able to keep up an exercise regimen that under normal conditions would lead to adverse physiological effects. The drugs prevent losing androgenic tone and increase sensitivity and the effect of the androgen processes in muscle growth, which makes muscle building possible despite overtraining, supported by reported efficacy in improving exercise tolerance and recovery time, and increase muscle mass dose-dependently (Eriksson et al., 2005; Finkelstein et a., 2013; Hildebrandt et al., 2011)

In summary, AAS decrease the adverse effects related to exercise while helping the individual reach the body they desire to attain, reducing both the negative experiences associated with overtraining and a negative body image. Furthermore, the negative effects following dysregulation of physiological systems when some individuals make efforts to discontinue the use make AAS dependence to appear negatively reinforcing. The experience of pleasure seems to be more secondary and related to changes in the HPG axis following increased androgen levels, which have been found to have some reinforcing effects, more specifically reinforcing the rewarding value of other activities, such as cocaine, sex and exercise (Clark & Henderson, 2003; Hildebrandt et al., 2014; Martínez-Sanchis et al., 2002). Moreover, AAS have been found to increase aggression and libido as noted previously. This can explain the tendency for some users to move from a steady and compulsive drug use pattern to an increasingly impulsive behavior involving natural, but risky behaviors related to

aggression and sex, and initiating use of other kinds of drugs (Chegeni et al, 2021a, 2021b; Clark & Henderson, 2003, Nelson et al., 2022). These kinds of behaviors could be associated with socially desirable characteristics, such as improved physical appearance, attracting partners and experience dominance in certain cultural contexts, and thus provide yet another secondary reinforcement for further AAS use (Hildebrandt et al., 2011).

After long-term use, there is evidence of a physiological adaptation leading to a dependence similar to other kinds of drug abuse, where the HPG axis is dependent on AAS to sustain normal functioning (Vilar Neto et al., 2018). This stage of dependence also seems related to the increased allostatic load as a consequence of the HPG axis' efforts to aim for hormonal balance and the intense level of exercise. The suppression of the HPG axis resulting from AAS use has been proposed to be a possible mechanism of dependence, referred to as the androgenic mechanism (Kanayama et al., 2018). When the HPG is suppressed, men will experience a decrease in testosterone and sperm production, which is one of the reasons for users to maintain a pattern of use characterized by on and off-cycles (Albano et al., 2021; Desai et al., 2022; Kanayama et al., 2009; Rahnema et al., 2014). Male users commonly experience hypogonadism temporarily, depending on how long they have been on-cycle when they end a cycle, but most of them will recover the HPG function by weeks or months. Some individuals, however, experience these issues for a prolonged amount of time. This condition can lead to different adverse effects, such as impaired sexual functioning and issues with sexual drive, increased fat and loss of attained muscle mass and fatigue (Albano et al., 2021; Rahnema et al., 2014). To avoid these symptoms, individuals may continue the use of AAS, which again serves as a negative form of reinforcement (Hildebrandt et al., 2011).

As the AAS use and exercise combination increases over time, it appears to have potentially severe consequences for the body, most evidently the cardiovascular system, and

some research suggests that these effects can persist after discontinued use. This is in line with allostatic overload leading to a physiological failure to adapt to the level of exercise muscle mass of some of these users, causing immense pressure on the cardiac system. Other examples of allostatic overload leading to homeostatic failure are liver toxicity, sexual adverse effects and problems related to fertility (Albano et al., 2021; El-Reshaid et al., 2018; Hardt et al., 2012; Herlitz et al., 2010; Hildebrandt et al., 2011; Pope & Kanayama, 2012; Rahnema et al., 2014.; Stoot et al., 2010; Woodward et al., 2019).

The present study

Considering the possible risks of long-term AAS use (Albano et al., 2021; Bond et al., 2022; Kanayama et al., 2020; Pope & Kanayama, 2012; Woodward et al., 2019), and current knowledge of the prevalence of global use (Sagoe et al., 2014b; Sagoe & Pallesen, 2018), developing an understanding and overview of AAS dependence is important. The existing literature indicates that use of AAS and the seemingly high estimates of dependence amongst users, especially among the male population of the world, is a serious public health issue that has not received enough attention. However, the literature on AAS dependence is, to our knowledge, limited to being unsystematic and narrative, not meta-analytic, or restricted to specific populations. Specifically, as noted previously, the two previous estimation literature reviews on the topic are vitiated by a systematic literature search and selection process (Kanayama et al., 2009; Pope et al., 2014), and the inclusion of only USA samples (Pope et al., 2014).

Therefore, the previous literature reviews on the topic are not comprehensive and lack external validity or generalizability to the larger global population (Sagoe et al., 2014; Sagoe & Pallesen, 2018) of AAS-using persons. They do not provide a global AAS dependence prevalence estimate or investigate the correlates and sequelae of AAS dependence. Accordingly, the aim of the present study is to conduct a systematic literature review, a meta-

analysis and meta-regression as well as a meta-synthesis to investigate the prevalence, correlates and sequelae of AAS dependence. The questions guiding the present study are: (1) what are the characteristics of studies on AAS dependence, (2) what is the prevalence of AAS dependence, (3) what are the correlates of AAS dependence prevalence, and (4) what are the sequelae of AAS dependence?

Methods

Search strategy and inclusion criteria

A systematic and comprehensive literature search was conducted in Google Scholar, ISI Web of Science, PsycNET, and PubMed. The following keywords were used: "anabolic-androgenic steroid dependence" OR "anabolic steroid dependence" OR "anabolic-androgenic steroid use and dependence" OR "anabolic steroid use and dependence". A total of 1634 hits were identified from the database search, and five records were identified through ad hoc searches. After deleting 1361 records by title and removing 64 duplicates, 214 records were available for screening. Of this pool, 151 records were removed after inspecting their abstracts. Thus, 63 full-text records were assessed for eligibility of which 25 were included in the review, and 17 in the meta-analysis.

The key inclusion criteria were that the study or record: (a) presented original data on the prevalence of AAS dependence, (b) as assessed with a valid measure (e.g., DSM-III-R), and (c) published in English. The literature search was conducted from 10th March, 2020 to 31st March, 2023. Literature selection was conducted in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) procedure (Moher et al., 2009), and the guidelines of the Meta-analysis of Observational Studies in Epidemiology (MOOSE; Stroup et al., 2000) group. Figure 1 presents the literature search and selection process.

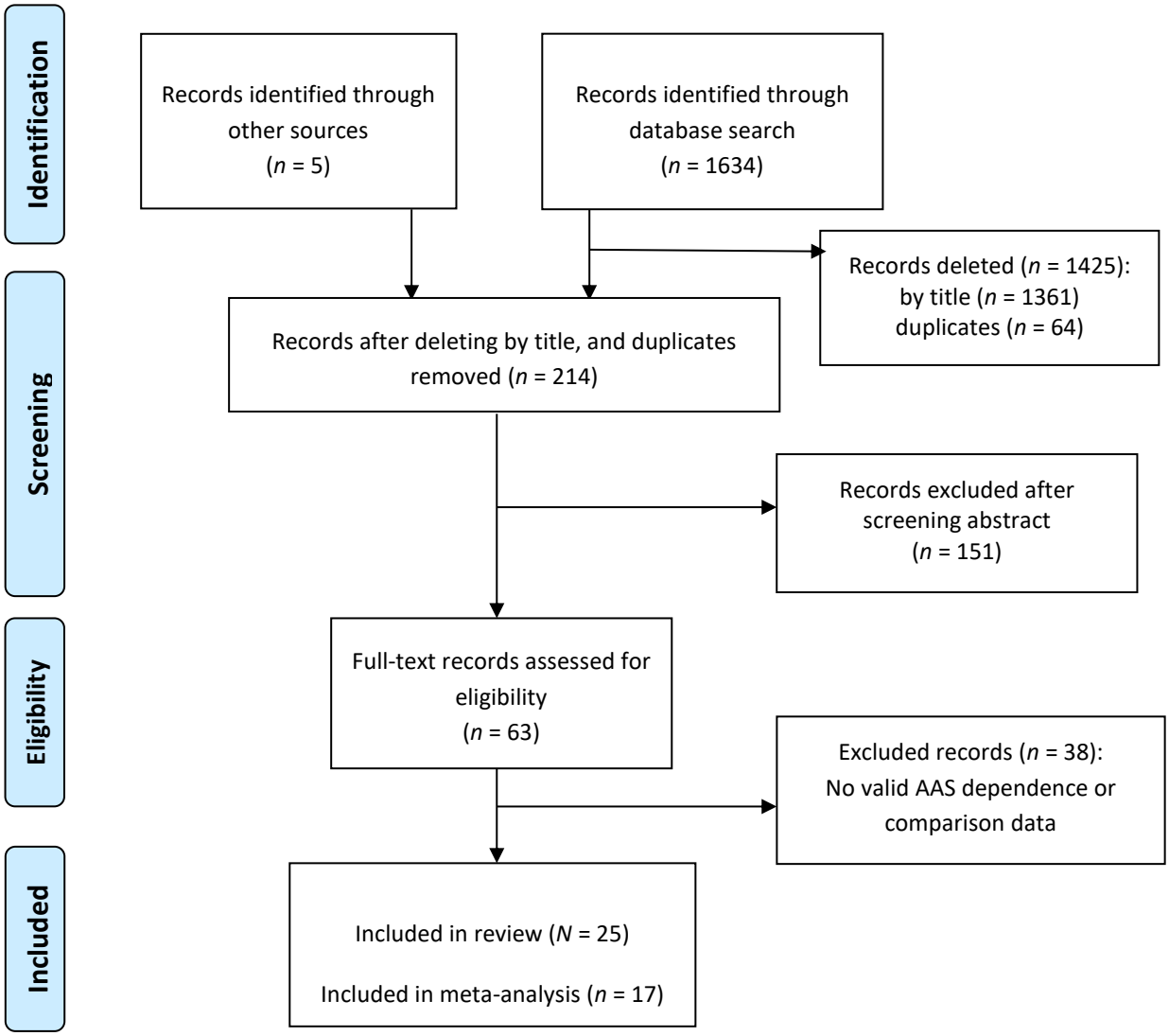

Figure 1. Flow diagram of systematic literature search on AAS dependence.

Data extraction

Using a standardized data extraction form, the following data were extracted from the identified studies and coded: first author name and publication year, country, sample, assessment method, AAS dependence measure, sample size (total, male, and female), participants' ages (range, $M \pm SD$), AAS dependence prevalence (overall, male, and female), and results of the comparison of AAS dependents to nonusers and AAS nondependents, or AAS dependence sequelae. See Table 1.

Table 1. Characteristics of studies on the prevalence, correlates and sequelae of AAS dependence.

1st author year	Country	Sample	Assessment	Measure	*N*	M	F	Age range	Age *M*±*SD*	T Prev %	M Prev %	F Prev %	Comparison/sequelae
Bjørnebekk 2016§	Norway	Weightlifters	I+Q	DSM-IV	82	82			33.0±8.2	53.7	53.7		AD-OSD: 26.8%. AD < AND & ANU: Cerebral cortex, total gray matter, putamen. AD-OSD < AND & ANU: Cerebral cortex, total gray matter, putamen
Brennan 2011	USA	Weightlifters	I+Q	DSM-IV	100	100		18-40		31.0	31.0		AD+HGH: 22.0%. AD-OSD (-Alcohol): 38.7%
Brower 1991	USA	Weightlifters	Q	DSM-III-R	49	49			24.4±5.7	57.1	57.1		AD > AND: Cycles, maximum dose, feeling not big enough, aggression symptoms
Clancy 1992‡	USA	Weightlifters	Q	DSM-III-R	68	64	4			69.1			
Copeland 2000	Australia	Athletes and weightlifters	I+Q	DSM-IV	100	94	6	18-50	29.2±6.9	23.0	22.3	33.3	
de Zeeuw 2023	The Netherlands	Gym visitors	Q	DSM-V	103	103			31.2±9.3	24.3	24.3		AD > AND: training per week (mins), recreational athletes, AAS use (weeks), average AAS dose (mg/week), oral AAS (weeks), injectable AAS (weeks), past year nonmedical insulin and/or DNP use, side effects.
Ganson 2023	Canada	Adolescents and young adults	Q	DSM-V	44	36	8	16-30	26.4±3.4	23.1?			
Goudy 1995	USA	Weightlifters	Q	DSM-III-R	3					66.7			
Gridley 1994	Australia	Gym exercisers	Q	DSM-III-R	21	21		25-30		57.1	57.1		AD > AND: Less knowledge of effects, polypharmacy, total number of cycles, use duration, weeks off cycle, weeks on cycle
Griffiths 2018	Australia	Exercisers and weightlifters	I	DSM-IV (SDS)	74	74							AD > AND: Social physique anxiety

Hauger 2019a§	Norway	Weightlifters	I+Q	DSM-IV	83	83		54.2	54.2	AD > AND > ANU: antisocial personality. AD < AND: Fear recognition [unadjusted/adjusted for antisocial personality; anxiety; depression; IQ; OSD], IQ. AD > AND: ADHD, Anxiety, avoidant personality, depression, side effects (cognitive, physical, psychological), somatic problems, years of use. AD < ANU: Education, emotion recognition, fear recognition (unadjusted and adjusted for IQ), IQ AD > ANU: ADHD, anxiety, avoidant personality, depression, OSU, somatic problems, T/E ratio, weight (kg)
Hauger 2019b§	Norway	Weightlifters	I+Q	DSM-IV	81	81		46.9	46.9	AD > AND: Aggression, anxiety, attention problems, blood pressure, depression, irritability, liver-related issues, memory problems, sexual dysfunction, side effects (cognitive, physical, psychological), sleep problems, total intra- and interpersonal problems, years of use. AD < AND: acumbens, appetite, cortical thickness (unadjusted and excluding OSU), sex drive
Hauger 2020§	Norway	Weightlifters	I+Q	DSM-IV	96	96		60.4	60.4	AD < AND & ANU: Education years, IQ. AD > AND: weekly dose, years of use. AD < ANU: [unadjusted: inhibition; adjusted for OSU: lower psychological distress, lower ADHD symptoms, problem-

											solving, working memory, mental flexibility, executive function]. AD < AND: [adjusted for OSU: executive function, lower psychological distress, lower ADHD symptoms]
Hildebrandt 2014	USA	Exercisers and weightlifters	I+Q	DSM-IV-TR	16	16	23-52	35.6±8.8			AD > AND: β-endorphin levels
Ip 2012	USA	Exercisers and weightlifters	Q	DSM-IV-TR	479				23.4		AD > AND: AAS types, Anxiety, depression, doses, duration of use, last 12 months' heroin use, married and not single, PEDs, psychiatric diagnosis, side effects, concern for side effects on long-term health
Kanayama 2003	USA	Substance users in treatment	I	DSM-IV	24	24		32.1±8.2	20.8	20.8	AD > AND: Duration of use. AD: AAS use is a gateway to opioid use
Kanayama 2009	USA	Weightlifters	I+Q	DSM-IV (AIM)	62	62	18-40		32.3		AD > AND & ANU: first degree relative with OSD, age, cocaine dependence, conduct disorder, more muscular, opioid abuse or dependence, OSD, AD < AND & ANU: Educational attainment AD > AND: Doses, duration of use, other PED use, single parent by age 13 AD > ANU: Body dysmorphic disorder
Midgley 1999	Scotland	Athletes, exercisers, and weightlifters	I+Q	DSM-III-R	50				26.0		
Perry 2005	USA	Athletes, exercisers, and weightlifters	Q	DSM-IV-TR	206			27.2±7.2	33.0		AD > AND: Stacking cycle length

Pope 2010	UK	Weightlifters	I	DSM-IV (AIM)	42	42	18-43	28.1±6.8	45.2	45.2		AD > AND: Age, doses, duration of use, hypothetical purchase of AAS, other PED use, perceived negative effects of AAS on mental health, sexual performance, and social life AD < AND: AAS initiation age
Pope 2014	USA	Weightlifters	I	DSM-IV (AIM)	102	102			36.3	36.3		
Scarth 2023§	Norway	Weightlifters	I+Q	DSM-IV (SCID-II)	153	153		35.78±9.95				Major dependence symptoms: continuing use despite physical and mental problems, longer use than planned, tolerance, work/life interference
Thiblin 1997	Sweden	Violent offenders	I	DSM-III-R	9				22.2			AD: Depression and suicide attempt upon withdrawal
Vaskinn 2020§	Norway	Weightlifters	I+Q	DSM-IV	51 §	44 §	7		54.3	56.4	43.8	AD < AND & ANU: Education, IQ, OSU. AD < AND: Side effects (cognitive, physical, psychological), years of use. AD < ANU: affective ToM, cognitive ToM, overmentalizing/undermentalizing errors, total ToM
Westlye 2017§	Norway	Weightlifters	I+Q	DSM-IV	66	66			54.5	54.5		AD < AND & ANU: Brain connectivity in emotional and cognitive regulation (amygdala and default-mode network; dorsal attention network and frontal node)

‡in Brower (2002). AD: AAS dependents. AD-OSD: AAS dependents without other substance dependence. AIM: AAS Interview Module. AND: AAS non-dependents. ANU: AAS non-users. DNP: 2,4-dinitrophenol. DSM: Diagnostic and Statistical Manual of Mental Disorders. FPE: Forensic psychiatric evaluation. HGH: Human growth hormone. IGF-1: Insulin-like growth factor-1. I: Interview. I+Q: Interview and questionnaire. MASC: Movie for the Assessment of Social Cognition test. MDI: Muscle Dysmorphia Inventory. OSD: Other substance dependence. OSU: Other substance use. PED: Performance enhancing drugs. Prev: Prevalence. Q: Questionnaire. RR: Response rate. SCID: Structured Clinical Interview for DSM-IV. SDS: Severity of Dependence Scale. ToM: Theory of mind. §: Sample overlap.

Data analysis

A meta-analysis was conducted to estimate the prevalence of AAS dependence. Heterogeneity was assessed using Cochran's *Q* and the I^2 statistic (Borenstein et al., 2017). Here, an I^2 of 0% indicates no heterogeneity, 25% denotes low heterogeneity, 50% signifies moderate heterogeneity, and 75% or higher reflects high heterogeneity (Higgins et al., 2003). Publication bias was investigated using Egger's test (Egger et al., 1997) as well as the trim-and-fill procedure (Duval & Tweedie, 2000).

Moreover, study quality or risk of bias was assessed using a checklist for prevalence studies (Hoy et al., 2012). The checklist contains 10 items for assessing included studies. Each item is scored 0 (low risk of bias) or 1 (high risk of bias). High risk or low quality is indicated by the following characteristics: (1) study target population is not representative of the national population, (2) sampling frame is not a close representation of the target population, (3) lack of random selection, (4) high likelihood of non-response bias, (5) lack of primary data, (6) inadequate operationalization, (7) low instrument reliability or validity, (8) inconsistent mode of data collection, (9) large span of the assessed prevalence, and (10) problematic prevalence estimation. Thus, the total quality or risk score ranges from 0 to 10 and each study is categorized as: high quality/low risk (0 to 3), moderate quality/risk (4 to 6), and low quality/high risk (7–10). The author and supervisor independently conducted the study quality or risk of bias assessment and reached consensus on conflicting assessments through discussion.

A random-effects model was used in the overall prevalence meta-analysis due to its propensity for higher external validity or generalizability of findings, and recommendation when included studies are assumed to represent different populations of studies (Borenstein et al., 2009). However, in the rest of the meta-analyses, a fixed-effect model was adopted due to the smaller number of studies (Borenstein et al., 2009; Lin et al., 2020). A meta-regression

analysis was also conducted to examine the correlates of the AAS dependence prevalence. Here, AAS dependence measure (DSM-III-R etc.) was not included in the meta-regression due to multicollinearity. Furthermore, using content analysis (Finfgeld-Connett, 2014), evidence on the correlates and sequelae of AAS dependence were extracted and synthesized under the following clusters: demographic, biophysical, cognitive, emotional, and psychosocial. Here, evidence from comparisons of AAS dependents to nonusers, and nondependents were extracted separately. The interrater reliability was calculated using SPSS 28 (IBM Corp.), and publication bias, the meta-analysis and meta-regression analyses using Comprehensive Meta-Analysis 4 (Biostat Inc.).

Results

What are the characteristics of studies on AAS dependence?

Description of studies

Of the 25 included studies, publication years range from 1991 (Brower, Blow, Young, & Hill, 1991) to 2023 (de Zeeuw et al., 2023; Ganson et al., 2023; Scarth et al., 2023). Studies were conducted in USA (*n* = 10), Norway (*n* = 7), Australia (*n* = 3), and one study each from the UK, Canada, Scotland, Sweden, and the Netherlands. Samples were predominantly weightlifters, exercisers, and athletes. Assessment methods comprised interviews and questionnaires (*n* = 12), interviews only (*n* = 5), and questionnaires only (*n* = 8). AAS dependence was assessed using the DSM-III-R (*n* = 6), DSM-IV (*n* = 14), DSM-IV-TR (*n* = 2), and DSM-V (*n* = 2). The studies included a total of 1,705 participants (range: 3 to 479, *M* = 89.74, *SD* = 24.61). Of this sample, 1,680 were males and 25 were females. Table 1 presents further characteristics of included studies.

Publication bias

There was no publication bias (Egger's *B*0 = 1.85, 95% CI: -0.94–4.65, $t = 1.41$, $p = 0.08$). Similarly, the trim-and-fill procedure imputed no study and did not change the overall prevalence estimate.

Quality assessment

Table 2 presents results of the study quality or risk of bias assessment. All studies were evaluated as of moderate quality or risk of bias. The inter-reviewer reliability was found to be kappa = 0.63 ($p < 0.001$) indicating substantial agreement between the two reviewers.

Table 2. Risk of bias/methodological quality (Hoy et al., 2012) of included studies.

Study	1. *N* representativeness	2. *N* frame	3. Randomization	4. Non-response bias	5. Primary data	6. Operationalization	7. Instrument	8. Consistency	9. Period	10. Estimation	Total risk score	Risk category✓
Bjørnebekk 2016§	1	1	1	1	0	0	0	0	0	0	4	Moderate
Brennan 2011	1	1	1	1	0	0	0	0	1	0	5	Moderate
Brower 1991	1	1	1	1	0	0	0	0	1	0	5	Moderate
Clancy 1992‡	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Copeland 2000	1	1	1	1	0	0	0	0	1	0	5	Moderate
de Zeeuw 2023	1	1	1	1	0	0	0	0	0	0	4	Moderate
Ganson 2023	0	0	1	1	0	1	0	0	1	0	4	Moderate
Goudy 1995	1	1	1	1	0	0	0	0	0	0	4	Moderate
Gridley 1994	1	1	1	1	0	0	0	0	1	0	5	Moderate
Griffiths 2018	1	1	1	1	0	0	0	0	1	1	6	Moderate
Hauger 2019a§	1	1	1	1	0	0	0	0	0	0	4	Moderate
Hauger 2019b§	1	1	1	1	0	0	0	0	0	0	4	Moderate
Hauger 2020§	1	1	1	1	0	0	0	0	0	0	4	Moderate
Hildebrandt 2014	1	1	1	1	0	0	0	0	1	1	6	Moderate
Ip 2012	1	1	1	1	0	0	0	0	1	0	5	Moderate
Kanayama 2003	1	1	1	0	0	0	0	0	1	0	4	Moderate
Kanayama 2009	1	1	1	1	0	0	0	0	1	0	5	Moderate
Midgley 1999	1	1	1	1	0	0	0	0	0	0	4	Moderate
Perry 2005	1	1	1	1	0	0	0	0	1	0	5	Moderate
Pope 2010	1	1	1	1	0	0	0	0	1	0	5	Moderate
Pope 2014	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Scarth 2023§	1	1	1	1	0	0	0	0	0	1	5	Moderate
Thiblin 1997	1	1	1	1	0	0	0	0	0	0	4	Moderate
Vaskinn 2020§	1	1	1	1	0	0	0	0	0	0	4	Moderate
Westlye 2017§	1	1	1	1	0	0	0	0	0	0	4	Moderate

Item score: (0: low risk, 1: high risk). ✓Total quality/risk score: (range [0–10]: high quality/low risk [0–3], moderate quality/risk [4–6], poor quality/high risk [7–10]). ‡In Brower (2002). §: Sample overlap. NA: Not applicable. Primary document not available.

What is the prevalence of AAS dependence?

Overall

The overall lifetime prevalence of AAS dependence from the 17 included studies was 36.0% (95% CI: 29.1–43.4, $Q = 102.6$, $I^2 = 84.4$, $p < .001$). Figure 2 presents the forest plot of the overall lifetime prevalence.

Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
Bjørnebekk 2016	0.537	0.429	0.641	0.662	0.508
Brennan 2011	0.310	0.227	0.407	-3.700	0.000
Brower 1991	0.571	0.431	0.701	0.997	0.319
Clancy 1992	0.691	0.572	0.789	3.069	0.002
Copeland 2000	0.230	0.158	0.322	-5.085	0.000
de Zeeuw 2023	0.243	0.170	0.335	-4.951	0.000
Goudy 1995	0.667	0.154	0.957	0.566	0.571
Ganson 2023	0.227	0.127	0.373	-3.402	0.001
Gridley 1994	0.571	0.360	0.760	0.652	0.514
Ip 2012	0.234	0.198	0.274	-10.994	0.000
Kanayama 2003	0.208	0.089	0.413	-2.656	0.008
Kanayama 2009	0.323	0.219	0.448	-2.731	0.006
Midgley 1999	0.260	0.157	0.398	-3.244	0.001
Perry 2005	0.330	0.269	0.397	-4.777	0.000
Pope 2010	0.452	0.310	0.603	-0.616	0.538
Pope 2014	0.363	0.275	0.460	-2.736	0.006
Thiblin 1997	0.222	0.056	0.579	-1.562	0.118
	0.360	0.291	0.434	-3.630	0.000

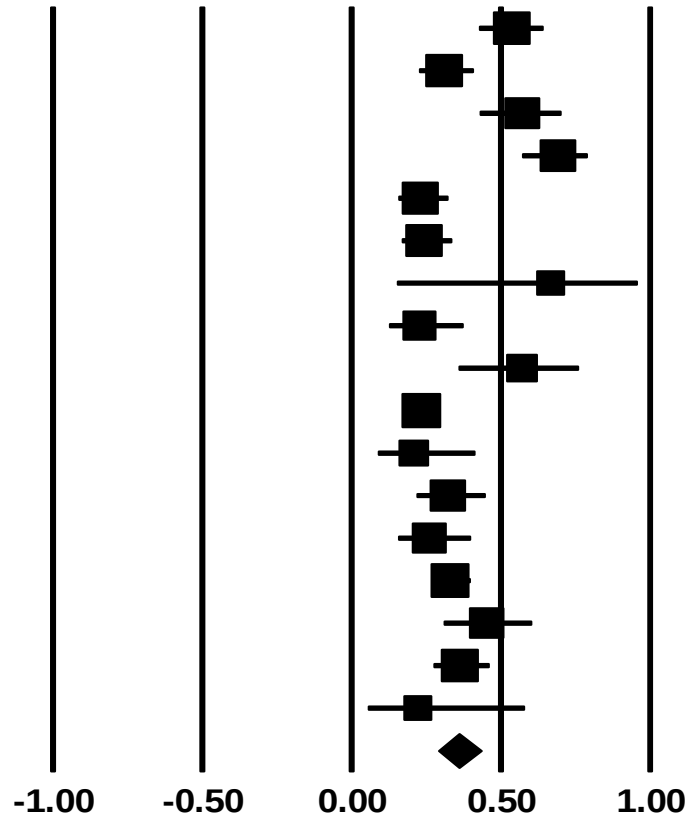

Figure 2. Forest plot of the lifetime prevalence of AAS dependence.

Regions

Table 3 presents the total number of studies, the prevalence rates and the confidence interval for the three regions. Also presented are their respective heterogeneity statistics. From Table 3, Europe had a prevalence rate of 36.9%, North America had a prevalence rate of 36.4%, and Oceania had a prevalence rate of 29.5%. There were no significant differences in prevalence rates between the regions.

Table 3. Regional prevalence rates, 95% confidence intervals, and heterogeneity statistics

Region	*N*	Prevalence (%)	95% CI	*Q*	I^2
Europe	5	36.9**	31.3–43.0	20.9**	80.9
North America	10	36.4*	27.5–46.4	69.8**	87.1
Oceania	2	29.5**	21.7–38.7	8.9*	88.8

** $p < .001$, * $p < .01$. *Q*: heterogeneity statistic. I^2: heterogeneity index.

Assessment

Table 4 presents the total number of studies, the prevalence rates and the confidence interval for the assessment methods as well as their heterogeneity statistics. From Table 4, studies using interviews as a method of assessment had a prevalence of 36.1%, studies based on questionnaires had a prevalence of 31.5%, and studies applying both interviews and questionnaires had a prevalence of 33.8%. There were no significant differences in prevalence rates between the three assessment methods.

Table 4. Assessment prevalence rates, 95% confidence intervals, and heterogeneity statistics

Assessment	*n*	Prevalence (%)	95% CI	*Q*	I^2
Interview	4	36.1*	29.3–43.6	4.5^{ns}	33.8
Questionnaire	8	31.5*	28.5–34.6	75.9*	90.8
Interview and questionnaire	5	33.8*	29.1–38.8	20.5*	80.5

* $p < .001$. *ns*: not significant. *Q*: heterogeneity statistic. I^2: heterogeneity index

Dependence measure

Table 5 presents the total number of studies, the prevalence rates, the confidence interval, and heterogeneity statistics for the dependence measures. From Table 5, DSM-III-R as a measure had a prevalence of 52.9%, DSM-IV had a prevalence of 35.5%, DSM-IV-TR had a prevalence of 26.5%, and DSM-V had a prevalence of 23.8%. Subgroup comparisons showed higher DSM-III-R prevalence compared to DSM-IV ($Q = 15.9$, $p < .001$), DSM-IV-TR ($Q = 42.3$, $p < .001$), and DSM-V ($Q = 27.1$, $p < .001$) prevalences. Additionally, DSM-IV prevalence was higher than DSM-IV-TR ($Q = 10.9$, $p < .01$) and DSM-V ($Q = 6.9$, $p < .01$) prevalences.

Table 5. Dependence measure prevalence rates, 95% confidence intervals, and heterogeneity statistics

Measure	*N*	Prevalence (%)	95% CI	*Q*	I^2
DSM-III-R	6	52.9$^{ns\ abc}$	45.5–60.2	23.5**	78.8
DSM-IV	7	35.5** ^{ade}	31.4–39.9	23.0*	73.8
DSM-IV-TR	2	26.5** ^{bd}	23.3–29.9	6.8*	85.4
DSM-V	2	23.8** ^{ce}	17.6–31.4	0.0^{ns}	0.0

** $p < .001$, * $p < .01$. *ns*: not significant. *Q*: heterogeneity statistic. I^2: heterogeneity index. Categories sharing a superscript are significantly different ($p < .05$).

Publication year

Table 6 presents the total number of studies, the prevalence rates and the confidence interval for publication year as well as their heterogeneity statistics. From Table 6, publications from 1990–1999 had a prevalence of 52.9%, 2000–2009 publications had a prevalence of 29.9%, and publications from 2010–2023 had a prevalence of 29.7%. Subgroup comparisons showed higher 1990–1999 publications prevalence compared to 2000–2009 publications ($Q = 26.6$, $p < .001$), and 2010–2023 ($Q = 33.8$, $p < .001$) prevalences.

Table 6. Publication year prevalence rates, 95% confidence intervals, and heterogeneity statistics

Publication year	*n*	Prevalence (%)	95% CI	*Q*	I^2
1990–1999	6	52.9$^{ns\ ab}$	45.5–60.2	23.5*	78.8
2000–2009	4	29.9** ^{a}	25.5–34.6	4.3^{ns}	30.0
2010–2023	7	29.7** ^{b}	26.8–32.8	39.1**	84.7

** $p < .001$, * $p < .01$. *ns*: not significant. *Q*: heterogeneity statistic. I^2: heterogeneity index. Categories sharing a superscript are significantly different ($p < .05$).

What are the correlates of AAS dependence prevalence?

Table 7 presents results of the meta-regression analysis of the correlates of AAS dependence prevalence. The meta-regression model was significant ($Q = 52.93$, $df = 7$, $p < 0.001$, $R^2 = 97.00\%$). Compared to European dependence prevalence, North America ($B = -0.69$, $p < 0.01$) and Oceania ($B = -1.12$, $p < 0.01$) were associated with lower dependence prevalence. Additionally, compared to dependence assessment using interviews, questionnaire assessment was associated with lower dependence prevalence ($B = -1.11$, $p < 0.01$). Furthermore, 2000–2009 ($B = -2.62$, $p < 0.001$) and 2010–2023 ($B = -2.32$, $p < 0.001$) publications were associated with lower dependence prevalence in comparison to 1990–1999 publications.

Table 7. Meta-regression analysis of the correlates of AAS use dependence prevalence.

Predictor	*B*	SE	95% CI	*Z*	*p*
Region					
Europe§					
North America	-0.69	0.26	-1.21–-0.17	-2.62	0.009
Oceania	-1.12	0.42	-1.93–-0.30	-2.67	0.008
Assessment					
Interview§					
Questionnaire	-1.11	0.36	-1.81–-0.41	-3.12	0.002
Interview and questionnaire	0.08	0.24	-0.39–0.54	0.32	0.749
Publication year					
1990–1999§					
2000–2009	-2.62	0.43	-3.47–-1.78	-6.08	0.000
2010–2023	-2.32	0.43	-3.16–-1.48	-5.42	0.000
Male sample proportion (%)	-0.04	0.05	-0.13–0.06	-0.77	0.439

R^2 = 97.0%. §: Reference category.

What are the sequelae of AAS dependence?

Table 8 presents results of the comparison of AAS dependents to nonusers as well as nondependents.

Demographic

Compared to nonusers, AAS dependents had lower age, educational attainment, education years and IQ. Furthermore, they were found to have higher weight (kg), muscularity, weekly AAS dose and more years of use (Ganson et al., 2023; Hauger et al., 2019a, 2020; Kanayama, 2009; Vaskinn et al., 2020).

Compared to nondependents, AAS dependents used more types of AAS and had higher age, number of cycles, doses and were more likely to purchase AAS in an experimental scenario. Additionally, AAS dependents had lower AAS initiation age, educational attainment, education years, IQ and knowledge of AAS effects. AAS dependents were also more likely to have had a single parent by the age of 13, to be married and not single, and to be recreational athletes. They also had a higher maximum dose, higher levels of muscularity, longer stacking cycle lengths, more training per week measured in minutes, duration of AAS use, higher weekly dose, more weeks off cycle, more weeks on cycle and more years of use compared to nondependents (Brower et al., 1991; de Zeeuw et al., 2023; Gridley et al., 1994; Hauger et al., 2019a, 2020; Ip et al., 2012; Kanayama et al., 2003, 2009; Perry et al., 2005; Pope et al., 2010; Vaskinn et al., 2020).

Table 8. Summary of comparison of correlates and sequelae of AAS dependence.

	Comparison		Comparison	
Domain	AAS dependents > nonusers	References	AAS dependents > nondependents	References
Demographic	Lower (age, educational attainment, education years, IQ), weight (kg) muscularity, weekly dose, years of use	Ganson 2023; Hauger 2019a; Hauger 2020; Kanayama 2009; Vaskinn 2020;	AAS types used, age, cycles, doses, hypothetical purchase of AAS, lower (AAS initiation age, educational attainment, education years, IQ, knowledge of effects), married and not single, maximum dose, muscularity, recreational athletes, single parent by age 13, stacking cycle length, training per week (mins), use duration, weekly dose, weeks off cycle, weeks on cycle, years of use	Brower 1991; de Zeeuw 2023; Gridley 1994; Hauger 2019a; Hauger 2020; Ip 2012; de Zeeuw 2023; Kanayama 2003; Kanayama 2009; Perry 2005; Pope 2010; Vaskinn 2020
Biophysical	Lower (cerebral cortex, total gray matter, putamen), somatic problems, T/E ratio	Bjørnebekk 2016; Hauger 2019a; Kanayama 2009; Vaskinn 2020	β-endorphin levels, blood pressure, liver-related issues, lower (acumbens, appetite, brain connectivity [amygdala and default-mode network, dorsal attention network and frontal node], cerebral cortex, cortical thickness [unadjusted and excluding OSU], total gray matter, putamen), somatic problems, physical side effects, sex drive, sexual dysfunction	Bjørnebekk 2016; Hauger 2019b; Hildebrandt 2014; Kanayama 2009; Vaskinn 2020; Westlye 2017
Cognitive	Lower (brain connectivity in emotional and cognitive regulation [amygdala and default-mode network; dorsal attention network and frontal node], problem-solving, working memory, mental flexibility, executive function)	Hauger 2020; Vaskinn 2020; Westlye 2017	Attention problems, cognitive side effects, lower (affective ToM, cognitive regulation, executive function [adjusted for OSU], cognitive ToM, overmentalizing/undermentalizing errors, total ToM), memory problems	Hauger 2019a; Hauger 2019b; Hauger 2020; Vaskinn 2020; Westlye 2017

Emotional	Lower emotion recognition, fear recognition (unadjusted/adjusted for IQ)	Hauger 2019a	Lower fear recognition (unadjusted/adjusted for antisocial personality; anxiety; depression; IQ; OSD), lower emotional regulation, irritability	Hauger 2019a; Hauger 2019b; Westlye 2017
Psychosocial	ADHD symptoms (adjusted for OSU), antisocial personality, anxiety symptoms, body dysmorphic disorder, cocaine dependence, conduct disorder, depression symptoms, first degree relative with OSD, lower inhibition, opioid abuse/dependence, OSD, OSU, psychological distress (adjusted for OSU), violent behavior	de Zeeuw 2023; Ganson 2023; Hauger 2019a; Hauger 2020; Kanayama 2009; Vaskinn 2020	ADHD symptoms and psychological distress (adjusted for OSU), ADHD symptoms, aggression symptoms, antisocial personality, anxiety symptoms, avoidant personality, cocaine dependence, concern for side effects on long-term health, conduct disorder, continuing use despite physical and mental problems, depression symptoms, feeling not big enough, first degree relative with OSD, intra- and interpersonal problems, past year heroin use, past year nonmedical insulin and/or DNP use, longer use than planned, lower inhibition, opioid abuse/dependence, other PED use, OSD, perceived negative effects of AAS on mental health, sexual performance and social life, polypharmacy, psychiatric diagnosis, psychological side effects, sleep problems, social physique anxiety, tolerance, work/life interference	Brower 1991; de Zeeuw 2023; Gridley 1994; Griffiths 2018; Hauger 2019a; Hauger 2019b; Hauger 2020; Ip 2012; Kanayama 2003; Kanayama 2009; Pope 2010; Scarth 2023; Vaskinn 2020

DNP: 2,4-dinitrophenol. OSD: Other substance dependence. OSU: Other substance use. PED: Performance enhancing drugs. ToM: Theory of mind.

Biophysical

Compared to nonusers, AAS dependents had lower mass volume in the cerebral cortex, total grey matter and putamen, higher levels of somatic problems, and higher testosterone/epitestosterone (T/E) ratio (Bjørnebekk et al., 2016; Hauger et al., 2019a; Kanayama et al., 2009; Vaskinn et al., 2020).

Compared to nondependents, AAS dependents had higher β-endorphin levels, blood pressure and liver-related issues. They also had lower levels of appetite, brain connectivity (amygdala and default-mode network, dorsal attention network and frontal node), smaller volume in the acumbens, cerebral cortex, cortical thickness, total grey matter, and putamen. Furthermore, they had more somatic problems, physical side effects, a higher sex drive and sexual dysfunction (Bjørnebekk et al., 2016; Hauger et al., 2019b; Hildebrandt et al., 2014; Kanayama et al., 2009; Vaskinn et al., 2020; Westlye et al., 2017).

Cognitive

AAS dependents had, compared to nonusers, lower brain connectivity in emotional and cognitive regulation shown in the amygdala, the default mode network, the dorsal attention network, and the frontal node. In addition, AAS dependents showed lower problem-solving skills, working memory, mental flexibility, and executive function compared to nonusers (Hauger et al., 2020; Vaskinn et al., 2020; Westlye et al., 2017).

Moreover, in comparison to nondependents, AAS dependents displayed higher levels of attention problems and more cognitive side effects of AAS use. They furthermore showed lower skills in affective, cognitive and total theory of mind, cognitive regulation, executive function, overmentalizing/undermentalizing errors, and higher levels of memory problems (Hauger et al., 2019a, 2019b, 2020; Vaskinn et al., 2020; Westlye et al., 2017).

Emotional

Compared to nonusers, AAS dependents scored lower on overall emotion recognition and fear recognition irrespective of IQ (Hauger et al., 2019a). Additionally, compared to AAS nondependents, dependents were associated with lower level of fear recognition irrespective of antisocial personality, anxiety, depression, IQ and other substance dependence, as well as lower levels of emotional regulation, and higher levels of irritability (Hauger et al. 2019a, 2019b; Westlye et al., 2017).

Psychosocial

In comparison to nonusers, AAS dependents had a higher prevalence of ADHD symptoms, antisocial personality disorder, anxiety and depression symptoms, body dysmorphic disorder, cocaine dependence, conduct disorder, and were more likely to have a first degree relative with other substance dependence. Furthermore, they showed lower inhibition skills, and higher rates of opioid abuse or dependence, other substance use and dependence, psychological distress irrespective of other substance use, and higher levels of violent behaviour (de Zeeuw et al., 2023; Ganson et al., 2023, Hauger et al., 2019a, 2020; Kanayama et al., 2009; Vaskinn et al., 2020).

Comparing AAS dependents to nondependents, dependents had higher levels of ADHD symptoms and psychological distress irrespective of other substance use. Moreover, AAS dependents had a higher prevalence of aggression symptoms, antisocial personality disorder, symptoms of anxiety, avoidant personality disorder, cocaine dependence, conduct disorder, continuation of use despite the experience of physical and mental problems, symptoms of depression, not feeling big enough, and concern for side effects of AAS on their long-term health compared to nondependents. AAS dependents were more likely to have a first degree relative with other substance disorder, have intra- and interpersonal problems, had a higher past year prevalences of heroin and insulin and/or DNP use, and had a longer use of

AAS than planned in comparison to nondependents. Moreover, AAS dependents exhibited lower levels of inhibition, higher levels of opioid abuse or dependence and other performance-enhancing drug use, other substance disorder, and polypharmacy compared to nondependents. Furthermore, AAS dependents reported more perceived negative effects of AAS on their mental health, sexual performance, and social life than nondependents (de Zeeuw et al., 2023; Gridley et al., 1994; Griffiths et al., 2018; Hauger et al., 2019a, 2019b, 2020; Ip et al., 2012; Kanayama et al., 2003, 2009; Pope et al., 2010; Scarth et al., 2023; Vaskinn et al., 2020).

Discussion

The aim of the present study was to investigate the characteristics of studies on AAS dependence, the global prevalence of AAS dependence, the correlates of AAS dependence prevalence, and the sequelae of AAS dependence. To achieve this, a systematic literature review with a meta-analytic investigation, a meta-regression analysis and a meta-synthesis were conducted.

Prevalence of AAS dependence

The overall lifetime prevalence of AAS dependence obtained from the meta-analysis (36.0%) is similar to the previously reported 30% estimate (Kanayama et al., 2009; Pope et al., 2014), albeit unsystematic and American biased as previously noted. In support of the overall prevalence estimate, similar prevalence estimates were observed across geographical regions (Europe, North America, and Oceania) and assessment methods (interviews, questionnaires, and combined interviews and questionnaires), and no significant differences were observed in subgroup comparisons per category. The downtrend of the dependence prevalence rates by publication year is explainable by historical trends in AAS use and legislation. The 1970s and 1980s were characterized by the proliferation of magazines and underground guides advertising AAS use, the availability of AAS as prescription drugs, and

loose regulation of AAS (Kanayama et al., 2008). Indeed, a global meta-analysis (Sagoe et al., 2014b) found the 1970s (9.2%) as having a higher lifetime prevalence of AAS use compared to the 1990s (2.9%). It is therefore plausible that the higher dependence prevalence in 1990–1999 reflects the user group of the 1970s and 1980s who had a risky user pattern in an environment characterized by higher levels of availability and less regulation of AAS by authorities (Kanayama et al., 2008).

Relatedly, during the 1990s, concerns regarding AAS use led to legislation enactments such as the 1990 Steroid Trafficking Act in the United States, and the 1991 Act Prohibiting Certain Doping Substances in Sweden (Kanayama et al., 2008; SFS, 1991). It is plausible that the concern for AAS use and the new legislation against AAS use in the 1990s and their increased regulation decreased AAS availability. Combined with growing concerns and accumulated research on the potential harms of use (Pope & Katz, 1988; Pope, Katz, & Champoux, 1988), it is reasonable that this generated apprehension regarding the legal and health consequences, and more consideration of user patterns and therefore the downtrend in the dependence prevalence rates for the next decades (McVeigh & Begley, 2017). This could be supported by the finding of less knowledge of effects associated with AAS use within the dependent group compared to nondependents (Gridley et al., 1994). The above historical trends and legislation explanation may also account for the downtrend of the dependence prevalence rates by dependence measure considering the publication of the DSM-III-R in 1987 (APA, 1987), the DSM-IV in 1994 (APA, 1994), the DSM-IV-TR in 2000 (APA, 2000), and the DSM-V in 2013 (APA, 2013).

Correlates of AAS dependence prevalence

The finding that Europe is associated with significantly higher dependence prevalence compared to North America and Oceania can be partially explained by the fact that AAS legislation started in North America and spread to Europe (Kanayama et al., 2008). Moreover,

the North American studies use questionnaire assessment in five out of the 10 included studies, compared to the European studies which used questionnaires in one out of five included studies.

Although questionnaire assessments are ‘populist’ and time-efficient, they can be affected by several factors such as misunderstandings, non-response errors and biased wording (Harris & Brown, 2010). Despite some limitations of interviews such as relatively low time efficiency, interviews provide the opportunity for respondents to elaborate and ask for or give clarifications if questions are misunderstood or unclear (Harris & Brown, 2010), which is advantageous in a clinical or diagnostic context (Rasmussen, Jensen, & Olesen, 1991). Thus, the association of questionnaire assessments with lower dependence prevalence compared to dependence prevalence assessment based on interviews is reasonable. This finding is also consistent with evidence from a global meta-regression analysis associating interviews with higher AAS use prevalence assessment relative to questionnaire AAS use prevalence assessment (Sagoe e al., 2014b). Finally, the association of publications from 2000–2009 and 2010–2023 with lower dependence prevalence relative to 1990–1999 publications is consistent with the results of the meta-analysis subgroup comparisons and understandable from historical and legal perspectives (Diethelm et al., 2022; Kanayama et al., 2008) as previously explained.

Comparison of AAS dependents to nonusers and nondependents

The present study found that AAS dependents differ on several demographic factors compared to both nonusers and nondependents. The younger age of dependents compared to nonusers can be interpreted in light of evidence of AAS use an element of youth culture with meta-analytic results indicating higher prevalence among persons 19 years and younger (2.5%) compared to 1.9% for those older than 19 years (Sagoe et al, 2014b), and about 80% of AAS users initiating use before age 30 (Pope et al., 2014). Also, the finding that AAS

dependents are heavier and more muscular, had more years of use and higher weekly dose compared to nonusers are understandable where the dependents in addition to AAS use have higher dedication to the lifestyle required to build bigger muscle mass as well as the ability to take part in more excessive training without experiencing overtraining syndrome due to AAS use (Hildebrandt, 2011).

Indeed, the finding that the dependents exercise more per week compared to the nondependents supports this, and also supports that AAS dependence could be reinforced through the effect it has on elevating the positive reinforcement of exercise and preventing overtraining syndrome, allowing the most dedicated users to continue what would normally be excessive training (Hildebrandt et al., 2011). The above findings are in line with the salience and tolerance criteria of the components model (Griffiths, 2005), as well as the body image (Brower, 2002; Kanayama et al., 2010) and allostatic (Hildebrandt et al., 2011) models of AAS dependence as explained previously.

The older age of AAS dependents compared to nondependents can be explained by the criteria for meeting dependence diagnosis such as the duration of the dependent user pattern for at least 12 months (APA, 2013; Piacentino et al., 2015). The older age of the dependents also explains their higher proportion of married and not single persons compared to the nondependents. The findings of younger AAS initiation age, and lower educational attainment, education years, IQ, and knowledge of AAS effects can also be interpreted in light of problem behavior theory and its proposed ‘problem behavior syndrome’ (Jessor & Jessor, 1977) where involvement in one problem behavior such as AAS use is linked to involvement in other problem behaviours such as delinquency and lower academic achievement.

Additionally, the higher proportion of recreational athletes in AAS dependents compared to nondependents is in line with meta-analytic evidence (Sagoe et al, 2014b) showing that recreational athletes constitute the largest subgroup (18.4%) of AAS users, and

is understandable from an anti-doping perspective (Mottram, 2022). Also, the identified AAS use characteristics such as more types of AAS used, higher doses and a higher number of cycles among AAS dependents compared to nondependents is in line with the components (Griffiths, 2005), body image (Brower, 2002; Kanayama et al., 2010) and allostatic (Hildebrandt et al., 2011) models of AAS dependence.

Furthermore, altogether, the consistent higher association of AAS dependents with a wide array of biophysical, cognitive, emotional, and psychosocial syndromes in comparison with nonusers and nondependents is explainable with problem behavior theory (Jessor & Jessor, 1977), the components (Griffiths, 2005), body image (Brower, 2002; Kanayama et al., 2010) and allostatic (Hildebrandt et al., 2011) models of AAS dependence. For instance, in line with the allostatic model of AAS dependence (Hildebrandt et al., 2011), the long-term AAS use and exercise combination over time may lead to allostatic overload and related biophysical syndromes such as liver toxicity, lower acumbens and brain connectivity, and sexual dysfunction (Hauger et al., 2019b; Hildebrandt et al., 2011; Kanayama et al., 2009).

Strengths and limitations

The present study is, to the author's knowledge, the first meta-analytic and meta-regression study of AAS dependence that provides a global prevalence of AAS dependence and in addition investigates the correlates and sequalae of AAS dependence. The systematic literature search, study quality or risk of bias assessment, and data analysis combining meta-analysis and meta-regression analysis are also notable strengths of the present study. Thus, unlike previous literature reviews on the topic (Kanayama et al., 2009; Pope et al., 2014) that lack comprehensiveness and generalizability, this study provides estimates with external validity and therefore generalizability to the global population of AAS users. In this regard, the present study contributes to a better understanding of AAS dependents.

However, there are some limitations of the study. The aim of the study was to estimate the global prevalence of AAS dependence. Yet, only studies from Europe, North America and Oceania were identified with lack of representation from the South American, Asian and African regions. Also, the measure of dependence in all the included studies are based on self-reports, which could be inaccurate and affected by subjective interpretations. Also, many of the studies assessed lifetime AAS dependence, which could be inaccurate considering they rely on the participants' memory of events. Most of the studies included also rely on non-randomized methods and samples from weightlifter communities and gyms, which could exclude some of the AAS users and information about use in different environments.

In addition, web-based recruitment methods were employed in some studies in addition to flyers and approaching members in relevant contexts, making non-participation rates and therefore generalizability of findings hard to assess. That means that most of the studies have no numbers or data describing the people who do not respond or choose to participate in the studies. There could for instance be common traits among the participants who decided to respond that differ from the ones who didn't, and in this way the results could favour a subgroup of AAS dependents. Relatedly, most of the data is also based on men which is reasonable based on the male preponderance of AAS use (Sagoe et al., 2014b). Indeed, the included studies had a total of 1,680 males and only 25 females with female dependence prevalence reported in only two (Copeland, Peters, & Dillon, 2000; Vaskinn, Hauger, & Bjørnebekk, 2020) studies making gender prevalence estimation and comparison untenable. Finally, the included studies are cross-sectional which makes conclusions about causality and directionality of the findings difficult. This explains, for the avoidance of causal insinuations, the careful use of "sequelae" instead of "effects" or "outcomes" in comparisons of AAS dependents to nonusers and nondependents.

Implications for practice and future research

The high lifetime prevalence of AAS dependence found in this study is alarming and should have implications for further research attention on AAS, prevention work and clinical practice. The serious issues experienced by this group related to both physical and psychological health and cognitive and psychosocial functioning is of a public health concern on a global level, and should affect awareness of AAS use, AAS dependence and related consequences among health professionals. The findings of the present study can contribute to preventive work and treatment for AAS dependence, as well as inform interventions for harm reduction and treatment. Interventions that focus on highlighting the present findings of a high risk of developing dependence to AAS and the wide array of associated syndromes may be useful in preventing AAS initiation, as well as harm reduction and treatment of AAS users (Brower, 1992; Petróczi et al., 2014; Sagoe et al., 2016).

Future research should include longitudinal designs to achieve a better understanding of a causal direction on the correlates and sequelae found in this study, as well as studies involving more representation from Asian, African and South American regions. Furthermore, future studies are encouraged to include randomized sampling, use recruitment methods that can provide information on potential differences between respondents and nonrespondents, as well as ensure more representative sample groups to aim for a more comprehensive understanding of AAS dependence.

Conclusions

Despite some limitations, the results of the present study show a concerningly high lifetime AAS dependence prevalence rate of 36%. This suggests that about 2 of 5 persons who initiate AAS use experience AAS dependence at least once in their lifetime. AAS dependents experience a wide array of demographic issues as well as biophysical, cognitive, emotional and psychosocial syndromes. These reduce their quality of life, life expectancy, and have been implicated in the premature mortality among this population (Petersson et al., 2006;

Pärssinen et al., 2000; Smoliga, Wilber, & Robinson, 2023). Thus, AAS use and dependence should be regarded a serious public health issue. Targeted health interventions are required to prevent AAS use initiation, and to reduce, prevent, and treat dependence and associated syndromes among the AAS-using population.

References

Aizawa, K., Iemitsu, M., Maeda, S., Otsuki, T., Sato, K., Ushida, T., Mesaki, N., & Akimoto, T. (2010). Acute exercise activates local bioactive androgen metabolism in skeletal muscle. *Steroids*, *75*(3), 219–223. https://doi.org/10.1016/j.steroids.2009.12.002

Al Hashimi, M., Farahat, Y., Kandil, H., & Al Khalidi, I. (2023). Androgenic-anabolic steroid abuse trend and management: A prospective, cross-sectional, questionnaire-based survey. *Health Science Reports*, *6*(1), e1032. https://doi.org/10.1002/hsr2.1032

Albano, G. D., Amico, F., Cocimano, G., Liberto, A., Maglietta, F., Esposito, M., Rosi, G. L., Di Nunno, N., Salerno, M., & Montana, A. (2021). Adverse effects of anabolic-androgenic steroids: A literature review. *Healthcare*, *9*(1), 97. https://doi.org/10.3390/healthcare9010097

Alexander, G. M., Packard, M. G., & Hines, M. (1994). Testosterone has rewarding affective properties in male rats. *Behavioral Neuroscience*, *108*(2), 424–428. https://doi.org/10.1037/0735-7044.108.2.424

American Psychiatric Association. (1987). *Diagnostic and Statistical Manual of Mental Disorders* (3rd ed., revised). Washington, D.C.: American Psychiatric Publishing.

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). Washington, D.C.: American Psychiatric Publishing.

American Psychiatric Association. (2000). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.). Washington, D.C.: American Psychiatric Publishing.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorder*s (5th ed.). Washington, D.C.: American Psychiatric Publishing. https://doi.org/10.1176/appi.books.9780890425596

Arnedo, M., Salvador, A., Martinez-Sanchis, S., & Gonzalez-Bono, E. (2000). Rewarding properties of testosterone in intact male mice: A pilot study. *Pharmacology,*

Biochemistry and Behavior, *65*(2), 327–332. https://doi.org/10.1016/S0091-3057(99)00189-6

Barceloux, D. G. M. D., & Palmer, R. B. P. (2013). Anabolic-androgenic steroids. *Disease-a-Month, 59*(6), 226–248. https://doi.org/10.1016/j.disamonth.2013.03.010

Becona, E. (2018). Brain disease or biopsychosocial model in addiction? Remembering the Vietnam Veteran Study. *Psicothema*, *30*(3), 270–275. https://doi.org/10.7334/psicothema2017.303

Bjørnebekk, A., Kaufmann, T., Hauger, L. E., Klonteig, S., Hullstein, I. R., & Westlye, L. T. (2021). Long-term anabolic–androgenic steroid use is associated with deviant brain aging. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *6*(5), 579–589. https://doi.org/10.1016/j.bpsc.2021.01.001

Bjørnebekk, A., Walhovd, K. B., Jørstad, M. L., Due-Tønnessen, P., Hullstein, I. R., & Fjell, A. M. (2016). Structural brain imaging of long term anabolic-androgenic steroid users and non-using weightlifters. *Biological Psychiatry (1969)*. https://doi.org/10.1016/j.biopsych.2016.06.017

Bond, P., Smit, D. L., & de Ronde, W. (2022). Anabolic-androgenic steroids: How do they work and what are the risks? *Frontiers in Endocrinology, 13*, 1059473. https://doi.org/10.3389/fendo.2022.1059473

Borenstein, M., Hedges, L. V., Higgins, J. P. T., and Rothstein, H. R. (2009). *Introduction to Meta-Analysis.* Chichester: Wiley. https://doi.org/10.1002/9780470743386

Borenstein, M., Higgins, J. P. T., Hedges, L. V., & Rothstein, H. R. (2017). Basics of meta-analysis: *I*2 is not an absolute measure of heterogeneity. *Research Synthesis Methods, 8*, 5–18. https://doi.org/10.1002/jrsm.1230

Brennan, B. P., Kanayama, G., Hudson, J. I., & Pope, H. G. (2011). Human growth hormone abuse in male weightlifters. *American Journal on Addictions*, *20*(1), 9–13. https://doi.org/10.1111/j.1521-0391.2010.00093.x

Brower, K. J. (1992). Anabolic steroids: Addictive, psychiatric, and medical consequences. American *Journal on Addictions, 1*(2), 100–114.

Brower, K. J. (2002). Anabolic steroid abuse and dependence. *Current Psychiatry Reports, 4*(5), 377–387. https://doi.org/10.1007/s11920-002-0086-6

Brower, K. J., Blow, F. C., Young, J. P., & Hill, E. M. (1991). Symptoms and correlates of anabolic-androgenic steroid dependence. *British Journal of Addiction, 86*(6), 759–768.

Cadegiani, F. A., & Kater, C. E. (2017). Hypothalamic-pituitary-adrenal (HPA) axis functioning in overtraining syndrome: Findings from endocrine and metabolic responses on overtraining syndrome (EROS) – EROS-HPA axis. *Sports Medicine - Open, 3*(1), 1–11. https://doi.org/10.1186/s40798-017-0113-0

Cafri, G., Thompson, J. K., Ricciardelli, L., McCabe, M., Smolak, L., & Yesalis, C. (2005). Pursuit of the muscular ideal: Physical and psychological consequences and putative risk factors. *Clinical Psychology Review, 25*(2), 215–239. https://doi.org/10.1016/j.cpr.2004.09.003

Carlezon, W. A., Jr & Thomas, M. J. (2009). Biological substrates of reward and aversion: A nucleus accumbens activity hypothesis. *Neuropharmacology, 56 Suppl 1*(Suppl 1), 122–132. https://doi.org/10.1016/j.neuropharm.2008.06.075

Chamberlain, S. R., Lochner, C., Stein, D. J., Goudriaan, A. E., van Holst, R. J., Zohar, J., & Grant, J. E. (2016). Behavioural addiction – A rising tide? *European Neuropsychopharmacology, 26*(5), 841–855. https://doi.org/10.1016/j.euroneuro.2015.08.013

Chegeni, R., Notelaers, G., Pallesen, S., & Sagoe, D. (2021a). Aggression and psychological distress in male and female anabolic-androgenic steroid users: A multigroup latent class analysis. *Frontiers in Psychiatry, 12*, 629428–629428. https://doi.org/10.3389/fpsyt.2021.629428

Chegeni, R., Pallesen, S., McVeigh, J., & Sagoe, D. (2021b). Anabolic-androgenic steroid administration increases self-reported aggression in healthy males: A systematic review and meta-analysis of experimental studies. *Psychopharmacology, 238*(7), 1911–1922. https://doi.org/10.1007/s00213-021-05818-7

Clancy, G. P., & Yates, W. R. (1992). Anabolic steroid use among substance abusers in treatment. *Journal of clinical Psychiatry, 53*, 97–100.

Clark, A. S., & Henderson, L. P. (2003). Behavioral and physiological responses to anabolic-androgenic steroids. *Neuroscience and Biobehavioral Reviews*, *27*(5), 413–436. https://doi.org/10.1016/S0149-7634(03)00064-2

Cohen, J., Collins, R., Darkes, J., & Gwartney, D. (2007). A league of their own: Demographics, motivations and patterns of use of 1,955 male adult non-medical anabolic steroid users in the United States. *Journal of the International Society of Sports Nutrition*, *4*, 12. https://doi.org/10.1186/1550-2783-4-12

Copeland, J., Peters, R., & Dillon, P. (2000). Anabolic-androgenic steroid use disorders among a sample of Australian competitive and recreational users. *Drug and Alcohol Dependence*, *60*(1), 91–96. https://doi.org/10.1016/S0376-8716(00)80011-3

de Zeeuw, T. I., Brunt, T. M., Van Amsterdam, J., Van De Ven, K., & Van Den Brink, W. (2023). Anabolic androgenic steroid use patterns and steroid use disorders in a sample of male gym visitors. *European Addiction Research*, 1–10. https://doi.org/10.1159/000528256

Diethelm, D., Ege, G., Claussen, M. C., & Iff, S. (2022). The criminal liability of health care professionals treating anabolic steroid users under the SpoPA. *Sports Psychiatry, 1*(4), 157–166. https://doi.org/10.1024/2674-0052/a000029

Duval, S., & Tweedie, R. (2000). Trim and fill: A simple funnel-plot–based method of testing and adjusted for publication bias in meta-analysis. *Biometrics, 56*, 455–463.

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal, 315*, 629–634. https://doi.org/10.1136/bmj.315.7109.629

El-Reshaid, W., El-Reshaid, K., Al-Bader, S., Ramadan, A., & Madda, J. (2018). Complementary bodybuilding: A potential risk for permanent kidney disease. *Saudi Journal of Kidney Diseases and Transplantation*, *29*(2), 326–331. https://doi.org/10.4103/1319-2442.229269

Eriksson, A., Kadi, F., Malm, C., & Thornell, L.-E. (2005). Skeletal muscle morphology in power-lifters with and without anabolic steroids. *Histochemistry and Cell Biology*, *124*(2), 167–75. https://doi.org/10.1007/s00418-005-0029-5

Finfgeld-Connett, D. (2014). Use of content analysis to conduct knowledge-building and theory-generating qualitative systematic reviews. *Qualitative Research, 14*, 341–352. https://doi.org/10.1177/1468794113481790

Finkelstein, J. S., Lee, H., Burnett-Bowie, S.-A. M., Pallais, J. C., Yu, E. W., Borges, L. F., Jones, B. F., Barry, C. V., Wulczyn, K. E., Thomas, B. J., & Leder, B. Z. (2013). Gonadal steroids and body composition, strength, and sexual function in men. *The New England Journal of Medicine*, *369*(11), 1011–1022. https://doi.org/10.1056/NEJMoa1206168

Ganson, K. T., Hallward, L., Cunningham, M. L., Murray, S. B., & Nagata, J. M. (2023). Anabolic-androgenic steroid use: Patterns of use among a national sample of Canadian adolescents and young adults. *Performance Enhancement & Health, 11*(1), 100241. https://doi.org/10.1016/j.peh.2022.100241

George, O., Le Moal, M., & Koob, G. F. (2012). Allostasis and addiction: Role of the dopamine and corticotropin-releasing factor systems. *Physiology & Behavior*, *106*(1), 58–64. https://doi.org/10.1016/j.physbeh.2011.11.004

Goldman, A. L., Pope, H. G., & Bhasin, S. (2019). The health threat posed by the hidden epidemic of anabolic steroid use and body image disorders among young men. *Journal of Clinical Endocrinology and Metabolism, 104*(4), 1069–1074. https://doi.org/10.1210/jc.2018-01706

Goudy, T. R. (1994). *The behavioral concomitants of anabolic-androgenic steroids in strength athletes* (PhD thesis). Pennsylvania: Pennsylvania State University.

Gridley, D. W., & Hanrahan, S. J. (1994). Anabolic-androgenic steroid use among male gymnasium participants: dependence, knowledge and motives. *Sport Health, 12*, 11-11.

Griffiths, M. (2005). A 'components' model of addiction within a biopsychosocial framework. *Journal of Substance Use, 10*(4), 191–197. https://doi.org/10.1080/14659890500114359

Griffiths, S., Jacka, B., Degenhardt, L., Murray, S. B., & Larance, B. (2018). Physical appearance concerns are uniquely associated with the severity of steroid dependence and depression in anabolic–androgenic steroid users. *Drug and Alcohol Review, 37*(5), 664–670. https://doi.org/10.1111/dar.12688

Hardt, A., Stippel, D., Odenthal, M., Hölscher, A. H., Dienes, H.-P., & Drebber, U. (2012). Development of hepatocellular carcinoma associated with anabolic androgenic steroid abuse in a young bodybuilder: A case report. *Case Reports in Pathology, 2012*, 195607–195605. https://doi.org/10.1155/2012/195607

Harris, L. R., & Brown, G. T. L. (2010). Mixing interview and questionnaire methods: Practical problems in aligning data. *Practical Assessment, Research & Evaluation, 15*, 1. https://doi.org/10.7275/959j-ky83

Harvey, O., Keen, S., Parrish, M., & van Teijlingen, E. (2019). Support for people who use anabolic androgenic steroids: A systematic scoping review into what they want and

what they access. *BMC Public Health*, *19*(1), 1024–1024. https://doi.org/10.1186/s12889-019-7288-x

Hauger, L. E., Havnes, I. A., Jørstad, M. L., & Bjørnebekk, A. (2021). Anabolic androgenic steroids, antisocial personality traits, aggression and violence. *Drug and Alcohol Dependence*, *221*, 108604–108604. https://doi.org/10.1016/j.drugalcdep.2021.108604

Hauger, L. E., Sagoe, D., Vaskinn, A., Arnevik, E. A., Leknes, S., Jørstad, M. L., & Bjørnebekk, A. (2019a). Anabolic androgenic steroid dependence is associated with impaired emotion recognition. *Psychopharmacology*, *236*(9), 2667–2676. https://doi.org/10.1007/s00213-019-05239-7

Hauger, L. E., Westlye, L. T., & Bjørnebekk, A. (2020). Anabolic androgenic steroid dependence is associated with executive dysfunction. *Drug and Alcohol Dependence*, *208*, 107874. https://doi.org/10.1016/j.drugalcdep.2020.107874

Hauger, L. E., Westlye, L. T., Fjell, A. M., Walhovd, K. B., & Bjørnebekk, A. (2019b). Structural brain characteristics of anabolic–androgenic steroid dependence in men. *Addiction*, *114*(8), 1405–1415. https://doi.org/10.1111/add.14629

Helfer, S. G., Elhai, J. D., & Geers, A. L. (2015). Affect and exercise: Positive affective expectations can increase post-exercise mood and exercise intentions. *Annals of Behavioral Medicine*, *49*(2), 269–279. https://doi.org/10.1007/s12160-014-9656-1

Herlitz, L. C., Markowitz, G. S., Farris, A. B., Schwimmer, J. A., Stokes, M. B., Kunis, C., Colvin, R. B., & D'Agati, V. D. (2010). Development of focal segmental glomerulosclerosis after anabolic steroid abuse. *Journal of the American Society of Nephrology*, *21*(1), 163–172. https://doi.org/10.1681/ASN.2009040450

Hildebrandt, T., Shope, S., Varangis, E., Klein, D., Pfaff, D. W., & Yehuda, R. (2014). Exercise reinforcement, stress, and β-endorphins: An initial examination of exercise in

anabolic–androgenic steroid dependence. *Drug and Alcohol Dependence*, *139*, 86–92. https://doi.org/10.1016/j.drugalcdep.2014.03.008

Hildebrandt, T., Yehuda, R., & Alfano, L. (2011). What can allostasis tell us about anabolic–androgenic steroid addiction? *Development and Psychopathology*, *23*(3), 907–919. https://doi.org/10.1017/S0954579411000393

Hoy, D., Brooks, P., Woolf, A., Blyth, F., March, L., Bain, C., Baker, P., Smith, E., & Buchbinder, R. (2012). Assessing risk of bias in prevalence studies: Modification of an existing tool and evidence of interrater agreement. *Journal of clinical epidemiology*, *65*(9), 934–939. https://doi.org/10.1016/j.jclinepi.2011.11.014

Ip, E. J., Barnett, M. J., Tenerowicz, M. J., & Perry, P. J. (2011). The Anabolic 500 Survey: Characteristics of male users versus nonusers of anabolic-androgenic steroids for strength training. *Pharmacotherapy*, *31*(8), 757–766. https://doi.org/10.1592/phco.31.8.757

Ip, E. J., Lu, D. H., Barnett, M. J., Tenerowicz, M. J., Vo, J. C., & Perry, P. J. (2012). Psychological and physical impact of anabolic-androgenic steroid dependence. *Pharmacotherapy*, *32*(10), 910–919. https://doi.org/10.1002/j.1875-9114.2012.01123

Jessor, R., & Jessor, S. L. (1977). *Problem behavior and psychosocial development: A longitudinal study of youth.* New York: Academic Press.

Kanayama, G., Brower, K. J., Wood, R. I., Hudson, J. I., & Pope, H. G. (2009). Anabolic-androgenic steroid dependence: An emerging disorder. *Addiction*, *104*(12), 1966–1978. https://doi.org/10.1111/j.1360-0443.2009.02734.x

Kanayama, G., Cohane, G., Weiss, R., & Pope, H. (2003). Past anabolic-androgenic steroid use among men admitted for substance abuse treatment: An underrecognized

problem? *Journal of Clinical Psychiatry*, *64*(2), 156–160. https://doi.org/10.4088/JCP.v64n0208

Kanayama, G., Hudson, J. I., & Pope, H. G. (2008). Long-term psychiatric and medical consequences of anabolic–androgenic steroid abuse: A looming public health concern? *Drug and Alcohol Dependence*, *98*(1), 1–12. https://doi.org/10.1016/j.drugalcdep.2008.05.004

Kanayama, G., Hudson, J. I., & Pope, H. G. (2020). Anabolic-androgenic steroid use and body image in men: A growing concern for clinicians. *Psychotherapy and Psychosomatics*, *89*(2), 65-73. https://doi.org/10.1159/000505978

Kanayama, G., Pope, H. G., & Hudson, J. I. (2018). Associations of anabolic-androgenic steroid use with other behavioral disorders: An analysis using directed acyclic graphs. *Psychological Medicine*, *48*(15), 2601–2608. https://doi.org/10.1017/s0033291718000508

Kirkwood, K. (2017). Addiction to anabolic-androgenic steroids: A review. *British Journal of Pharmaceutical Research*, *16*, 1–6. https://doi.org/10.9734/BJPR/2017/33224

Koob, G. F. (1992). Drugs of abuse: Anatomy, pharmacology and function of reward pathways. *Trends in Pharmacological Sciences*, *13*(5), 177–184. https://doi.org/10.1016/0165-6147(92)90060-J

Koob, G. F., & Le Moal, M. (1997). Drug abuse: Hedonic homeostatic dysregulation. *Science*, *278*(5335), 52–58. https://doi.org/10.1126/science.278.5335.52

Koob, G. F., & Le Moal, M. (2001). Drug addiction, dysregulation of reward, and allostasis. *Neuropsychopharmacology*, *24*(2), 97–129. https://doi.org/10.1016/S0893-133X(00)00195-0

Lamarche, L., Gammage, K. L., & Ozimok, B. (2018). The gym as a culture of body achievement: Exploring negative and positive body Image experiences in men

attending university. *SAGE Open, 8*(2), 215824401877810. https://doi.org/10.1177/2158244018778103

Le Moal. (2009). Drug abuse: Vulnerability and transition to addiction. *Pharmacopsychiatry*, *42*(1), 42–55. https://doi.org/10.1055/s-0029-1216355

Lin, E., Tong, T., Chen, Y., & Wang, Y. (2020). Fixed-effects model: The most convincing model for meta-analysis with few studies. *arXiv,* doi: arXiv:2002.04211

Martínez-Sanchis, S., Aragon, C. M., & Salvador, A. (2002). Cocaine-induced locomotor activity is enhanced by exogenous testosterone. *Physiology & Behavior*, *76*(4), 605–609. https://doi.org/10.1016/S0031-9384(02)00764-3

McEwen, B. S., & Wingfield, J. C. (2003). The concept of allostasis in biology and biomedicine. *Hormones and Behavior*, *43*(1), 2–15. https://doi.org/10.1016/S0018-506X(02)00024-7

McVeigh, J., & Begley, E. (2017). Anabolic steroids in the UK: An increasing issue for public health. *Drugs: Education, Prevention & Policy*, *24*(3), 278–285. https://doi.org/10.1080/09687637.2016.1245713

Midgley, S. J., Heather, N., & Davies, J. B. (1999). Dependence-producing potential of anabolic-androgenic steroids. *Addiction Research*, *7*(6), 539–550. https://doi.org/10.3109/16066359909004404

Moher, D., Liberati A., Tetzlaff J., Altman, D. G., & The PRISMA Group. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA statement. *PLoS Medicine, 6*(7), e1000097. https://doi.org/doi:10.1371/journal.pmed1000097

Morton, J. P., Kayani, A. C., McArdle, A., & Drust, B. (2009). The exercise-induced stress response of skeletal muscle, with specific emphasis on humans. *Sports Medicine, 39*(8), 643–662. https://doi.org/10.2165/00007256-200939080-00003

Mottram, D. R. (2022). The evolution of doping and anti-doping in sport. In D. R. Mottram, & N. Chester (Eds.), *Drugs in sports* (8th ed., pp. 17–36). Abingdon, Oxon: Routledge. https://doi.org/10.4324/9781003096160-4

Nelson, B. S., Hildebrandt, T., & Wallisch, P. (2022). Anabolic-androgenic steroid use is associated with psychopathy, risk-taking, anger, and physical problems. *Scientific Reports*, *12*(1), 9133–9133. https://doi.org/10.1038/s41598-022-13048-w

Pärssinen, M., Kujala, U., Vartiainen, E., Sarna, S., & Seppälä, T. (2000). Increased premature mortality of competitive powerlifters suspected to have used anabolic agents. *International Journal of Sports Medicine*, *21*(3), 225–227. https://doi.org/10.1055/s-2000-304

Perry, P. J., Lund, B. C., Deninger, M. J., Kutscher, E. C., & Schneider, J. (2005). Anabolic steroid use in weightlifters and bodybuilders: An internet survey of drug utilization. *Clinical Journal of Sport Medicine*, *15*(5), 326–330. https://doi.org/10.1097/01.jsm.0000180872.22426.bb

Petersson, A., Garle, M., Granath, F., & Thiblin, I. (2006). Morbidity and mortality in patients testing positively for the presence of anabolic androgenic steroids in connection with receiving medical care: a controlled retrospective cohort study. *Drug and Alcohol Dependence*, *81*(3), 215–220. https://doi.org/10.1016/j.drugalcdep.2005.07.001

Petróczi, A., Dodge, T., Backhouse, S. H., & Adesanwo, C. (2014). Review of the literature on negative health risks based interventions to guide anabolic steroid misuse prevention. *Performance Enhancement & Health*, *3*(1), 31–44. https://doi.org/10.1016/j.peh.2014.08.001

Piacentino, D., Kotzalidis, G., Casale, A., Aromatario, M., Pomara, C., Girardi, P., & Sani, G. (2015). Anabolic-androgenic steroid use and psychopathology in athletes. A

systematic review. *Current Neuropharmacology*, *13*(1), 101–121. https://doi.org/10.2174/1570159x13666141210222725

Pope, H. G., & Kanayama, G. (2012). Anabolic–androgenic steroids. In J. C. Verster, K. Brady, M. Galanter, & P. Conrod (Eds.), *Drug abuse and addiction in medical illness: Causes, consequences and treatment* (pp. 251–264). New York, NY: Springer New York. https://doi.org/10.1007/978-1-4614-3375-0_19

Pope, H. G., & Katz, D. L. (1988). Affective and psychotic symptoms associated with anabolic steroid use. *American Journal of Psychiatry*, *145*(4), 487–90. https://doi.org/10.1176/ajp.145.4.487

Pope, H. G., Kanayama, G., & Hudson, J. I. (2012). Risk factors for illicit anabolic-androgenic steroid use in male weightlifters: A cross-sectional cohort study. *Biological Psychiatry*, *71*(3), 254–261. https://doi.org/10.1016/j.biopsych.2011.06.024

Pope, H. G., Kanayama, G., Athey, A., Ryan, E., Hudson, J. I., & Baggish, A. (2014). The lifetime prevalence of anabolic-androgenic steroid use and dependence in Americans: Current best estimates. *American Journal on Addictions*, *23*(4), 371–377. https://doi.org/10.1111/j.1521-0391.2013.12118.x

Pope, H. G., Katz, D. L., & Champoux, R. (1988). Anabolic-androgenic steroid use among 1,010 college men. *Physician and Sportsmedicine*, *16*(7), 75–81. https://doi.org/10.1080/00913847.1988.11709554

Pope, H. G., Kean, J., Nash, A., Kanayama, G., Samuel, D. B., Bickel, W. K., & Hudson, J. I. (2010). A diagnostic interview module for anabolic-androgenic steroid dependence: Preliminary evidence of reliability and validity. *Experimental and Clinical Psychopharmacology*, *18*(3), 203–213. https://doi.org/10.1037/a0019370

Pope, H. G., Khalsa, J. H., & Bhasin, S. (2017). Body image disorders and abuse of anabolic-androgenic steroids among men. *JAMA, 317*(1), 23–24. https://doi.org/10.1001/jama.2016.17441

Rahnema, C. D., Lipshultz, L. I., Crosnoe, L. E., Kovac, J. R., & Kim, E. D. (2014). Anabolic steroid–induced hypogonadism: Diagnosis and treatment. *Fertility and Sterility, 101*(5), 1271-1279. https://doi.org/10.1016/j.fertnstert.2014.02.002

Rasmussen, B. K., Jensen, R., & Olesen, J. (1991). Questionnaire versus clinical interview in the diagnosis of headache. *Headache: Journal of Head and Face Pain, 31*(5), 290–295. https://doi.org/10.1111/j.1526-4610.1991.hed3105290.x

Romero, L. M., Dickens, M. J., & Cyr, N. E. (2009). The reactive scope model — A new model integrating homeostasis, allostasis, and stress. *Hormones and Behavior*, *55*(3), 375–389. https://doi.org/10.1016/j.yhbeh.2008.12.009

Sagoe, D. (2014). *Anabolic steroid use is not just about bodybuilding.* The Conversation. https://theconversation.com/anabolic-steroid-use-is-not-just-about-bodybuilding-29180

Sagoe, D., Molde, H., Andreassen, C. S., Torsheim, T., & Pallesen, S. (2014b). The global epidemiology of anabolic-androgenic steroid use: A meta-analysis and meta-regression analysis. *Annals of Epidemiology*, *24*(5), 383–398. https://doi.org/10.1016/j.annepidem.2014.01.009

Sagoe, D., & Pallesen, S. (2018). Androgen abuse epidemiology. *Current Opinion in Endocrinology, Diabetes and Obesity*, *25*, 185–194. https://doi.org/10.1097/MED.0000000000000403

Sagoe, D., Andreassen, C. S., & Pallesen, S. (2014a). The aetiology and trajectory of anabolic-androgenic steroid use initiation: a systematic review and synthesis of

qualitative research. *Substance Abuse Treatment, Prevention and Policy,* 9(1), 27. https://doi.org/10.1186/1747-597X-9-27

Sagoe, D., Holden, G., Rise, E. N. K., Torgersen, T., Paulsen, G., Krosshaug, T., Lauritzen, F., & Pallesen, S. (2016). Doping prevention through anti-doping education and practical strength training: The Hercules program. *Performance Enhancement & Health, 5*(1), 24–30. https://doi.org/10.1016/j.peh.2016.01.001

Scarth, M., Westlye, L. T., Havnes, I. A., & Bjørnebekk, A. (2023). Investigating anabolic-androgenic steroid dependence and muscle dysmorphia with network analysis. *Research Square*, https://dx.doi.org/10.21203/rs.3.rs-2514206/v1

SFS. (1991). *Lagen om förbud mot vissa dopningsmedel. [Act prohibiting certain doping substances.].* Stockholm, Sweden: Government of Sweden.

Sharma, A., Grant, B., Islam, H., Kapoor, A., Pradeep, A., & Jayasena, C. N. (2022). Common symptoms associated with usage and cessation of anabolic androgenic steroids in men. *Best Practice & Research Clinical Endocrinology & Metabolism*, *36*(5), 101691–101691. https://doi.org/10.1016/j.beem.2022.101691

Smoliga, J. M., Wilber, Z. T., & Robinson, B. T. (2023). Premature death in bodybuilders: What do we know? *Sports Medicine, 53*(5), 933–948. https://doi.org/10.1007/s40279-022-01801-0

Solomon, R. L., & Corbit, J. D. (1974). An opponent-process theory of motivation: I. Temporal dynamics of affect. *Psychological Review*, *81*(2), 119–145. https://doi.org/10.1037/h0036128

Stoot, J. H. M. B., Coelen, R. J. S., De Jong, M. C., & Dejong, C. H. C. (2010). Malignant transformation of hepatocellular adenomas into hepatocellular carcinomas: A systematic review including more than 1600 adenoma cases. *HPB, 12*(8), 509–522. https://doi.org/10.1111/j.1477-2574.2010.00222.x

Stroup, D. F., Berlin J. A., Morton S. C., Morton, S. C., Olkin, I., Williamson, G. D., Rennie, D., Moher, D., Becker, B. J., Sipe, T. A., & Thacker, S. B. (2000). Meta-analysis of observational studies in epidemiology: A proposal for reporting. *JAMA*, 283, 2008e12. http://dx.doi.org/10.1001/jama.283.15.2008

Thiblin, I., Kristiansson, M., & Rajs, J. (1997). Anabolic androgenic steroids and behavioural patterns among violent offenders. *Journal of Forensic Psychiatry*, *8*(2), 299–310. https://doi.org/10.1080/09585189708412012

Tsatsoulis, A., & Fountoulakis, S. (2006). The protective role of exercise on stress system dysregulation and comorbidities. *Annals of the New York Academy of Sciences*, *1083*(1), 196–213. https://doi.org/10.1196/annals.1367.020

Vaskinn, A., Hauger, L. E., & Bjørnebekk, A. (2020). Theory of mind in users of anabolic androgenic steroids. *Psychopharmacology*, *237*(10), 3191–3199. https://doi.org/10.1007/s00213-020-05603-y

Vilar Neto, J. de O., da Silva, C. A., Lima, A. B., Caminha, J. de S. R., Pinto, D. V., Alves, F. R., Araújo, J. S., & Daher, E. de F. (2018). Disorder of hypothalamic–pituitary–gonadal axis induced by abusing of anabolic–androgenic steroids for short time: A case report. *Andrologia*, *50*(9), 13107. https://doi.org/10.1111/and.13107

Westlye, L. T., Kaufmann, T., Alnæs, D., Hullstein, I. R., & Bjørnebekk, A. (2017). Brain connectivity aberrations in anabolic-androgenic steroid users. *Neuroimage: Clinical*, *13*, 62–69. https://doi.org/10.1016/j.nicl.2016.11.014

Wood, R. I. (2004). Reinforcing aspects of androgens. *Physiology & Behavior*, *83*(2), 279–289. https://doi.org/10.1016/j.physbeh.2004.08.012

Wood, R. I. (2006). Anabolic steroids: A fatal attraction? *Journal of Neuroendocrinology*, *18*(3), 227–228. https://doi.org/10.1111/j.1365-2826.2006.01407.x

Woodward, C., Smith, J., Acreman, D., & Kumar, N. (2019). Hepatocellular carcinoma in body builders; An emerging rare but serious complication of androgenic anabolic steroid use. *Annals of Hepato-Biliary-Pancreatic Surgery*, *23*(2), 174–177. https://doi.org/10.14701/ahbps.2019.23.2.174

World Health Organization (WHO). (1993). *The ICD-10 classification of mental and behavioural disorders*. Geneva: World Health Organization.

PRISMA 2009 Checklist

Section/topic	#	Checklist item		Reported on page #
TITLE				
Title	1	Identify the report as a systematic review, meta-analysis, or both.		1
ABSTRACT				
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.		4–5
INTRODUCTION				
Rationale	3	Describe the rationale for the review in the context of what is already known.		24–25
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).		24–25
METHODS				
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.		–
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.		25–36, 31
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.		4–5, 25
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.		25
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).		4–5, 25–26
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.		26, 31
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.		25, 31–32
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.		31, 33–34

PRISMA 2009 Checklist

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).		4–5, 35–40
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.		4-5, 31–33, 35–46

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4-5, 26, 31–33
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	4–5, 37–46
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4-5, 25-26, 31-32
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	27–30
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	33–34
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	4–5, 35–46
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	4–5, 35–39
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	4–5, 31–33
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	4–5, 37–46
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	4–5, 45–53

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	50–51
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	4–5, 52-53
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	–

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097