

Anabolic-Androgenic Steroids and Aggression in Humans: Experimental Studies, Subgroups, and Longitudinal Risk

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Thesis for the degree of Philosophiae Doctor (PhD)
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I dedicate this thesis to my beloved brother

Scientific environment

I completed this dissertation at the Department of Psychosocial Science of the Faculty of Psychology, University of Bergen. I was affiliated to the Graduate School of Clinical and Developmental Psychology and the Human Enhancement and Body Image Lab (HEBI Lab) of the Bergen Addiction Research Group. My main supervisor has been Assoc. Prof. Dominic Sagoe with Prof. Ståle Pallesen as co-supervisor.

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Abbreviations

AAS	Anabolic-Androgenic Steroid(s)
AIDS	Acquired Immunodeficiency Syndrome
ATLAS	Adolescents Training and Learning to Avoid Steroids
CMA	Comprehensive Meta-Analysis
DSM	Diagnostic and Statistical Manuals of Mental Disorders
GDR	German Democratic Republic
ICD	International Classification of Diseases
LHT	Life History Theory
MLCA	Multigroup Latent Class Analysis
NSP	Needle and Syringe Program
PBT	Problem Behavior Theory
PBS	Problem Behavior Syndrome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomized Controlled Trials
SCT	Social Cognitive Theory
SLT	Social Learning Theory
SPSS	Statistical Package for Social Sciences
YOLO	You Only Live Once
WADA	World Anti-Doping Agency
WHO	World Health Organization

Abstract

Anabolic-androgenic steroid (AAS) use is a global public health concern. However, the relationship between AAS use and its psychological side effects, specifically aggression needs further elucidation. Results from experimental studies on this topic are inconsistent. Moreover, no previous study has examined patterns of aggression and psychological distress among male and female AAS users. Finally, although some studies have examined risk factors of AAS use in cross-sectional samples, there is a dearth of longitudinal studies on prevalence and risk factors for AAS use, particularly aggression, from late adolescence to early adulthood. Three studies were conducted to shed light on the aforementioned gaps in the literature. The aim of the first study was to systematically review and meta-analyse results from human randomized controlled trials (RCTs) on the effect of AAS administration on aggression. The second study aimed to investigate the patterns of aggression and psychological distress among AAS users among male and female AAS users. The third study aimed to examine the prevalence of AAS use, and longitudinal risk factors for AAS use intent, especially physical and verbal aggression, from late adolescence to early adulthood.

A systematic review and meta-analysis was conducted to accomplish the first study's aim. Twelve RCTs comprising a total of 562 healthy males were identified and included in the meta-analysis after systematic searches of MEDLINE, PsycINFO, ISI Web of Science, ProQuest, Google Scholar, and the Cochrane Library. The Q -statistic and I^2 index were utilized to assess heterogeneity. Additionally, to achieve the aim of the second study, a cross-sectional survey was conducted on 206 AAS users (females = 58.30%) in Iran. Participants' ages ranged from 14 to 56 ($M = 26.86$, $SD = 7.12$). Data was collected from Tehran, Iran. The questionnaire comprised questions on demographics, AAS use, aggression and psychological distress. A multigroup latent class analysis (MLCA) was conducted to

elucidate patterns of aggression and psychological distress among this sample. Measurement invariance examined sex-specificity of identified patterns of aggression and psychological distress. Moreover, to accomplish the aim of the third study, a longitudinal study of the prevalence of AAS use, and risk factors of AAS use intent, particularly the role of physical and verbal aggression from age 18 to 19 was conducted in Norway. At the first wave, 1,333 18-year-olds (females = 58.9%) completed a questionnaire containing demographic, AAS use and intent, other substance (alcohol, cigarette, and snus) use, aggression, anxiety, and depression. At age 19 ($N = 1277$, females = 61.7%), they completed the same set of questionnaires. To analyse the data descriptive statistics, correlations, and hierarchical multiple regression were utilized

Results of the first study, after excluding an outlier, indicated that AAS administration is associated with a small increase in self-reported aggression using a random-effects model. This result was replicated when restricting the analysis to the effect of acute AAS administration on self-reported aggression under a fixed-effect model. For the second study, the MLCA identified five subgroups of AAS users. The first and smallest subgroup (7.63%) comprised highly aggressive and moderately distressed users. The second subgroup (18.64%) consisted of moderately aggressive and distressed users. The third subgroup (22.95%) was composed of users with moderate levels of direct aggression (physical and verbal aggression) as well as distress, and mild levels of indirect aggression (anger and hostility). The fourth subgroup (11.71%) was made up of users with mild levels of direct aggression and moderate levels of indirect aggression and psychological distress. Finally, the fifth and largest subgroup (39.06%) encompassed users with low levels of aggression and mild levels of psychological distress. Results from measurement invariance analysis indicated that a homogenous five-class solution is the best model for both sexes. However, sex was significantly associated with the probability of belongingness to subgroups with

members of the highly aggressive and moderately distressed subgroup more likely to be male users whereas members of the fifth subgroup were more likely to be female. Results of the third study indicated an AAS use prevalence of 1 person at age 18 to 4 persons at age 19. AAS use intent, being male, living alone, and actual AAS use at age 18 were predictive risk factors of AAS use intent at age 19. From age 18 to 19, physical aggression and verbal aggression decreased significantly in both sexes and, did not predict AAS use intent at age 19.

Altogether, it can be inferred from the above results that AAS administration increases aggression in RCTs. Additionally, the above results provide evidence of the idiosyncratic patterns of aggression and psychological distress among male and female AAS users, and denote the lack of prospective associations between physical or verbal aggression and AAS use intent from ages 18 to 19. Findings from these studies contribute to the evidence base on AAS use and aggression. Potential applications of these findings in future research, policymaking and public health interventions is also discussed.

List of papers

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

1.1 Anabolic-androgenic steroids

Anabolic-androgenic steroids (AAS) are a family of drugs comprising the male hormone testosterone and its synthetic derivatives (Kanayama & Pope, 2018). These drugs have been developed over the last 75 years. AAS possesses both anabolic (i.e., facilitating muscle building and fat loss) and androgenic (i.e., masculinization properties such as deepening of the voice, sperm production, and growth of pubic hair) effects. Even though the pharmaceutical industry has produced substances in which the androgenic effects have been minimized and the main effects are anabolic, yet both effects of AAS are inseparable (Pope et al., 2013). Thus, in this thesis, AAS refers to testosterone and its synthetic derivatives which have inseparable anabolic and androgenic effects.

During the early years of the twentieth century, testicular dysfunction was treated with transplanting animal and human testicular material into patients (Hoberman & Yesalis, 1995). In the 1930s scientists isolated and synthesized the hormone testosterone and showed its anabolic effects, abolishing the aforementioned practice (Butenandt & Hanisch, 1935). Shortly thereafter, testosterone and its synthetic derivatives were available for both oral and injectable administration to the medical community. In the 1940s, AAS was used in the medical community to treat hypogonadism, anemia (Behre & Nieschlag, 2012) and depression in men (Altschule & Tillotson, 1948). AAS was shown to be effective with several patients reporting euphoria and increased libido after use (Altschule & Tillotson, 1948). In recent years, AAS have been clinically administered for revitalizing aging in men, and for the treatment of male hypogonadism (Behre & Nieschlag, 2012). AAS have also been prescribed for patients with muscle contusion injury, breast cancer, and for the prevention of muscle wasting in patients suffering from diseases such as AIDS, osteoporosis, and chronic obstructive pulmonary disease (Beiner et al., 1999; Bhasin et al., 2010; Ferreira

et al., 1998; Johns et al., 2005; Rabkin et al., 1995; Tenover, 1994). Additionally, it has been suggested that AAS can be used by males with type 2 diabetes or hypogonadism to increase their libido, energy level, and bone density and decrease their anemia and fat storage thereby improving their overall quality of life (Caliber & Hackett, 2019). AAS are also administered to postmenopausal women to increase their libido (Islam et al., 2019).

Boje (1939) first suggested that sex hormones improve physical performance. Simultaneously, the anabolic effects of testosterone were being assessed in normal men and women (Kenyon et al., 1940; Simonson et al., 1944). From the 1960s however, non-medical use of AAS has been associated with 'doping'. In this period, AAS was mainly used by elite athletes and bodybuilders in order to increase their muscle mass and their performance. Additionally, during this era, the German Democratic Republic (GDR) arranged a program about AAS doping for their Olympic athletes. After the collapse of GDR in 1990s, classified documents indicated that from 1966 onward, the program consisted of physicians and scientists who worked on development and administration of AAS on thousands of athletes (Hoberman, 1992).

From the 1970s, AAS use shifted from elite athletes and bodybuilders into the non-athletic population (Kanayama & Pope, 2018; Maravelias et al., 2005). Today, they are predominantly used as illicit self-administration drugs, where supratherapeutic doses are typically used to enhance performance and physical appearance among the general population (Bahrke & Yesalis, 2004). Thus, being a professional athlete and sports participation are no longer the primary risk factor for AAS use (Harmer, 2010). A meta-analysis on the global prevalence of AAS use estimated that 3.3% of the world's population has used AAS at least once with use being, expectedly, more popular among men (6.4%) compared to women (1.6%) (Sagoe et al., 2014a). Indeed, in this meta-analysis AAS was most prevalent among recreational sportspersons (18.4%) followed by athletes (13.4%).

AAS can be self-administered orally in the form of pills, parenterally by intramuscular injection, or transdermally in the form of patches or topical gel (van de Ven et al., 2020). It has been indicated that since data on AAS are increasingly being collected within Needle and Syringe Programs (NSPs), non-injectors have become an overlooked group of AAS users and require attention (van de Ven et al., 2020). Users typically administer AAS in phases known as “cycles”. The two main cycles are “on cycle” which is the phase in which AAS is used and typically lasts from 6 to 18 weeks (Copeland et al., 2000) and the “off cycle” which is a phase where no AAS is used. The purpose of the “off cycle” is to prevent tolerance and the experience of side-effects as well as getting the natural production of androgens back to their normal activity and level. In this off period some facilitates this by drugs, such as clomiphene, which blocks the estrogen receptors in the hypothalamus, with increased release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) as result. Also, other drugs may be used to reduce catabolic effects of cortisol.

Collectively, the measures taken to lessen the side-effects of AAS and to re-initiate the natural production of androgens are referred to as post cycle therapy (Griffiths et al., 2017). Another mode of AAS use is called “blitz-cycling” which is when users constantly change the type of AAS they administer in order to avert tolerance and androgen receptor down-regulation. Also, the “blast and cruise” mode of use is when users do not have an “off cycle” phase but instead switch between administering high (blast) and low (cruise) dosages (Sagoe et al., 2015a). “Stacking” is another mode of administration AAS referring to the use of different types of AAS concurrently in order to ensure saturation of all androgen receptors, increase metabolism, enhance performance, build muscle, or counter unwanted effects of other AAS (Backhouse, 2012; Hoffman & Ratamess, 2006). Additionally, AAS is often used concurrently with other licit or illicit drugs in order to increase the effectivity of

AAS or for other purposes (Dodge & Hoagland, 2011). AAS users typically self-administer supraphysiologic doses over relatively long periods (Pope & Kanayama, 2012).

1.2 Typologies of AAS users

AAS users are a heterogeneous population amongst which there is variation in terms of motives for use, predispositions, and risk factors for use. Some studies have sought to identify subgroups of AAS users based on motives for use and approaches toward AAS. After systematically synthesizing studies regarding the experiences of AAS users, a review identified four main subgroups of AAS users: aesthetic users, occupational (non-sporting) users, psychological users, and sports users (Sagoe, 2014). Aesthetic users are mostly concerned with their body image and their main purpose of AAS use is to enhance their appearance and sexual attractivity. Occupational users engage in AAS use to enhance their aggression and body strength, personal security, and sexual attraction. This group typically include criminals, security workers, and male models. Psychological users such as persons with psychological problems, like low self-esteem or depression utilize AAS in order to enhance their confidence, and psychological well-being. Finally, sports users include competitive and recreational sportspeople (e.g., bodybuilders, athletes, and weightlifters) with enhanced aggression and muscle mass, physiological recovery, athletic performance and injury prevention as their main purposes for AAS use. It should be noted that some individuals may belong to one or more subgroups.

A qualitative study (Christiansen et al., 2017) presented a typology based on men's approach to AAS use in which four user types are proposed. These typologies have received empirical support from a study of 611 AAS users from England, Scotland and Wales (Zahnnow et al., 2018). First is the expert type (24.9%) in which the user chooses the safest and most effective way of AAS utilization by achieving knowledge regarding dosage, concurrent use with other drugs, and possible cycles on websites and blogs. Second is the

well-being type (38.6%) comprising users whose priority is to experience physical, mental, and social well-being. Such users try to keep the risks of AAS use as low as possible. The “You Only Live Once” (YOLO) type (11.1%) represents users who are more likely into junk food, alcohol consumptions, and other recreational drugs. These AAS users’ main aim is looking muscular in order to achieve high social status and are not concerned with AAS side-effects. The YOLO type is more likely to be aggressive and end up in fights and they are more likely to use stimulants concurrently (Zahnow et al., 2018). The athlete type (25.4%) represents a user committed to competitive sports and his/her main focus is to achieve his goal. He/she trains hard and avoids junk food and alcohol. If he notices that fellow competitors are using higher dosages of AAS, he will typically utilize higher dosages as well (Christiansen et al., 2017; Zahnow et al., 2018).

Subgroups of appearance- and performance-enhancing drug (APED) users have also been examined by Hildebrandt et al. (2007). Results of that study indicated that patterns of APED use depend on different training goals and identities. The first subgroup of APED users was heavy polypharmacy users including body builders who used high dosages for long periods. The second subgroup comprised the fat-burning group who identified themselves as power lifters and used APED in order to add muscle mass. The third subgroup primarily included the mass-making group consisting of users who preferred lean muscles and were more likely to be fitness or endurance athletes. Finally, the fourth subgroup consisted of the normal APED group including the majority of participants and they used low to moderate dosages of AAS for shorter periods of time. Those in this group identified themselves as recreational weightlifters (Hildebrandt et al., 2007). Identifying the motives and risk factors for AAS use and subgroups of AAS users can help design prevention policies and identify at risk subgroups of users (Harvey, 2020).

1.3 Adverse effects of AAS use

The benefits of AAS mentioned by users include gained muscle mass, improved performance and enhanced appearance, boosted confidence, elevated mood, and increased libido (Davis & Arnocky, 2020; Mey et al., 2018; Smit et al., 2020). However, it has been shown that when administered illicitly, users experience various side effects or harms particularly after a long-term use of supraphysiologic doses or when concurrently used with other substances (Mey et al., 2018). Some of these harms to health can be permanent (Torrise et al., 2020).

1.3.1 Harms to the physiological system

One of the major concerns regarding AAS use is cardiovascular disorders induced by AAS use such as cardiomyopathy, high blood pressure, fibrosis, and myocardial infarction (Angell et al., 2012; Neto et al., 2018; Baggish et al., 2017; Pirompol et al., 2016). Other general effects of AAS encompass sleep abnormalities, hematologic effects, hepatic, neuromuscular and skeletal, dermatologic, immunological, and renal impairment (Ganesan et al., 2020; Pope et al., 2014a). In males, AAS use has been associated with decreased libido, increase in prostate-specific antigen, testicular atrophy, benign prostatic hypertrophy, low testosterone level, erectile dysfunction, and oligospermia (Armstrong et al., 2018; Christou et al., 2017; Ganesan et al., 2020). In females, AAS use has been linked to lower-pitched voice, hirsutism, breast atrophy, male-pattern baldness, clitoromegaly, and irregular menses (Bensoussan & Anderson, 2019; Christou et al., 2017).

1.3.2 Harms to the brain and cognition

AAS permeate the blood-brain barrier and act on the central nervous system (Bertozi et al., 2018). Recent laboratory and neuroimaging studies have reported deviant brain aging (Bjørnebekk et al., 2020), brain abnormalities (Bjørnebekk et al., 2017; Hauger et al., 2019) and cognitive impairments such as deficits in retrospective and prospective

memory (Heffernan et al., 2015) in long-term AAS users. Additionally, long-term AAS use has also been linked to higher risk of dementia (Kaufman et al., 2019). Deficiencies in connectivity between brain structures important for normal cognitive and emotional functioning such as the amygdala and the default-mode network, the dorsal attention network and the superior and inferior frontal gyri, as well as the anterior cingulate cortex are also associated with AAS use (Seitz et al., 2017; Westlye et al., 2017).

1.3.3 Harms to adolescents' health

Many studies have raised concerns about the prevalence of AAS use among adolescents (Cohen et al., 2007; Dunn & White, 2011; Sagoe et al., 2015c). Evidence from systematic reviews suggest that about 13% of AAS users initiate use in adolescence and about 20% of adolescents have at least one AAS-using acquaintance (Pope et al., 2014b; Sagoe et al., 2014a; Sagoe et al., 2015c). Results from the Youth Risk Behavior Surveillance System survey in the United States suggested that 3.2% of all students in grades 9 through 12 have taken AAS illicitly at some point in their life (Kann et al., 2013). Many adolescents believe that they are invulnerable to the physical and psychological harms of AAS use (Blahshill, 2014).

In addition to the harmful effects of AAS mentioned earlier, adolescent AAS use is also linked to stunted growth, brain and neurological disorders, and alteration of cognition as well as emotional reactivity to social encounters (Cunningham et al., 2013). During adolescence some brain organizations which are related to gonadal steroids such as testosterone, start to remodel (McCarthy, 2008; Schulz et al., 2009). For example, it has been suggested that testosterone levels are positively linked to increase in gray matter in adolescent boys (Peper et al., 2009). Moreover, several studies suggest that AAS exposure during adolescence can affect amygdala function in anxiety and fear inducing situations (Ernst et al., 2007). AAS use during adolescence have been shown to affect different

neurotransmitters' level such as serotonin, catecholamines (e.g., dopamine and norepinephrine), and GABA (Frahm et al., 2011). Overall, all these changes in neurotransmitters' levels and brain organizations can increase the likelihood of behavioral and emotional disorders (Cunningham et al., 2013) since adolescents' brains are still developing, they are more susceptible to the detrimental effects of AAS use (Bahrke et al., 2000) and these harms may be permanent (Hildebrandt et al., 2014).

1.3.4 Risks of AAS administration

AAS can be administered orally or can be injected (van de Ven et al., 2020). The oral use of AAS has been uniquely linked to liver toxicity (Niedfeldt, 2018). It has been found that oral AAS users are more likely than injecting AAS users to use psychoactive substances and less likely to be informed about harm reduction and medical advice programs (van de Ven et al., 2020). People who inject drugs such as AAS are at risk of bacterial, fungal, and viral infections (Hope et al., 2013). A significant proportion of AAS users experience hepatitis B or C and HIV infections (Hope et al., 2013). The prevalence of HIV among AAS injectors is similar to that amongst psychoactive substance injectors (McVeigh & Begley, 2017; Hope et al., 2016). Additionally, AAS are mostly produced in underground 'laboratories' (Brennan et al., 2018) and sold on the illicit market. In addition, they are usually combined with various ancillary or supplemental substances, of which a large proportion are illegal in many jurisdictions (Evans-Brown et al., 2012). Indeed, an analysis of AAS products in a recent study indicated that the content of these product oftentimes does not match the label information (Smit et al., 2020). Hence, AAS may be contaminated with toxic biological or chemical matter and pathogens thereby causing additional and unexpected harms to AAS users (Smit et al., 2020; Weber et al., 2017).

As indicated previously, AAS are often concurrently used with other licit or illicit drugs in order to enhance AAS effect, reduce the side effects of AAS, or for other purposes

(Dodge & Hoagland, 2011). Robust evidence indicates that polydrug use, denoting the concurrent use of multiple drugs or substances, is common among AAS users (Dodge & Hoagland, 2011; Molero et al., 2017; Sagoe et al., 2015a). In the 1990s, polypharmacy was mostly restricted to a small number of AAS combined with tamoxifen citrate and human growth hormone (i.e., human chorionic gonadotrophin) (Korkia & Stimson, 1993; Lenehan et al., 1996). A systematic review of quantitative studies on polypharmacy among AAS users indicated that the main supplementary or ancillary drugs they use are alcohol, cannabinoids, amphetamine, clenbuterol, cocaine, ecstasy, ephedrine, somatropin, insulin, thyroxine, selective estrogen receptor modulators, aromatase inhibitors, and human chorionic gonadotropin (hCG) (Hakansson et al., 2012; Molero et al., 2017; Zahnow et al., 2020). Moreover, non-AAS substances are also used to enhance performance, increase fat burn, counter the side effects of AA, and relax muscles after intense exercises. Polydrug use among AAS users has been shown to increase the risk of short- and long- term consequences of cross-drug interactions about which AAS users mostly are unaware of. Polypharmacy use can also lead to complicated medical responses in case of medical emergency and increase risk of adverse health effects (Molero et al., 2017; Nieschlag & Vorona, 2015).

1.3.5 Harms to mental health

AAS dependence

Substance use disorders are among the most prevalent psychological disorders (Hoaken et al., 2012). In assessing the harms of substance use, people who are diagnosed with substance use dependence are known to be at greater risk of harm. Like other substances users, AAS users sometimes develop a dependence syndrome (Brower, 2002) which is also characterized by experiencing withdrawal symptoms and continued use despite experiencing adverse effects (Kanayama et al., 2009a; Brower, 2002). The medical,

cognitive, and psychological side effects of AAS use can be found in those users who fulfill criteria for AAS dependence syndrome (Kanayama et al., 2009a). It has been estimated that 30% of AAS users experience a dependence syndrome (Kanayama et al., 2009a). Compared to nondependent users, AAS dependent users experience higher physical (Bjørnebekk et al., 2020; Hauger et al., 2020), cognitive (Hauger et al., 2020; Vaskinn et al., 2020), emotional (Ip et al., 2012; Westlye et al., 2017), and psychosocial harms (Hauger et al., 2019, 2020). Particularly, AAS dependents are more likely to be involved in social conflicts and they show higher levels of aggression and antisocial behaviors compared to non-dependents (Brower et al., 1991; Hallgren et al., 2015; Hauger et al., 2019; Kanayama et al., 2009a). Like tobacco, alcohol, and opiates dependence, withdrawal symptoms such as decreased libido, depressed mood, and fatigue that arise from discontinuation are also observed among AAS dependents (Kanayama et al., 2009a).

Mood disorders

During the 1980s, some case and field studies began to report manic or hypomanic symptoms during AAS exposure and depressive symptoms, suicidal thoughts, and sometimes committed suicide upon AAS withdrawal (Choi et al., 1990). Not all AAS users experience manic or hypomanic symptoms (Clark & Henderson, 2003). However, among those who experience these symptoms, they appear within days or weeks after AAS use initiation. Another factor affecting the appearance of these symptoms is AAS dosage as they are more common among persons using more than 1000 mg of testosterone equivalent per week which is 15-20 times more than the testosterone a healthy male produce (Pope & Katz, 1994). It has been suggested that the manic or hypomanic symptoms are associated with aggressive and violent behaviors among AAS users as well (Pagonis et al., 2006). Depressive symptoms, on the other hand, can appear within weeks of AAS withdrawal (Mey et al., 2018). These symptoms are also idiosyncratic and not all the AAS users experience

them upon withdrawal (Kanayama et al., 2020). Further, AAS use has been associated with increased sexual coercion and sexual motivation (Keleta et al., 2007). Several reports of severe psychiatric side effects including psychosis and extreme mood swings induce worries because these mental states are associated with violent harm to AAS users and/or others (Brower, 2009).

1.4 Aggression

Aggression can be explained as any forms of behavior that delivers harm (Ramírez, 2010). Aggressive behaviors may be representative of psychological adaptations useful for survival with the goal of taking advantage when resources are limited and when harmful behaviors are more effective than negotiation (Buss, 1961; Haller & Haller, 2014). Further, aggression is intentional, and goal-centered with the recipient of the aggressive behavior is typically aversive towards it (Allen & Anderson, 2017). From an evolutionary perspective, aggression evolved as a means to gain and assert social status and in order to access or protect resources such as mates, food, territory and offspring (Buss, 1961; Darwin, 1871). Social psychologists define violence as severe form of aggression with serious physical and/or psychological harm as its main goal or consequence (Allen & Anderson, 2017; Piosiadlo et al., 2014). In this thesis, violence is perceived as a form of aggression and “aggression” is used in reference to both aggression and violence. Aggression can cause physical, emotional, and/or social harm (Allen & Anderson, 2017; Carroll & McCarthy, 2018).

In general, the bimodal classification of aggression identifies aggression as proactive aggression which is also called instrumental aggression and reactive aggression which is also called impulsive aggression (Haller, 2013). Proactive aggressive behaviors are mostly purposeful and offensive and have low emotional activity (Smeijers et al., 2018). The main motivation of proactive aggression is gaining an incentive through aggressive means and not

harming others (Smeijers et al., 2018). Proactive aggression involves low levels of guilt, emotional activity, and moral inhibition (Bussey et al., 2015; Euler et al., 2017; Nagy et al., 2012). These characteristics help persons who deploy proactive aggression justify their behavior and achieve their goal (Smeijers et al., 2018). Proactive aggression results from excessive activation of reward circuits and same circuits are activated due to the rewarding effect of substance use (Bussey et al., 2015). Indeed, it has been shown that proactive aggressive behaviors are associated with drug addiction and substance use (Golden & Shaham, 2018). In addition to proactive aggression outlined above, aggression may also be affective (e.g., reflecting more immediate expressions of emotions; Ramírez, 2010). Reactive aggression is described as aggression that is impulsive, hostile, violent, and characterized by high emotional reactivity (Haller, 2013). Reactive aggression happens as a response to external threats or frustrating stimuli. The main motivation of reactive aggression is to remove the threat or stimuli and it is associated with a cortical control failure (Wrangham, 2018).

Another classification of aggression identifies aggressive behavior as direct and indirect aggression. Direct aggression includes physical and verbal acts of aggression and there is risk of serious physical, psychological and sexual harm when direct aggressive behaviors are severe (Wyckoff & Kirkpatrick, 2016). Indirect aggression includes hostile behaviors such as gossip in order to manipulate social situations (Björkqvist, 2018). The main motivation of indirect aggression is causing a psychological and/or social harm to the targeted person (Björkqvist, 2018).

Aggression is used by all species and it is a normal and necessary component of social behavior (van Staaden et al., 2011). In general, an aggressive behavior is abnormal when it is goalless, or when its costs outweigh its benefits (World Health Organization; WHO, 2002; Vaughn et al., 2015). In humans, aggressive behaviors have decreased due to a

civilization process such as the centralization of the state and a change in cultural norms which has made some forms of aggression abnormal or illegal (Wrangham, 2018), for example, when the aggressive behavior is life threatening or it increases chances of future post-traumatic stress disorder or other types of psychiatric disease in victims and observers of the aggressive behavior. Aggression is predicted to threaten more lives by 2030 than the most prevalent diseases such as Alzheimers and breast cancer (World Health Organization, 2010).

1.4.1 Assessment of aggression

Aggression in humans is assessed using laboratory behavioral measures, self-reports, and observer reports (Björkqvist et al., 1994; Buss & Perry, 1992; Chester & Lasko, 2019). As each form of assessment has strengths and limitations, triangulation and meta-analysis provide the best evidence of aggression assessment (Murad, Asi, Alsawas, & Alahdab, 2016; Warburton, 2014). Aggression measures used in investigating the relationship between AAS use and aggression are described next.

Laboratory behavioral measures

Laboratory behavioral measures assess aggression in laboratory settings (McCarthy et al., 2018). The Point Subtraction Aggression Paradigm (PSAP; Cherek, 1981) is a popular behavioral measure assessing aggression and competitiveness mostly in experimental settings (Geniole et al., 2017). The PSAP is an online computer game with the main goal of the game being winning over a fictitious opponent, gaining as many points as possible and exchanging the points for money at the end of the game. To provoke participants, the fictitious opponent starts taking points from the participants once they start collecting many points. At this point, participants are given three options: they can press the same predetermined key that they have been pressing from the beginning of the game, they can

press a different key that protects the points they already have for some time, or they can press a key that helps them steal points from the fictitious opponent. However, the researcher mentions to the participants that they are randomly assigned to a condition where they don't get to keep the points they steal from the opponent. The main idea of provoking participants and later using the concept of stealing is that participants are put in a competitive environment with stealing as a means of harming (i.e., aggressive behavior) the opponent. Previous studies suggest that the relationship between AAS administration and aggression are stronger when assessed by behavioral aggression measures compared to self-report measures (Archer et al., 2005; Carré et al., 2017)

Self-report measures

Using self-report measures, respondents indicate their aggressive behaviors, emotions and cognitions typically via questionnaires. Self-report measures are popular in the assessment of AAS use and aggression. The Buss-Perry Aggression Questionnaire (BPAQ; Buss & Perry, 1992) is a self-report measure that assesses four different factors. These are anger (i.e., an aggressive affection linked to high psychophysiological activation and frustration), hostility (i.e., an aggressive cognitive attitude towards others), physical aggression, and verbal aggression (Sanz et al., 2010). The Buss-Durkee Hostility Inventory (BDHI; Buss & Durkee, 1975) is another widely used self-report measure for the assessment of cognitive (hostility) and affective (anger) aggression. This inventory consists of eight subscales. Two subscales assess two different types of hostility (resentment and suspicion), five subscales assess five different types of aggressive behaviors (assault, indirect aggression, irritability, negativism, verbal aggression, and guilt). Anger, the affective aspect of aggression, can also be assessed using the Multidimensional Anger Inventory (MAI; Siegel, 1986). The MAI assesses the frequency, duration, magnitude, mode of expression

(i.e., anger-in vs. anger-out, guilt, brooding, and anger-discuss), hostile-outlook, and range of anger-eliciting situations.

Another widely used measure of aggression is the Profile of Mood States (POMS; McNair et al., 1992) that consists of 65 adjectives that describe temporary and discrete mood states. The POMS consists of six bipolar factors including anxious-composed, hostile-agreeable, depressed-elated, unsure-confident, tired-energetic, and confused-clearheaded. The Aggressive Provocation Questionnaire (APQ; O'Connor et al., 2001) is also a self-report used in studies examining the relationship between AAS administration and aggression (e.g., O'Connor et al., 2002, 2004). The APQ consists of 21 vignettes that represent real provocative situations. Participants read the vignettes and report how they feel at that moment about each situation with the response alternatives being: angry, frustrated, and irritated. Next, participants report how they would react in each situation with response alternatives being: avoiding, no response, getting angry, showing assertive behavior, and showing direct aggression.

Observer reports

Observer-report measures of aggression (e.g., the Partner Aggression Questionnaire: AQ-P; O'Connor et al., 2001) are typically adapted versions of self-report measures (e.g., the Aggression Questionnaire: AQ; Buss & Perry, 1992). They are used to decrease possible problems associated with self-reports (e.g., social desirability response bias) and for obtaining an evaluation of the subject's aggressive behaviors and emotions from their partner, acquaintance or other observer (O'Connor et al., 2004). Observer report aggression measures are usually completed in a private room in the subject's absence. It has been shown that observer reports provide different information than self-reports in the same study due to differences in perspective (Abernethy, 2015). Although observer-report measures of aggression do not take into account internal processes such as the motives and intentions of

the subject, they are useful for obtaining information about the aggressive behavior, emotions, and personality of a subject (Mount et al., 1994; O'Connor et al., 2001).

1.5 Substance use and aggression

Substance use and aggression frequently co-occur (Pihl & Sutton, 2009; Tomlinson et al., 2016). There is robust evidence on the association between substance use (e.g., alcohol, psychostimulants, opioids, and hallucinogens) and aggression in adolescence, adulthood, as well as in intimate relationships (Tomlinson et al., 2016). These associations present important legal, social, and psychological dilemmas (Hammersley, 2011). Further, since substance use disorders are among the most prevalent mental disorders, the association between substance use and aggression induces serious concerns (Hoaken et al., 2012). Overall, studies on the relationship between substance use and aggression have found differing unidirectional and bidirectional associations between these two behaviors. Studies supportive of a unidirectional relationship indicate that substance use predicts aggression and/or aggression predicts substance use (Leober et al., 1998; Scal et al., 2003). On the other hand, studies supporting a bidirectional relationship suggest that these two behaviors reinforce each other mutually (Huang et al., 2001). There is also available evidence that does not support significant relationships between substance use and aggression in either direction (Brook et al., 1995).

1.6 AAS use and aggression

The most well-known psychological adverse effect of AAS use among the general population is lack of impulse control, hostility, and high levels of aggressive and violent behavior sometimes referred to as “roid rage” or “steroid rage” (Nelson, 1989; Pope & Katz, 1987; Taylor, 1987). In the 1940s, Arnold A. Berthold castrated developing male chicken and observed that they stopped developing secondary sexual characteristics and aggressive

behavior (Berthold & Quiring, 1944). Later, Berthold transplanted testes taken from another male chicken to the castrated male chicken and noticed that the chicken regained their secondary sexual characteristics. This study and later animal studies in which animals were castrated (Nelson et al., 1989; Takeshita et al., 2017) suggested that testosterone may also modulate aggressive behavior in humans. In the 1980s, there was an emergence of case studies (Pope & Katz, 1987; Tragger, 1988) linking AAS use to aggression particularly homicide and near-homicide with an accumulation of case studies over the years (Choi et al., 1990; Khodoruth & Khan, 2020; Papazisis et al., 2007; Pope & Katz, 1990; 1994). In one case study, a man with a complex history of mental health and alcohol use murdered and dismembered his wife after using AAS for two weeks (Seppänen & Eronen, 2016). It must be noted that case studies are restricted in their nature and therefore lack external validity and do not enable causal inferences.

It has been suggested that compared to non-AAS-users, AAS users experience increased aggression and hostility over time (Choi et al., 1990). Moreover, it has also been shown that after 6 to 14 weeks of AAS use, recreational sportspeople report higher feelings of aggression towards objects (especially while training) and verbal aggression (Parrott et al., 1994). AAS users do not only have an increased risk of premature death but also have an increased risk of violent death compared to people who use other types of drugs (Hall et al., 2005). Case and survey studies also describe many male users with no history of psychological disorders or criminal background who were convicted of a violent crime or committed murder during AAS exposure (Christoffersen et al., 2019; Hall et al., 2005; Pope et al., 2014a). Numerous cross-sectional survey studies indicate that AAS use is associated with aggression particularly when concurrently used with alcohol (Jenssen & Johannessen, 2015; Sagoe et al., 2016a; van Amsterdam et al., 2010). In one cross-sectional study (Lundholm et al., 2015), lifetime AAS use had a strong positive association with criminal

conviction but this association diminished after adjusting for polydrug use. Some qualitative studies have also provided evidence from AAS users in which they have self-reported increased aggressiveness and willingness to fight after AAS exposure (Skårberg et al., 2008; Bates & McVeigh, 2016, Bahri et al., 2017). In a study of monozygotic twins, it was found that the twin who administered AAS became more aggressive, hostile, anxious, and paranoid compared to the twin who did not use AAS (Pagonis et al., 2006).

The evidence base on AAS use and aggression strongly relies on an experimental approach since the main goal in laboratory studies is to establish causation. Experimental animal studies on the AAS use and aggression relationship indicate robust positive effects with the AAS type, age of ingestion, the environmental context, and species as moderators (Bronson, 1996; Carrillo et al., 2011; Clark & Henderson, 2003; Cunningham & McGinnis, 2008; Onakomaiya et al., 2014). For example, although male rats are not normally aggressive towards female rats, when exposed to AAS, they show aggressive behaviors towards ovariectomized females (Cunningham & McGinnis, 2006). These behaviors are augmented when nandrolone is administered on adolescent male rats (Kalinine et al., 2014). Animal studies of female rodents also indicated that they became more behaviorally aggressive after AAS administration (Oberlander & Henderson, 2012).

However, results from human placebo-controlled randomized studies show an inconsistent association between AAS administration and aggression. Findings comprise negative (Björkqvist et al., 1994), positive (Panagiotidis et al., 2017; Wagels et al., 2018) and non-significant results (Tricker et al., 1996). Thus, it is still not clear whether aggression is an antecedent or consequence of AAS use (Dunn, 2015; Lundholm et al., 2015) and this relationship presents an ongoing serious concern (Christoffersen et al., 2019; Hoaken et al., 2012; McVeigh & Begley, 2017; McVeigh et al., 2020).

1.7 Theoretical associations of AAS use and aggression

Various theories have been proposed in order to highlight the relationship between use of AAS and aggression. These theories present biological, evolutionary, psychosocial and cognitive perspectives and altogether provide a deeper explanation of the link between AAS use and aggression.

1.7.1 The dual-hormone hypothesis

The dual-hormone hypothesis (Mehta & Josephs, 2010) was initially proposed to explain the relationship between testosterone and status-seeking related behaviors such as aggression and dominance. The dual-hormone hypothesis proposes that in status-seeking contexts, testosterone levels (which are implicated in aggression and dominance) are usually higher, and cortisol levels (which are implicated in submissive behavior and lower anxiety levels) are lower (Denson et al., 2013; Eisenegger et al., 2010). It has been shown that testosterone and cortisol levels measured at the same time of the day are stable (Mehta & Josephs, 2010). However, their levels change when exposed to status-seeking contexts (Mehta & Prasad, 2015). The dual-hormone hypothesis suggests that an increase in testosterone level is associated with increased aggression only when the level of cortisol is low (Mehta & Josephs, 2010). Using the dual-hormone hypothesis, researchers have found that the balance between testosterone and cortisol levels can be predictive of proactive and reactive aggressive behaviors (van Honk et al., 2010).

The dual-hormone hypothesis has been supported by cross-sectional studies using aggression measures in different age groups (Mehta & Prasad, 2015). For example, it has been shown that adolescent prisoners' aggressiveness is positively associated with their testosterone levels and negatively associated with their cortisol levels (Debbs et al., 1991). Results from clinical studies using samples with conduct disorder and clinical psychopathy as well as healthy persons also support the dual-hormone hypothesis (Glenn et al., 2011; Mehta & Josephs, 2010). However, results from experimental studies does not consistently

support this hypothesis (Denson et al., 2013; Geniole et al., 2011). Moreover, a recent meta-analysis that tested the interaction of testosterone and cortisol levels on status-seeking behaviors found a small significant effect and provided some support for the dual-hormone hypothesis (Dekkers et al., 2019).

1.7.2 The challenge hypothesis

The challenge hypothesis (Wingfield et al., 1990) was originally proposed to explain the relationship between testosterone and aggression in monogamous birds (Wingfield et al., 1990). When males need to guard their mate and offspring from rivals or mark their territory, testosterone levels increase, facilitating aggressive behavior. However, in situations where males need to express parental care, their testosterone level and aggressive behavior decreases (Wingfield et al., 2000). It has been suggested that since maintaining elevated testosterone levels is cost inflicting (e.g., decreased paternal care, decreased immune function, elevated risk of death/injury), the endocrine system have been evolutionary wired to modulate testosterone level according to different social and environmental contexts (Wingfield et al., 2000).

Since 1990, human studies have been examining the challenge hypothesis to investigate whether the testosterone-aggression relationship in humans can be explained by this evolutionary-based hypothesis (Carré & Archer, 2018). Consistent with the challenge hypothesis, numerous studies have supported the notion that intrasexual competition and social status seeking increases testosterone and aggressive behaviors (Gray et al., 2020). Further, it has been shown that testosterone increases in competitive contexts, which is followed by willingness to compete and increased aggression (Zilioli & Bird, 2017). The challenge hypothesis has been supported by studies on prenatal and adolescents' development. Studies on postnatal (i.e., birth to 6 months) testosterone levels have suggested that exposure to testosterone is associated with higher rates of aggression and risky

behaviors in unpredictable environments (Kuzawa et al., 2010). Thus, according to the challenge hypothesis, the association between acute changes in testosterone and aggression is context dependent (Carré & Archer, 2018). In light of the challenge hypothesis, numerous human studies have suggested that acute testosterone change can lead to aggressive behaviors in competitive interactions and/or socially provocative contexts (Carré & Olmstead, 2015).

1.7.3 Life history theory

Evolutionary psychologists apply life history theory (LHT) to understand adaptive and maladaptive human social behaviors (Del Giudice, 2018). According to this theory, human beings invest in different survival and reproductive strategies based on variability in environmental conditions they are evolved in (Hill & Kaplan, 1999). A harsh and unpredictable environment can promote a fast life history which is characterized by increased risky, short-term, and opportunistic behaviors as well as earlier sexual debut and substance use (Figueredo et al., 2006). Individuals who adopt a fast life history strategy believe that “life is too short not to risk”, and “future is unpredictable, uncontrollable, and unknown”. These beliefs are basically immediate survival focused (Mittal & Griskevicius, 2014) and motivate individuals to engage in risky behaviors such as substance use (Hill et al., 1997).

The evolutionary rationale for individuals who apply fast life history strategies is that these behaviors are adaptive and increased survival and reproductive fitness in the evolutionary past especially among individuals that could take advantage of immediate opportunities with short-term benefits and long-term costs (Del Giudice, 2009). For example, engaging in risky behaviors such as substance and alcohol use as a result of peer pressure can result in more popularity among peers in the short-term but, in the long-term, they result in various physical and psychological harms (Belsky et al., 2012).

Overall, it has been shown that substance use and aggressive and antisocial behaviors are byproducts of adaptations to harsh and unpredictable environmental conditions such as lower family cohesion and greater family hostility (Nation & Heflinger, 2006; Richardson & Hardesty, 2012). LHT has been used in explanations of the associations between substance use and impulsivity (Brumbach et al., 2009), psychosocial stress and insecure attachment (Del Giudice, 2009), intimate partner aggression (Figueredo et al., 2011, 2018), and aggression (Figueredo et al., 2018). In the context of LHT, the association between AAS use and aggression can be explained as a byproduct of adaptations to harsh and unpredictable environmental conditions such as the bodybuilding context and security workplace (e.g., night club door, police and military) where displaying an imposing macho physique may be advantageous (Givens et al., 2016; Hoberman, 2017; Simoni & Huhtaniemi, 2017).

1.7.4 Social learning/cognitive theory

In 1971, Bandura proposed the social learning theory which suggests that a behavior is learnt by observing and modelling behaviors and attitudes of significant others (Bandura, 1986). Bandura referred to this type of learning as vicarious learning. Through vicarious learning, a person observes the model's behavior, cognitively maintains the observed behavior, and when motivated executes the learnt behavior (Bandura, 1986). Bandura (1986) further suggested that the environment plays a very important role in learning and later exhibiting maladaptive behaviors such as substance use and aggression (Conger & Rueter, 1996). Numerous studies on acquisition of maladaptive behaviors during childhood and exhibiting them later during adolescence and in adulthood have supported the SLT (Egan et al., 1998; Weiss et al., 1992).

Bandura (1986) integrated the prominent role of personal influences in his theory by introducing a conceptual framework termed “triadic reciprocity” or “triadic reciprocal determinism” (see figure 1) into his initial theory and rearticulated SLT as social cognitive

theory (SCT). Triadic reciprocity includes three sets of factors: behavioral, environmental, and personal factors that interact together to influence learning and maintaining of behavior (Bandura, 1986). In the context of SCT, aggression can be explained as a product of the reciprocal interaction of behavioral factors (AAS use), environmental factors (the bodybuilding and security contexts), and personal factors (lack of self-regulation, status seeking, and impulsivity) as supported by a meta-synthesis of qualitative studies on AAS use initiation (Sagoe et al., 2014b).

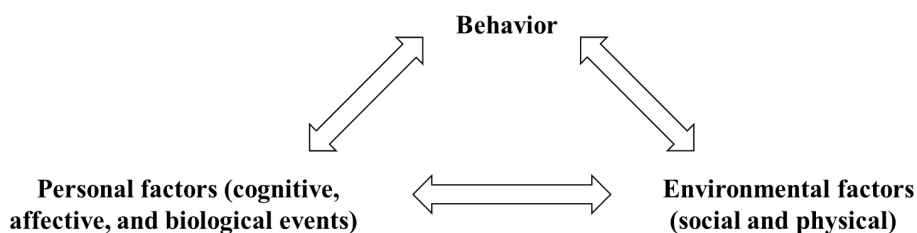


Figure 1: Triadic reciprocal determinism

1.7.5 Problem behavior theory

Jessor and Jessor (1977) proposed problem behavior theory (PBT) which asserts that there are common risk and protective factors underlying problem behaviors such as substance use, aggression, delinquency, and crime (Jessor, 2016). According to PBT, risk factors increase the likelihood of engaging in problem behaviors whereas protective factors diminish the likelihood of engaging in problem behaviors (Jessor, 2016; Jessor & Turbin, 2014). In PBT, the co-occurrence of multiple problem behaviors has been termed problem behavior syndrome (PBS; Willoughby et al., 2004). PBS suggests that engaging in one problem behavior such as substance use is associated with engagement in other problem behaviors such as aggressive and violent behaviors (Miller et al, 2005; Sagoe et al., 2016a).

In explaining the organization and patterning of PBS, Jessor (2016) delineated a social ecology of problem behaviors in that problem behaviors are learnt and performed together.

In 1991, Jessor reformulated PBT and introduced three psychosocial explanatory systems in the theory: 1) perceived environment system which includes proximal (e.g., awareness of friends influence) and distal (e.g., positive relations with adults) social factors, 2) personality system including motivational-instigation (e.g., value on academic achievement), personal belief (e.g., social criticism), and personal control (e.g., religiosity), and 3) behavioral system including conventional (e.g., church attendance) and deviant (e.g., poor school achievement) behaviors. These psychosocial protective factors and risk factors can predict involvement in problem behaviors such as substance use, aggression, delinquency, and early sexual intercourse (Jessor, 2018). PBT has been one of the most influential theories of deviant behaviors the last two decades (Jessor, 2016).

PBT has been empirically supported in the AAS use literature with numerous studies finding associations between AAS use and contemplation on one hand and aggression as well as use of narcotics, alcohol, and marijuana, risky sexual behavior, anti-social behaviors, and delinquency (Farrell et al., 2020; Hallgren et al., 2015; Miller et al., 2005; Pallesen et al., 2006; Sagoe et al., 2016a; Wichstrøm, & Pedersen, 2001) on the other. Particularly, a cross sectional study indicated that aggression is a risk factor of adolescents' AAS use contemplation (Sagoe et al., 2016a). Other recent evidence suggests that the likelihood of engaging in school and teen dating aggression is higher among adolescent AAS users compared to nonusers (Elkins et al., 2017; Ganson & Cadet, 2019). Additionally, it has been shown that adolescents who were in the proxy of AAS milieu, but did not use them, were also more likely to involve in violent behaviors than those who were not in the proxy of such environments (Pedersen et al., 2001).

1.8 Aims

1.8.1 Thesis aims

From the foregoing literature review, it can be deduced that the association between AAS use and aggression is still unclear. Particularly, the association between AAS use and aggression remains inconsistent in human randomized controlled trials (RCTs). Additionally, although aggression and psychological distress seem to be major behavioral outcomes of AAS use, no previous study has examined subgroups of AAS users based on their aggression and psychological distress profiles. Here, female AAS users seem particularly to be understudied and it is further unclear if there are unobserved intersex differences. Finally, there is a dearth of longitudinal research on the correlates, particularly physical and verbal aggression, of AAS use and intent in adolescence and emerging adulthood.

This thesis aimed to contribute to the evidence base on AAS use and aggression by: (a) systematically reviewing and quantitatively synthesizing results from human RCTs on AAS administration and aggression, (b) examining subgroups of aggression and psychological distress in AAS users as well as investigating sex differences in the subgroups, and (c) examining the longitudinal correlates, with emphasis on the role of physical and verbal aggression, of AAS use and intent in adolescence and emerging adulthood. In this thesis, three studies were conducted to address the aforementioned gaps in the literature.

1.8.2 Aims of Study 1

Study 1 aimed to synthesize and integrate findings from human placebo-controlled RCTs using systematic review and meta-analysis to examine the effect of AAS administration on self-reported as well as observer-reported aggression in healthy persons.

1.8.3 Aims of Study 2

Study 2 sought to identify subgroups of male and female AAS users based on their physical aggression, verbal aggression, anger, hostility, and psychological distress profiles and whether these subgroups can be applied to both sexes.

1.8.4 Aims of Study 3

Study 3 aimed to longitudinally investigate the associations between aggression, sex, living situation, grade point average, AAS, alcohol, cigarette and snus use as well as depression and anxiety symptoms and AAS use intent from age 18 to 19, highlighting the role of physical and verbal aggression. Another aim was to investigate the prevalence of AAS use at age 18 and 19 in a representative sample of Norwegian adolescents.

2. Methods

2.1 Measures

2.1.1 Measures of Study 2

Demographics

AAS users who participated in the study were asked to indicate their age, sex, weight (kg), and height (cm). The educational level of participants was assessed by means of a single item: “What is your highest level of education completed?”. Response alternatives included: high school (1), diploma (2), technician (3), bachelor (4), master (5), and PhD (6). Marriage status was assessed with the question: “What is your marital status?”. For the Iranian setting, response alternatives were: single (0) and married (1). Finally, participants indicated their job status by responding to the question “What is your job status?”. Response alternatives for this question consisted of: full time (1), part time (2), self-employed (3), jobless (4), student (5), and other (6).

Sports participation and weight training

Participants indicated their involvement in sports based on the following response alternatives: competitive sport (1), recreational sport (2), competitive bodybuilding (3), and recreational bodybuilding (4). They also answered a question about how many years in total they have been regularly engaged in weight training and how many times per week they trained with weights.

AAS use and type

Current AAS use was assessed with the question: “Do you currently use anabolic-androgenic steroids?” with ‘yes’ scored ‘1’ and ‘no’ scored ‘0’. Participants also indicated

the type of AAS they used. Response alternatives were: Anadrol (Oxymetholone), Anavar (Oxandrolone), Deca-Durabolin (Nandrolone decanoate), Depo-Testosterone, Dianabol (Methandrostenolone), Durabolin, Equipoise (Boldenone), Finajet (Trenbolone), Maxibolim (Ethylestrenol), Methyltestosterone, Oxandrolone, Primobolan, Steroid cocktail, Sustanon, Testosterone, and Stanozolol (Winstrol). There was also an open-ended section for participants to indicate any other AAS they had used. Finally, for the assessment of AAS use duration, participants indicated how many years they had been using AAS regularly.

Aggression

Physical and verbal aggression were assessed using the physical aggression and verbal aggression subscales of the Short-Form Buss-Perry Aggression Questionnaire (BPAQ-SF; Diamond & Magaletta, 2006). The physical aggression subscale consists of four items (e.g., “I have trouble controlling my temper”) while the verbal aggression subscale contains three items (e.g., “My friends say that I’m somewhat argumentative”). Items for each subscale are answered on a five-point response scale with ‘very unlike me’ scored ‘1’ to very like me’ scored ‘5’. Higher scores on each subscale suggest higher propensity toward the corresponding type of aggression.

Psychological distress

Symptoms of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS; Montazeri et al., 2003; Zigmond & Snaith, 1983). HADS consists of 14 items. Depression symptoms are assessed by seven items (e.g., “I feel as if I am slowed down”). Anxiety symptoms are also assessed by seven items (e.g., “I feel restless as I have to be on the move”). Items are answered on a four-point response scale. However, response alternatives are unique for each item. A composite score of anxiety and depression was computed to indicate psychological distress of participants. The computation of a composite

HADS score is in line with previous studies in which a superior factor loading of one general factor has been shown (Kjærgaard et al., 2014).

2.1.2 Measures of Study 3

Demographics

Participants indicated their sex with being male scored as 0 and being female scored as 1. They also indicated their grade point average (GPA). Additionally, participants were asked about their living situation with the question: “Who do you live with?”. Response options were: live with both parents (1), live with only one of the parents (2), shuttling between parents (3), live alone (4), live in a household/dormitory (5), and other (6).

Use of AAS, snus, and cigarette

Participants answered whether they had used AAS in the past 12 months. “Yes” responses were scored 1 and “no” responses scored 0. They were also asked about how often they smoked during the last month with ‘every day’ scored ‘2’, ‘less than every day’ scored ‘1’, and ‘not at all’ scored ‘0’. They also specified how often they used snus, using the same response alternatives as for smoking as above.

AAS use intent

The Intent to Use AAS Scale (IUAS; MacKinnon et al., 2001), was used to assess AAS use intent. IUAS consists of five items measured on a five-point response scale; ‘strongly disagree’ scored ‘1’ to ‘strongly agree’ scored ‘5’. Higher scores on the IUAS indicates greater intention to use AAS. An example item is “I am curious to try anabolic steroids”.

Aggression

Aggression was examined using the Short-Form Buss-Perry Aggression Questionnaire (BPAQ-SF; Diamond & Magaletta, 2006; Samani, 2008). This questionnaire consists of four subscales. These are physical aggression, verbal aggression, anger, and hostility. Physical aggression and verbal aggression subscales are defined in Measures of Study 2 section. The anger subscale consists of two items (e.g., “I sometimes feel like a powder keg ready to explode”) and the hostility subscale consists of three items (e.g., “I wonder why sometimes I feel so bitter about things”). Items are answered on a five-point response scale ranging from very unlike me (1) to very like me (5).

Anxiety and depression

Psychological distress was assessed using the HADS (Montazeri et al., 2003; Zigmond & Snaith, 1983). Subscales and their response alternatives are explained in Measures of Study 2 section. A score of 8 or higher on each subscale denotes mild anxiety and depression (Carroll et al., 1993). The time frame for the HADS is the past week.

Alcohol misuse

The Alcohol Use Disorder Identification Test-Consumption (AUDIT-C; Bush et al., 1998) is a short instrument with three items and it was used to assess alcohol misuse. Items include: “How often do you drink alcohol?”, “How many units of alcohol (a drink, a glass of wine, a shot, and/or small bottle of beer)?”, and “How often do you drink six or more units of alcohol at once?”. Response alternatives are unique for each item. AUDIT-C’s items are answered on a five-point response scale ranging from never (0) to four times or more per week (4). A total score is calculated with a score of 5 or higher indicating alcohol misuse.

2.2 Samples and procedures

2.2.1 Included studies and procedure of Study 1

Search strategy and inclusion criteria

MEDLINE, PsycINFO, ISI Web of Science, ProQuest, Google Scholar, and Cochrane Library were systematically searched for research literature with no time constraints. The latest literature search was conducted on 31st December 2019. In 2020, ad hoc searches were conducted to corroborate comprehensiveness. Keywords for the literature search are presented in Appendix A.

Studies that met the following inclusion criteria were included: studies that (a) investigated the effects of AAS administration on aggression among healthy persons, (b) were randomized controlled trials (RCTs), (c) assessed aggression utilizing valid aggression measures, and (d) were published in English. From a total of 30,407 hits, 3,772 were duplicates and 7,647 were grey literature. Of the remaining 18,988 hits, 18,752 were removed after screening by title and abstract. Thus, 238 full-text articles were retrieved for further evaluation. Of the remaining records, 226 full-text records comprised animal experimental studies, cross-sectional, case studies, and narrative reviews and were therefore removed at the eligibility assessment stage of the selection process leaving 12 studies that passed the inclusion criteria and were included in the meta-analysis. The literature search was conducted in adherence to the guidelines and recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA; Moher et al., 2009).

Data extraction

Data on study authors, country, design (e.g., double-blind), sample type (i.e., healthy males), sample size, age (range, $M \pm SD$), study groups (e.g., placebo group), AAS type, AAS dose, AAS administration mode (e.g., injection), study duration, assessment type (e.g.,

self-report), aggression measure, and results were extracted from the final identified hits using a standardized data extraction sheet form by two reviewers independently. The two reviewers discussed any possible discrepancies in data extraction and reached consensus.

2.2.2 Sample and procedure of Study 2

Sample

A total of 206 current AAS-using weightlifters took part in this study (females = 58.30%). Participants' age ranged from 14 to 56 with a mean age of 26.89 ($SD = 7.12$) years.

Procedure

This study was a cross-sectional survey and self-report questionnaires were used to collect data. Participants were recruited from training centers and sports supplement stores in Tehran, Iran. Eligibility criteria for participation in this study were: (a) being a current weightlifter, and (b) having used AAS regularly for at least the past six months before data collection. Participation was voluntary and anonymous, and all participants provided oral consent prior to data collection. No incentive or compensation were given to participants upon partaking in the study. Data were collected in June 2019. The study was conducted in accordance with the Declaration of Helsinki. Alzahra University in Tehran, Iran provided ethical approval for the study.

2.2.3 Sample and procedure of Study 3

Sample

Participants were pooled from an initial sample of 3000 17-year-olds that were randomly selected from the Norwegian Population Registry in 2012 (wave 1). In wave 1, 2055 (female = 53.0%) participants completed the questionnaires (response rate = 70.4%). In

2013, when the participants were 18 years old, they were contacted again to complete the questionnaire for wave 2. This time, of the 2055 participants from wave 1, a total of 1333 persons (females = 58.9%, response rate = 64.9%) completed the questionnaire. The last wave (wave 3) was collected in 2014 when the participants entered adulthood (19 years old). A total of 1277 of the participants returned completed questionnaires (females = 61.7%, response rate = 62.1%).

Procedure

The study was a longitudinal survey by means of a self-report questionnaire. Participants were selected from the Norwegian National Population Registry in 2012 using a random selection method. They received postal invitations containing the following material: an information sheet explaining the purpose of the study, information about the confidentiality of the study, information about compensation (NOK200, ~ €25), and the questionnaire. Answering the survey was regarded as providing informed consent. Participants were provided with a pre-paid envelope for returning completed questionnaires. In 2013, the Intent to Use AAS Scale (IUAS; MacKinnon et al., 2001) was included in the questionnaire and same participants from wave 1 were contacted to complete the questionnaire again for wave 2. The same process was repeated in 2014 (wave 3). The Regional Committee for Medical and Health Research Ethics in South East Norway provided ethical approval for the study (REK 2012/914).

2.3 Statistical procedures

2.3.1 Statistical analysis in Study 1

The analysis examined the effects of AAS administration on self-reported aggression in RCTs under the random-effects model. Moreover, three separate analyses were conducted

to examine the effects of high-dose (over 500 mg) AAS administration, long-term (from 3 days to 14 weeks) AAS administration, and acute AAS administration on self-reported aggression. Analysis was also conducted to examine the effect of AAS administration on observer-reported aggression. Due to the small number of included studies, analyses of the effects of acute ($k = 4$) and high-dose AAS administration ($k = 5$) on self-reported aggression, as well as the effect of AAS administration on observer-reported aggression ($k = 3$) were conducted using a fixed-effect model (Borenstein, 2009). Additionally, analysis of the effect of long-term AAS administration ($k = 7$) on self-reported aggression was conducted under a random-effects model. Finally, using meta-regression analysis, the effect of AAS dose on self-reported aggression was examined.

Some of the studies included in the current meta-analysis used multiple aggression measures. In order to combine scores from multiple measures, instruments should be highly correlated and measure the same construct (Gleser & Olkin, 2009). Here, the analysis combined scores from different aggression measures and calculated a final effect size estimate from each study in the analysis as recommended (Gleser & Olkin, 2009). Using previous validation studies on aggression instruments, a correlation of 0.6 was used to provide the best estimates of study variance and corresponding confidence intervals (Gleser & Olkin, 2009). For crossover studies, previous longitudinal studies on aggression were used to estimate a correlation between aggression scores over time (Krahé & Möller, 2010). An average correlation of 0.5 between aggression measures over time was estimated to provide optimal estimates of effect sizes. For studies with multiple groups (i.e., a passive control group, a placebo group, and a treatment group), only data from the placebo and treatment groups were used.

The fixed-effect model assumes that all factors that could affect the effect size are the same in all the included studies. Hence, the common (true) effect size is assumed to be the

same in all the included studies. In contrast, the random-effects model assumes that the variability in effect size estimates can be decomposed into two parts: heterogeneity due to random population effects and sampling variance (Borenstein, 2009). For the assessment of heterogeneity, the Q -statistic and the I^2 statistic were used. The Q -statistic is calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies. The I^2 is a percentual statistic (0-100) that describes the proportion of the observed variance across studies that reflects real differences in effect size with 0% indicating no heterogeneity, 25% indicating low heterogeneity, 50% indicating moderate heterogeneity and 75% suggesting high heterogeneity (Higgins et al., 2003). Moreover, Duval and Tweedie's (2000) trim and fill method, and Orwin's (1983) fail-safe N were utilized to examine publication bias. The Cochrane risk of bias tool (Higgins et al., 2003) was used to assess the risk of each study. The meta-analysis was preregistered in PROSPERO (CRD 42019117834). The Comprehensive Meta-Analysis software version 3.3.070 (Borenstein et al., 2014) was utilized to conduct the meta-analysis and meta-regression.

2.3.2 Statistical analysis in Study 2

Standard descriptive statistics were used to determine characteristics of the sample. A multilevel latent class analysis (MLCA; Lazarsfeld & Henry, 1968) was conducted to determine how male and female AAS users can be categorized based on their direct (i.e., physical and verbal aggression), indirect aggression (i.e., anger and hostility), and psychological distress levels, and whether the identified classes can be applied to both sexes. MLCA is a model-based clustering method that uses the manifest variables found in a survey to identify unobserved classes of response patterns. Different model fit criteria are used in order to determine the number of classes. The likelihood-ratio chi-square (L^2) criteria is used as a standard measure of the difference between observed and expected frequencies in the

model. A significant L^2 indicates that the model does not fit the data. The Bayesian Information Criterion (BIC; Schwarz, 1978) penalizes models with larger numbers of factors and is one of the most used information criteria for estimating the number of classes (Collins & Lenza, 2010). Models with lower BIC values have a better fit to the data (Kankaraš et al., 2010). Finally, the quality of the classification was examined using entropy R^2 and total proportion of adjacent classification error.

Additional analysis examined whether the identified subgroups of AAS users could be applied to both sexes. A MLCA assumes the presence of three types of variables: observed variables (here direct and indirect aggression and psychological distress), unobserved variable(s) that accounts for the relationship between the observed variables, and a grouping variable (here sex) which is a categorical manifest variable that can be associated with both the observed variables and the latent class(es). The analysis aimed to examine whether class-specific conditional response probabilities (class structures) were equivalent across male and female AAS users therein defining measurement equivalence. When comparing latent classes across groups, the analysis imposes across-group equality restrictions on specific sets of model parameters which leads to three different levels of homogeneity or measurement invariance.

First, when all the model parameters are set to be equal across the grouping variable and the latent classes have the same structure in each group, the model is homogeneous. Here the direct effect of the grouping variable on the observed variables and the interaction of the grouping variable with the latent classes are eliminated from the model. Second, when there are no restrictions on both the direct effect of the grouping variable on the observed variables and the effect of the interaction of the grouping variable with the latent classes the model is heterogeneous. Third, interaction effects exist when the grouping variable differs in the effects of latent classes on the observed variables whereas the direct effect exists when

differences in scores of grouping variable respondents are not related to differences in a given latent class (Kankaraš et al., 2010). If some of these effects are restricted to be equal across all groups while some of the effects are kept in the model, the model is partially homogeneous. The present study examined measurement invariance by conducting homogeneous, partially homogeneous, and heterogeneous multigroup latent class analyses with sex as the grouping variable. To analyze the invariance of each observed variable, the direct effect of the grouping variable was added onto each indicator in the partially homogeneous model.

Finally, the analysis compared the models in order to choose the best model fit for the data. For this purpose, L^2 differences between two consecutively nested models was used. The fully restricted homogeneous model served as the reference model for this comparison. When moving from the homogeneous model to the heterogeneous model, if the difference in L^2 between the two consecutive nested models (i.e., one model is obtained from a general model by imposing complex and decreasing homogeneity on the former) is significant, the best-fitting model is the one with more heterogeneity and less degrees of freedom (Schermelleh-Engel et al., 2010). After selecting the best model for the data, class proportions for each group were examined. Here, participants' likelihood of belonging to a subgroup was based on the proportional assignment rule (Goodman, 2007; Magidson & Vermunt, 2002). The association between sex and group membership was examined using the Walt test. Descriptive analyses were conducted using RStudio version 1.1.463 (RStudio, Inc), and the LCA was performed using advanced LatentGOLD 5.1 (Vermunt & Magidson, 2016).

2.3.3 Statistical analysis in Study 3

Standard descriptive statistics were used to determine frequencies of females and males, past year AAS use, living situation, past month cigarette use, past month snus use,

and alcohol misuse in both waves. Mean, standard deviation and log-transformed skewness and kurtosis scores for intent to use AAS, physical aggression, verbal aggression, and grade point average were calculated. Correlations between the independent variables at both waves were also estimated using Pearson product-moment correlations, point-biserial correlations, and phi coefficients. Mean differences of physical aggression, verbal aggression, intent to use AAS from wave 2 to wave 3 were examined using paired *t*-test.

The influence of the independent variables (i.e., intent to use AAS at wave 2, physical aggression and verbal aggression at wave 2, sex, living situation, grade point average, last year AAS use, alcohol misuse, last month cigarette use, last month snus use, anxiety and depression levels) on the intent to use AAS at wave 3 were examined using hierarchical multiple regression analysis. The hierarchical regression analysis included three steps; with intent to use AAS scale at wave 2 in the first step, physical and verbal aggression at wave 2 added to model at the second step, and the last step including all the indicators. Preliminary analysis of assumptions (i.e., normality, linearity, multicollinearity, and homoscedasticity) of hierarchical multiple regression analysis was conducted. With residuals of the intent to use AAS variable not normally distributed, this variable was log-transformed to improve its statistical properties. Since living situation was a nominal variable with six categories (both parents, single parent, shuttling between parents, alone, household/dormitory, and other), it was dummy coded with 'other' as the reference category. RStudio version 1.1.463 (RStudio, Inc) was used to conduct the analysis.

3. Results

3.1 Results of Study 1

After the final round of screening 238 full-text records, 12 studies were included in the meta-analysis. Altogether, 562 healthy males (females: $n = 0$) participated in the included studies and their age ranged from 18 (Su et al., 1993) to 49 (Carré et al., 2017) with a grand mean of 25.83 ($SD = 3.80$). Publication year ranged from 1992 (Anderson, Bancroft, & Wu, 1992) to 2017 (Carré et al., 2017; Cueva et al., 2017; Panagiotidis et al., 2017) with four studies conducted in the US (Pope et al., 2000; Su et al., 1993; Tricker et al., 1996; Yates et al., 1999), four in the UK (Anderson et al., 1992; Cueva et al., 2017; O'Connor et al., 2002, 2004), and one study each in Germany (Panagiotidis et al., 2017), Ireland (Dreher et al., 2016), Finland (Björkqvist et al., 1994), and Canada (Carré et al., 2017), respectively.

Of the total of twelve studies included, one study was a single-blind RCT (Anderson et al., 1992) and the rest were double-blind RCTs. Half of the included studies were cross-over studies (Anderson et al., 1992; Cueva et al., 2017; O'Connor et al., 2004; Pope et al., 2000; Su et al., 1993; Yates et al., 1999) and the other half were between-subject studies (Björkqvist et al., 1994; Carré et al., 2017; Dreher et al., 2016; O'Connor et al., 2002; Panagiotidis et al., 2017; Tricker et al., 1996).

The included studies varied in the type of AAS administered to the participants. Four studies administered testosterone enanthate (Anderson et al., 1992; Dreher et al., 2016; O'Connor et al., 2002; Tricker et al., 1996), two studies administered testosterone cypionate (Pope et al., 2000; Yates et al., 1999), two studies administered testosterone undecanoate (Björkqvist et al., 1994; O'Connor et al., 2004), three studies administered testosterone gel (Carré et al., 2017; Cueva et al., 2017; Panagiotidis et al., 2017), and one study administered methyltestosterone (Su et al., 1993). AAS doses ranged from a one-time application of 50 mg of testosterone gel (Panagiotidis et al., 2017) to the injection of 1000 mg of testosterone

undecanoate (O'Connor et al., 2004), and the injection of a total of 7000 mg of testosterone enanthate over a 14-week period (Yates et al., 1999).

Moreover, the included studies varied in the measures used to assess aggression. Three studies (O'Connor et al., 2002, 2004; Pope et al., 2000) utilized the Buss-Perry Aggression Questionnaire (Buss & Perry, 1992), three studies (O'Connor et al., 2002, 2004; Yates et al., 1999) utilized the Buss-Durkee Hostility Inventory (Buss & Durkee, 1957), two studies (Carré et al., 2017; Pope et al., 2000) utilized the Point Subtraction Aggression Paradigm (Cherek, 1992), and three studies (Dreher et al., 2016; O'Connor et al., 2002, 2004) utilized the Profile of Mood States (McNair et al., 1992). In addition to the Profile of Mood States, O'Connor et al. (2002, 2004) utilized the Aggression Provocation Questionnaire (O'Connor et al., 2001). Moreover, one study (Björkqvist et al., 1994) utilized the Self-Estimated Mood Checklist (Lindman, 1985), one study (Panagiotidis et al., 2017) utilized the Technical Provocation Paradigm (Panagiotidis et al., 2017) and emotional self-ratings (Schneider et al., 1994). Furthermore, two studies (Cueva et al., 2017; Su et al., 1993) utilized visual analogue scales (Cline et al., 1992; Norris, 1971), one study (Tricker et al., 1996) utilized the Multidimensional Anger Inventory (Siegel, 1986), and one study (Anderson et al., 1992) used daily ratings of irritability, readiness to fight, and being easily angered.

There was no significant effect of AAS administration and aggression in ten of the included studies (Anderson et al., 1992; Carré et al., 2017; Cueva et al., 2017; Dreher et al., 2016; O'Connor et al., 2002, 2004; Panagiotidis et al., 2017; Pope et al., 2000; Tricker et al., 1996; Yates et al., 1999). Further, one study (Su et al., 1993) reported a significant positive effect of AAS administration on aggression, whereas one study (Björkqvist et al., 1994) reported a significant negative effect of AAS administration on aggression.

The two reviewers who assessed the risk of bias for all the included studies disagreed once on the random sequence generation dimension of the selection bias which led to a Cohen's kappa of .58 (Cohen, 1988). All the included studies were assessed as having a high risk of selection bias on the random sequence generation dimension and unclear risk of selection bias on the allocation concealment dimension. One single-blinded study (Anderson et al., 1992) was assessed to have a high risk of performance and detection bias whereas the rest of included studies were assessed to have unclear risk of performance and detection bias. In addition, all studies were evaluated as having low risk of attrition bias as the outcome data was reported. Moreover, except for one study (Björkqvist et al., 1994) that did not report means and standard deviations of measured aggression, all studies were assessed to have low reporting bias.

Under a random-effects model, after eliminating an outlier which did not overlap with the 95% confidence interval of the overall pooled effect size (Björkqvist et al., 1994), a small significant and positive effect of AAS administration on self-reported aggression was observed ($g = 0.171$, 95% CI: 0.029–0.312, $k = 11$, $p = .018$; $I^2 = 0.000$, $Q = 8.891$, $p = .542$). Under a random-effects model, the effect of administering AAS over longer periods (3 days to 14 weeks) on self-reported aggression was not significant ($g = 0.100$, 95% CI: -0.079–0.278, $p = .273$; $I^2 = 5.286$, $Q = 6.335$, $p = .321$).

Under a fixed-effect model, the effect of acute administration of AAS on self-reported aggression was significant ($g = 0.291$, 95% CI: 0.014–0.524, $p = .014$, $Q = .867$, $p = .833$). Under a fixed-effect model, the effect of administering higher doses of AAS (over 500 mg) on self-reported aggression was not significant ($g = 0.191$; 95% CI: -0.007–0.388, $p = .059$, $Q = 1.399$, $p = .844$). Similarly, results from the fixed-effect meta-regression analysis on the effect of AAS dose on self-reported aggression was not significant [$B = 0.000$, $SE = 0.000$ (95% CI: -0.000–0.000), $p = .096$]. Furthermore, the overall fixed-effect

of AAS administration on observer-reported aggression was not significant ($g = 0.157$, 95% CI: -0.026 – 0.581 , $p = .469$, $Q = .249$, $p = .833$)

3.2 Results of Study 2

Stanozolol (Winstrol, $n = 136$), Testosterone ($n = 114$), oxandrolone ($n = 73$), Dianabol (methandrostenolone, $n = 71$), and Anadrol (oxymetholone ($n = 62$)) were the most frequently used type of AAS among both sexes.

A five-class solution was the best model fit for the data (BIC = 4326.81, $L^2 = 2220.11$, $p = 0.000$, ACE = .02, entropy $R^2 = .94$). MLCA was conducted to examine whether the same profiles of direct and indirect aggression and psychological distress can be applied to both sexes. Results of the MLCA indicated that the homogenous model was the best model and that patterns of direct and indirect aggression and psychological distress are not dependent on the sex of AAS users.

For the five-class solution, Class 1 comprised members with the highest levels of direct and indirect aggression and moderate levels of psychological distress (high aggression moderate distress users: HAMoD; 7.63%). Class 2 members were characterized by moderate levels of direct and indirect aggression and psychological distress (moderate aggression distress users: MoAD; 18.64%). Class 3 consisted of users with moderate levels of direct aggression, mild levels of indirect aggression, and moderate levels of psychological distress (moderate direct aggression-mild indirect aggression moderate distress users: ModA-MiiA MoD; 22.95%). Class 4 comprised users with mild levels of direct aggression and moderate levels of indirect aggression as well as psychological distress (mild direct aggression-moderate indirect aggression-distress users: MidA-MoiAD; 11.71%). Finally, Class 5 comprised users with lowest levels of direct and indirect aggression and mild psychological distress (low aggression mild distress users: LAMiD; 39.06%).

Additionally, sex was significantly related to class membership (Wald = 31.04, $p < .001$). In particular, members of the HAMoD subgroup had a higher likelihood of being male ($z = -5.02, p < .001$). In contrast, members of the LAMiD subgroup were more likely ($z = 3.51, p < .001$) to be female.

3.3 Results of Study 3

The prevalence of AAS use among participants increased from 1 person at wave 2 to 4 persons at wave 3. Intent to use AAS did not change from 18 to 19 years old. From wave 2 to wave 3, physical aggression and verbal aggression decreased significantly in both sexes (males: wave 2: $M = 6.6, SD = 3.1$, wave 3: $M = 5.9, SD = 2.9$; $t = 4.40, p < .01$; and females: wave 2: $M = 6.1, SD = 3.0$, wave 3: $M = 5.5, SD = 2.4$; $t = 8.15, p < .01$). Correlation coefficients among the study variables at wave 2 and wave 3 indicated that intent to use AAS at Wave 2 was negatively correlated to GPA ($r = -.07, p < .05$), alcohol misuse ($r = -.06, p < .01$), past month cigarette use ($r = -.13, p < .01$), and snus use ($r = -.10, p < .01$).

Intent to use AAS at wave 2 was positively associated with shuttling between parents (living situation, $r = .06, p < .05$), anxiety ($r = .09$), depression ($r = .11, p < .01$), and physical ($r = .16, p < .01$) and verbal aggression ($r = .10, p < .01$). Intent to use AAS at Wave 3 was positively correlated with last year AAS use ($r = .22, p < .01$), anxiety ($r = .06, p < .05$), depression ($r = .12, p < .01$) and verbal ($r = .12, p < .01$) and physical aggression ($r = .18, p < .01$) but negatively correlated with past month cigarette use ($r = -.10, p < .01$).

Results from the first step of the hierarchical linear regression of predictors of intent to use AAS at wave 3 indicated that AAS use intent at wave 2 significantly accounted for 8.2% of the variance in AAS use intent at wave 3 ($F(1, 1268) = 114.8, p < .01$). The second step explained 8.4% of the variance in intent to use AAS at the wave 3 ($F(3, 1266) = 40.05, p < .01$). Here, physical aggression and verbal aggression at wave 2 were not associated with

intent to use AAS at wave 3. The third step included all the independent variables and significantly explained 15% of the variance of the AAS use intent at wave 3 ($F(16, 957) = 13.36, p < .01$) with being male (sex: $\beta = -.066, p < .01$), living alone ($\beta = .068, p < .05$), and past year AAS use at wave 2 ($\beta = .296, p < .05$) positively associated with AAS use intent at wave 3.

4. Discussion

The main aim of this thesis was to contribute to the existing evidence on the relationship between AAS use and aggression by: 1) systematically reviewing and synthesizing effects from RCTs on the association between AAS use and aggression, 2) exploring the patterns of aggression and psychological distress among male and female AAS users, and 3) examining the relationship between AAS use intent and aggression and exploring risk factors of AAS use intent across time. To attain these aims, three studies were conducted. The following discussion consists of findings from the aforementioned studies as well as implications for practice and future research, strengths, and limitations of the thesis.

4.1 Main findings

Based on the notion that RCTs and meta-analyses are methodologically superior to cross-sectional and longitudinal studies (Murad et al., 2016), in Study 1, a meta-analysis of RCTs examining the effect of AAS use on self-reported as well as observer-reported aggression was conducted. Under a random-effects model, after eliminating an outlier from the included studies, a significant positive effect of AAS administration on self-reported aggression was observed. This finding is in line with the finding from a recent meta-analysis (Geniole et al., 2020) suggesting that AAS administration has a marginally significant and positive correlation with aggressive behavior. Further, when restricting the analysis to studies in which acute (one dosage) AAS administration effects on aggression were examined, results were also significant. The meta-analysis by Geniole et al. (2020) attests to the finding that acute testosterone increase is positively associated with aggressive behavior.

The positive effect of testosterone administration on aggression in RCTs can be explained in light of the dual-hormone hypothesis as well as the challenge hypothesis. Some of the included RCTs in the meta-analysis used behavioral measures of aggression and

assessed aggression after provoking the participants in a competitive context (Carré et al., 2017; Dreher et al., 2016; Panagiotidis et al., 2017). Both the dual-hormone hypothesis and the challenge hypothesis emphasize the role of a competitive context for increased aggression (Mehta et al., 2015; Zilioli & Bird, 2017). In particular, the dual-hormone hypothesis suggests that in a competitive context, humans evolutionarily have lower levels of cortisol and higher levels of testosterone in order to execute aggressive and dominant behavior in favor of survival. The positive effect of acute AAS administration on self-reported aggression can also be explained in light of the challenge hypothesis (Archer, 2006). According to the challenge hypothesis, the relationship between testosterone levels and aggression depends on the social context. Testosterone levels tend to be higher in social contexts characterized by competition and aggression (Archer, 2006; Zilioli & Bird, 2017). In terms of the challenge hypothesis, it has been suggested that increased testosterone is associated with increased ongoing and/or future aggression (Geniole et al., 2020; Zilioli & Bird, 2017).

However, no significant effects of long-term and high-dose AAS administration on self-reported aggression was observed. Further, there was no significant relationship between AAS administration and observer-reported aggression. In addition, results from the meta-regression on the relationship between AAS administration and aggression using dose as the moderator was also insignificant. An important explanation for the above findings is that ecological settings are different from laboratory settings on various factors such as dosage, AAS types, and duration of use. AAS use is often part of a polydrug abuse pattern with AAS dosages ranging from 125 to 7,000 (mean = 1,278) mg per week over an average period of 9.1 years (Bjørnebekk et al., 2017; Salinas et al., 2019). Moreover, in another study, it was shown that when adjusting for polysubstance use, the association between AAS use and aggressiveness diminished (Lundholm, 2013).

The notion that AAS use is predominantly a male practice (Sagoe et al., 2014a; Sagoe & Pallesen, 2018) was also observed in samples from RCTs included in Study 1. All participants in the RCTs on the relationship between AAS use and aggression were healthy males. It is known that female AAS users are generally understudied in terms of the psychological side effects of AAS use (Abrahin et al., 2017; Börjesson et al., 2016; Grogan et al., 2006; Havnes et al., 2020). Hence, in Study 2, the majority of the sample were female AAS users. More importantly, due to the paucity of knowledge about AAS users in non-Western countries, particularly female AAS users, the data for Study 2 were collected from Iran.

The first class identified in Study 2 comprised mostly male AAS users and it was the smallest subgroup with highest levels of direct aggression (i.e., physical and verbal aggression) and indirect aggression (i.e., anger and hostility) and moderate levels of psychological distress. The second subgroup also consisted of more males and users in this subgroup had moderate levels of direct aggression, indirect aggression, and psychological distress. These two subgroups corroborate previous findings from clinical observations, case reports and anecdotes that indicate a positive relationship between AAS use and aggression (Choi & Pope, 1994; Thiblin et al., 1997). As the aggression and psychological distress scores started to decrease, the proportion of females in the latent classes started to grow. The third subgroup consisted of users reporting moderate levels of direct aggression, mild levels of indirect aggression, and moderate levels of psychological distress. Further, the fourth subgroup consisted of mild levels of direct aggression and moderate levels of indirect aggression as well as psychological distress. Finally, the fifth subgroup which was the largest subgroup comprised mostly female AAS users, and was characterized by the lowest levels of direct and indirect aggression and psychological distress. Results from Study 2 corroborate result from other studies in which majority of AAS users experienced aggressive

cognitions and affects (e.g., hostility, irritability, anger) instead of involvement in direct acts of aggression (Panagiotidis et al., 2017; Pope et al., 2000).

Results of measurement invariance assessment indicates that the identified subgroups of aggression and psychological distress apply to both male and female AAS users. However, the proportion of male AAS users in the highly aggressive and psychological distress subgroups are significantly higher than female users. Hence, it can be inferred that AAS users who experience high aggression and psychological distress comprise of a higher proportion of males compared to females. This finding may be attributed to the fact that compared to females, males initiate AAS use at a younger age, use higher weekly doses, a higher number of AAS per cycle and over their lifetime, and practice more stacking, polypharmacy and pyramiding (Ip et al., 2010). Altogether, discrepancies in the patterns of aggression and psychological distress among AAS users in Study 2 are in line with previous studies indicating that not all AAS users experience high levels of aggression and psychological distress (Trenton & Currier, 2005), and that the effect of AAS administration on aggressive behaviors are stronger in males in comparison to females (Geniole et al., 2020).

Life history theory (LHT; Del Giudice, 2018) provides explanations for the above finding from Study 2. According to LHT, maladaptive aggression can be promoted by growing up in an unpredictable and harsh environment leading to a fast life history strategy (Del Giudice, 2018). It is plausible that AAS users in the more aggressive and psychologically distressed classes exhibit a fast life history strategy characterized by a “You Only Live Once” (YOLO; Christiansen et al., 2017; Zahnw et al., 2018) perspective. According to LHT, persons with a slow life history strategy are less likely to engage in risky behaviors and aggression since these behaviors may help immediate survival but do not optimize lifelong survival (Mittal & Griskevicius, 2014). Further, LHT posits that females

are evolutionary wired to inhibit maladaptive emotional and behavioral responses in order to optimize reproduction and childbearing likelihood (Bjorklund & Kipp, 1996).

In line with the prevalence estimates from earlier Norwegian studies (Wichstrøm, 2006; Wichstrøm & Pedersen, 2001), results from Study 3 showed that the prevalence of AAS use increased from 1 person at 18 years old to 4 persons at 19 years in Norway. These results could be attributed to evidence that only about 13% of AAS users are below 18 years old (Pope et al., 2014b) and most persons initiate use of AAS after age 18 (Sagoe et al., 2014b). Moreover, Study 3 evidenced a temporal stability in AAS use intent from age 18 to 19. Importantly, it was observed in Study 3 that physical and verbal aggression decreased in both sexes from late adolescence to early adulthood. This finding is consistent with results from previous studies which did not observe any increase in aggression level among adolescents longitudinally from age 15 to 17 (Olweus et al., 1988). It can also be supported by the maturation of brain areas in charge of inhibiting responses (e.g., aggressiveness) such as the frontal lobe during adolescence (Leon-Carrion et al., 2004). The finding of decreased physical and verbal aggression from age 18 to 19 can be explained by decreased endogenous testosterone level during this period (Steinberg, 2008) in support of the challenge and (Wingfield et al., 1990) dual-hormone (Mehta & Josephs, 2010) hypotheses. Additionally, the lack of a longitudinal relationship between physical or verbal aggression and AAS use intent from age 18 to 19 in Study 3 indicates that the positive relationship between AAS use intent and aggression at age 18 found using a cross-sectional design (Sagoe et al., 2016a) is not applicable longitudinally from age 18 to 19.

In corroboration of previous studies suggesting that living alone is a risk factor for problem behaviors such as substance use and aggression among adolescents (Makanjuola et al., 2007), results from Study 3 indicated that living alone at age 18 is related to higher AAS use intent at age 19. In the context of problem behavior theory (Jessor & Jessor, 1977), the

finding that living alone is a risk factor for AAS use intent in Study 3 is understandable since adolescents living alone may have less parental supervision and higher exposure to problem behaviors such as AAS use and aggression (Fellmeth et al., 2018; Gestsdottir et al., 2020). Being male was another risk factor for AAS use intent at age 19 consistent with the traditional notion that AAS use is predominantly a male practice (Sagoe et al., 2014a; Sagoe & Pallesen, 2018). Overall, results from Study 3 are in line with previous studies suggesting that environmental risks, aggression, impulsiveness, and social problems during early adolescence are related to intent to and actual substance use in late adolescence (Ernst et al., 2006; Harvey, 2020).

4.2 Implications for practice and future research

Findings from the studies included in this thesis have implications for AAS-related prevention, harm reduction and treatment as well as future research. One of the effective preventive approaches to AAS use is providing balanced information about its health consequences (Petróczi et al., 2014; Sagoe et al., 2016b). Including information on the behavioral consequences of AAS use, in particular emphasizing that AAS use increases aggression and the likelihood of engaging in violent crime (Christoffersen et al., 2019; Ganson & Cadet, 2019; Hauger et al., 2021), is important for effective information-based preventive approaches. Relatedly, preventive interventions addressing the factors identified in Study 3 as associated with the maintenance of high AAS use intent in the transition from adolescence and early adulthood (i.e., being male, living alone, and past or current use of AAS), may be effective in reducing AAS use intent and initiation. Moreover, evidence of an acute increase in aggression following AAS administration should be considered in harm reduction and treatment interventions. Here, mindfulness-based interventions may be effective in helping AAS users be more mindful of the increased tendency for aggression

especially when “on cycle” and facilitate AAS abstinence and cessation (Gardner & Moore, 2012; Steyn et al., 2016).

A systematic review on negative health consequences-based interventions suggests that the impact of such interventions highly depends on how the target group consider the intervention to be relevant to their group (Petróczi et al., 2014). Utilizing results from Study 2, it is suggested that AAS-using females should be considered as an important group in policy making particularly in relation to the tendency for aggression. Additionally, findings on the heterogeneity denote the need for tailored interventions considering AAS users’ different profiles of aggression and psychological distress.

The findings also have implications for future research. RCTs on the effect of AAS administration on aggression have several limitations including low doses, lack of personality and polypharmacy controls, small sample sizes, risk of bias, short study duration, and the inclusion of only healthy males. Premorbid functioning may also predispose some persons to the aggression-instigating effects of AAS (Piacentino et al., 2015; Pope & Katz, 1990). Future RCTs considering these factors are also suggested to design experiments that are closer to ecologically valid settings so that they can contribute better to the evidence base on how AAS administration affects aggression in humans. It is also recommended that self-report measures of aggression are systematically supplemented with other measures, which may have higher ecological validity, such as observer reports as well as more advanced methods such as virtual reality (Lobbestael, 2015).

Also, considering the emphasis on the importance of personality traits in doping in general (Nicholls et al., 2017) and as a moderator of the relationship between AAS use and aggression in particular (Carré & Archer, 2018; Hauger et al., 2021; Pope et al., 2000), it would be of interest to examine the personality traits of the identified subgroups of AAS-related aggression and psychological distress. Research on this topic could also benefit from

longitudinal designs in highlighting potential transitions between the identified subgroups of AAS-related aggression and psychological distress. In addition, it could be of interest to replicate the identified subgroups and investigate the AAS types associated with members of each subgroup. Finally, further studies especially of longitudinal design should be conducted to shed light on the link between aggression and AAS use and intent. Larger sample sizes and innovative means of attrition prevention are recommended. Finally, in order to further elucidate the present findings, conducting similar research using different methods, samples particularly including females, factors, and in other cultural as well as geographic contexts is recommended.

4.3 Strengths and limitations

This thesis is methodically diverse comprising meta-analytic, cross-sectional, and longitudinal designs. Study 1 represents the first comprehensive systematic review and meta-analysis on RCTs of the relationship between AAS administration and aggression. Study 2 is the first to identify typologies of aggression and psychological distress among male and female AAS users. Additionally, the use of multilevel latent class analysis (MLCA) to identify the subgroups is a strength as MLCA is superior to traditional categorization of subgroups using cut-off points (Berzofsky et al., 2008). Also, given the dearth of AAS research in nonwestern countries and particularly among females (Sagoe et al., 2014a; Sagoe & Pallesen, 2018), the inclusion of a large proportion of female AAS users from Iran in Study 2 is a strength. Moreover, Study 3 is the first to investigate the longitudinal associations between AAS use intent and aggression. Standardized and validated measures were used to examine this relationship in a nationally representative sample in the critical transition from late adolescence to early adulthood. Another strength of Study 3 is that the sample was randomly selected from the Norwegian Population Registry and the response rate was also relatively high.

Limitations of the studies also need to be pointed out. One major limitation pertains to the assessment of aggression. Most of these were based on self-report. However, a major limitation of such measures is that they often do not correspond well with actual behavior (Lobbestael, 2015), which may be due to social desirability bias (Vigil-Colet et al., 2012). Another limitation is that such measures seldom make a distinction between reactive and proactive aggression. This may be problematic given that testosterone exerts a direct causal influence on provoked aggressive behavior but correlates lower and only indirectly with unprovoked aggressive behavior (Olweus et al., 1988).

The experimental settings in Study 1 had important gaps compared to ecological settings in which AAS use happens. As noted previously, these gaps include very low dosages, absence of polypharmacy control, small sample sizes, lack of gender diversity, including only healthy subjects, risk of bias, variation in aggression measures, and short duration of AAS exposure which may have diminished the robustness of the relationship between AAS use and aggression. It is therefore plausible that the identified positive effect of AAS administration on aggression may be exacerbated in ecological settings where AAS are obtained from ‘underground laboratories’ and sometimes contaminated with other toxic chemicals (Turnock, 2020; van de Ven et al., 2020) and are administered in supraphysiological doses for longer durations (Bjørnebekk et al., 2017; Salinas et al., 2019) concurrently with other substances (Dodge & Hoagland, 2011; Sagoe et al., 2015a). Another limitation of Study 1 is that there was substantial heterogeneity in the measurement of aggression (e.g., self-reports, observer reports, and behavioral) across the included RCTs.

Additionally, considering the elevated psychological distress as a major symptom of AAS withdrawal (Harvey, 2020; Malone & Dimeff, 1992; Perry et al., 1990; Su et al., 1993), whether participants in Study 2 were “on cycle” or “off cycle” might have affected the subgroups of aggression and psychological distress identified. Altogether, the three studies

included in this thesis were quantitative, and qualitative explorations may throw further light on AAS use and aggression. Also, Studies 2 and 3 were cross-sectional and longitudinal respectively and causality can thus not be inferred from such designs. Additionally, in longitudinal studies, attrition is always a threat to external and internal validity of study results since it may result in underrepresentation of relevant subgroups (Barry, 2005). Further, the use of self-reports in Studies 2 and 3 is noteworthy as self-reports may be affected by social desirability bias and inaccurate responses (Hickman et al., 2002; Kanayama et al., 2007; Sagoe & Pallesen, 2018). In both Study 2 and Study 3, more females responded than men. This can be attributed to the notion that, overall, females respond to surveys more often than men do (Sax et al., 2003). In terms of power analysis, it should be noted that Study 1 is a meta-analysis. It is well known that meta-analyses increase statistical power for fixed effect models, and sometimes also for random effects models (Cohn & Bcker, 2003). Still, a formal a priori power analysis (Boresnstein et al., 2014) was not conducted for Study 1. Although power analysis was not conducted for Study 2, the sample size seems adequate in terms of what is recommended for such analyses (Park & Yu, 2018). Study 3 is based on data from a larger research project focusing mainly on gambling among adolescents. A power calculation for this project showed that the sample size is sufficient to detect small effects in hierarchical multiple regression analyses (Faul et al., 2007). Furthermore, although most of the included measures in Studies 2 and 3 showed acceptable reliability, Cronbach's alpha for the anger subscale of BPAQ-SF was .69 in Study 2 and around .67 for the verbal aggression subscale in Study 3.

5. Conclusions

In the current thesis, three studies on the relationship between AAS and aggression are presented. Results of Study 1, based on a meta-analysis of RCTs, indicate a positive effect, although small, of AAS administration on aggression as well as a positive effect of acute AAS administration on aggression. In Study 2, using MLCA, male and female AAS users were classified into five subgroups according to their aggression and psychological distress levels. This underlines the sex homogeneity of AAS users' aggression and psychological distress, although the proportion of male AAS users in the highly aggressive and psychological distress subgroups are significantly higher than female users. Results of Study 3 indicate that there is no longitudinal relationship between AAS use intent and physical and verbal aggression. Finally, in a longitudinal context, many other factors are influential in the maintenance of the relationship between AAS use intent and aggression. The three studies presented in this thesis have implications for AAS-related preventive, harm reduction and treatment interventions as well as future research on AAS and aggression.

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Appendix A

Search terms for the literature search on the effect of AAS administration on aggression (Study 1).

Keywords/search terms for AAS

'anabol*', 'androgen*', 'steroid', 'doping', 'testosterone', '4-Hydroxytestosterone', '11-Ketotestosterone', 'Boldenone', 'Clostebol', '4-Androstenediol', '4-Dehydroepiandrosterone', '4-DHEA', '5-Androstenedione', '5-Dehydroandrosterone', '5-DHA', '11 β -Hydroxyandrostenedione', '11 β -OHA4', 'Adrenosterone', '11-ketoandrostenedione', '11-KA4', 'Androstenediol', '5-androstenediol', 'A5', 'Androstenedione', '4-androstenedione', 'A4', 'Atamestane', 'Boldione', '1,4-androstadienedione', 'Dehydroepiandrosterone', 'DHEA', '5-DHEA;prasterone', 'androstenolone', 'Exemestane', 'Formestane', 'Cloxotestosterone', 'Quinbolone', 'Silandrone', 'Dihydrotestosterone', 'DHT', 'Androstanolone', 'stanolone', '1-Testosterone', 'dihydro-1-testosterone', 'dihydroboldenone', '11-Ketodihydrotestosterone', '11-KDHT', 'Drostanolone', 'Epitiostanol', 'epithioandrostanol', 'Mesterolone', 'Metenolone', 'methenolone', 'Methylandrostenolone', 'Nisterime', '1-Androsterone', '1-Andro', '1-DHEA', '1-Androstenediol', 'dihydro-1-androstenediol', '5 α -Androst-2-en-17-one', 'Androsterone', 'Epiandrosterone', 'Mepitiostane', 'Mesabolone', 'Prostanozolol', 'Bolazine', 'di(drostanolone)azine', '2 α -methyl-5 α -androstan-17 β -ol-3-one', 'Nandrolone', 'nortestosterone', '11 β -Methyl-19-nortestosterone', '11 β -MNT', 'Dienolone', 'Dimethandrolone', 'Norclostebol', 'Oxabolone', 'Trenbolone', 'Trienolone', 'Trestolone', 'MENT', '7 α -Methyl-19-nor-4-androstenedione', 'Mentdione', 'Trestione', '19-Nor-5-androstenediol', 'Bolandiol', 'nor-4-androstenediol', 'Dienedione', 'nor-4,9-androstadienedione', 'Methoxydienone', 'methoxygonadiene', 'Bolmantalate', 'nandroloneadamantoate', 'Bolasterone', 'Calusterone', 'Chlorodehydromethyltestosterone', 'CDMT', 'Enestebol', 'Fluoxymesterone', 'Formebolone', 'Hydroxystenozole', 'Metandienone', 'Methandienone', 'methandrostenolone', 'Methylclostebol', 'chloromethyltestosterone', 'Oxymesterone', 'Tiomesterone', 'Thiomesterone', 'Chlorodehydromethylandrostenediol', 'CDMA', 'Chloromethylandrostenediol', 'CMA', 'Methandriol', 'methylandrostenediol', 'Methyltestosterone 3-hexyl ether', 'Penmesterol', 'Penmestrol', 'Androisoxazole', 'Desoxymethyltestosterone', 'Furazabol', 'Mestanolone', 'methyl-DHT', 'Methasterone', 'Methyldrostanolone', 'Methyl-1-testosterone', 'methyldihydro-1-testosterone', 'Methylepitiostanol', 'Methylstenbolone', 'Oxandrolone', 'Oxymetholone', 'Stanozolol', 'Mebolazine', 'Dimethazine', 'Di(methasterone)azine', 'Dimethyltrienolone', '7 α ,17 α -dimethyltrenbolone', 'Ethylendienolone', 'Ethylestrenol', 'ethylnandrol', 'Methyldienolone', 'Methylhydroxynandrolone', 'MOHN', 'MHN', 'Metribolone', 'methyltrienolone,R-1881', 'Mibolerone', 'Norboletone', 'Norethandrolone', 'ethylnandrolone', 'ethylestrenolone', 'Normethandrone', 'methylestrenolone', 'normethisterone', 'Tetrahydrogestrinone', 'THG', 'Bolenol', 'ethylnorandrostenediol',

'Propetandrol', 'Vinyltestosterone', 'Norvinisterone', 'vinylnoretestosterone', 'Etyndiol', 'Ethyndiol', '3 β -hydroxynorethisterone', 'Gestrinone', 'R-2323', 'ethylnorgestrienone', 'Levonorgestrel', '(-)-norgestrel', 'Lynestrenol', '3-deketonorethisterone', 'Norgestrel', '18-methylnorethisterone', 'Norgestrienone', 'ethynyltrenbolone', 'Tibolone', '7 α -methylnoretynodrel', 'Quingestanol', 'Etyndioldiacetate', 'ethynioldiacetate', 'Norethisteroneacetate', 'norethindroneacetate', 'Norethisteroneenanthatate', 'norethindroneenanthatate', and 'Quingestanolacetate'

Keywords/Search terms for aggression

'Aggress*', 'Hostil*', 'Anger*', 'Irritab*', 'Violen*', 'Impuls*', 'Angry', and 'Agres*'



Anabolic-androgenic steroid administration increases self-reported aggression in healthy males: a systematic review and meta-analysis of experimental studies

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Abstract

Rationale Aggression and irritability are notable psychiatric side effects of anabolic-androgenic steroid (AAS) use. However, no previous study has systematically reviewed and quantitatively synthesized effects reported by experimental studies on this topic. **Objective** We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) investigating the effect of AAS administration on self-reported and observer-reported aggression. **Methods** Twelve RCTs comprising a total of 562 healthy males were identified through systematic searches of MEDLINE, PsycInfo, ISI Web of Science, ProQuest, Google Scholar, and the Cochrane Library. **Results** After excluding one outlier, AAS administration was associated with an increase in self-reported aggression under a random-effects model, albeit small (Hedges' $g = 0.171$, 95% CI: 0.029–0.312, $k = 11$, $p = .018$), and when restricting the analysis to the effect of acute AAS administration on self-reported aggression under a fixed-effect model ($g = 0.291$, 95% CI: 0.014–0.524, $p = .014$). However, the above effects were neither replicated in the analysis of observer-reported aggression nor after restricting the analysis to the effects of the administration of higher (over 500 mg) and long-term (3 days to 14 weeks) doses. **Conclusions** The present meta-analysis provides evidence of an increase, although small, in self-reported aggression in healthy males following AAS administration in RCTs. Ecologically rational RCTs are warranted to better explore the effect of AAS administration on aggression in humans.

Keywords Anabolic-androgenic steroids · Aggression · Meta-analysis · Randomized controlled trial

Introduction

Anabolic-androgenic steroids (AAS) are a family of hormones comprising the androgen hormone testosterone as well as its synthetic derivatives (Kanayama and Pope 2018). Use of AAS was historically associated with weightlifters and later with professional bodybuilders and elite athletes in various sports. Since the 1980s, use of AAS has gradually spread to

recreational athletes as well as the general population (Pope and Kanayama 2012). Use of AAS normally comprises long-term administration of suprphysiological doses often 10–100 times the natural production or therapeutic doses of androgens (Kanayama et al. 2013). A meta-analysis on the global prevalence of AAS use indicated that 3.3% of the world's population has used AAS at least once with use being more frequent among males (6.4%) compared to (1.6%) females (Sagoe et al. 2014b; Sagoe and Pallesen 2018).

Despite benefits such as increased muscle growth, improved body image, and enhanced sports performance (Evans 2004; Sagoe et al. 2014a; Smit et al. 2020a), human case studies, surveys, and experimental studies suggest that AAS induce a plethora of physical and psychological adverse side effects. Cardiovascular disorders, particularly cardiomyopathy, are major physical side effects of AAS use (Baggish et al. 2017). Other somatic side effects of AAS include hypertension, sleep abnormalities,

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immunological dysregulation, decreased libido in males, and hirsutism and clitoromegaly in females (Bensoussan and Anderson 2019; Ganesan et al. 2020). Notable psychological side effects comprise manic and depressive symptoms as well as psychotic symptoms (Brower 2009; Kanayama et al. 2020). Human case studies, surveys, and experimental studies further suggest that AAS induce a plethora of symptoms such as irritability and unprovoked aggression sometimes referred to as “roid rage” or “steroid rage” (Nelson 1989; Pope and Katz 1987; Taylor 1987; Tragger 1988). Experimental animal studies show consistently that injections of AAS increase aggression (Clark and Henderson 2003; Lumia et al. 1994). For human studies, cross-sectional (Ganson and Cadet 2019; Pereira et al. 2019), case-control (Klötz et al. 2007; Lundholm et al. 2010; Thiblin et al. 2015), and longitudinal (Beaver et al. 2008) researches indicate a positive relationship between AAS use and aggression. However, results from human placebo-controlled randomized studies show an inconsistent association between AAS administration and aggression comprising negative (Björkqvist et al. 1994), positive (Panagiotidis et al. 2017; Wagels et al. 2018), and non-significant findings (Tricker et al. 1996).

Most previous reviews on this topic are merely narrative (Haug et al. 2004; Huo et al. 2016; Johnson et al. 2013). Additionally, a recent review (Geniole et al. 2020) on this topic lacks some studies (Anderson et al. 1992; Björkqvist et al. 1994; Su et al. 1993; Tricker et al. 1996). Hence, a comprehensive systematic review quantifying findings on the topic is overdue in line with the merit of meta-analyses in science and evidence-based medicine (Murad et al. 2016). Against this backdrop, we conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) examining the effect of AAS administration on self-reported as well as observer-reported aggression in healthy males.

Methods

Literature search strategy

Systematic literature searches were conducted in MEDLINE, PsycInfo, ISI Web of Science, ProQuest, Google Scholar, and Cochrane Library. There was no time constraint for the search. Keywords for AAS were combined with keywords for aggression. An overview of the keywords and search strategy can be found in Appendix A in the Supplementary information. The latest systematic literature search was conducted on 31 December 2019 followed by additional ad hoc searches to ensure comprehensiveness. The search and selection process are presented in Fig. 1.

Inclusion criteria and data extraction

Included studies were as follows: (1) RCTs, (2) investigating the effects of AAS administration on aggression in healthy persons, (3) based on valid aggression measures, and (4) published in English. The first author (RC) independently conducted the search and selection of articles based on the aforementioned criteria. Using a standardized data extraction form, the first and last (RC and DS) authors independently extracted the following data from the identified studies: study authors, country, design (e.g., double-blind), sample type (e.g., healthy males), sample size, age (range, $M \pm SD$), study groups (e.g., placebo group), AAS type, AAS dose, AAS administration mode (e.g., injection), study duration, assessment type (e.g., self-report), aggression measure, results, and risk of bias (see Table 1). Furthermore, the testosterone levels both at baseline and post-administration for each study are shown in Table 2. The two authors reached consensus in cases of discrepant extractions through discussions, with the involvement of the second author (SP) when necessary. We also contacted corresponding authors or, when unavailable, coauthors via email for missing information.

Statistical analysis

We first investigated the overall effect of AAS administration on self-reported aggression using a random-effects model. AAS users typically administer supraphysiologic doses of AAS for 4 to 28 weeks (Kanayama et al. 2013; Copeland et al. 2000). We therefore subsequently pooled studies in which higher doses (over 500 mg) of AAS were administered for the examination of the effect of high-dose AAS administration on self-reported aggression (O'Connor et al. 2004; Pope et al. 2000; Su et al. 1993; Tricker et al. 1996; Yates et al. 1999). Furthermore, we pooled studies in which AAS were administered over longer periods (i.e., 3 days to 14 weeks: Anderson et al. 1992; Cueva et al. 2017; O'Connor et al. 2002; O'Connor et al. 2004; Pope et al. 2000; Su et al. 1993; Yates et al. 1999) as well as studies investigating acute AAS effects (Carré et al. 2017; Dreher et al. 2016; Panagiotidis et al. 2017; Tricker et al. 1996). Due to the low number of studies administering higher doses ($k = 5$) or investigating acute AAS effects ($k = 4$), a fixed-effect model was used for these analyses (Borenstein 2009). Moreover, we conducted a meta-regression analysis to elucidate a potential dose-response association, regressing AAS dose (mg) on self-reported aggression. Finally, we investigated the overall effect of AAS administration on observer-reported aggression using a fixed-effect model due to the low number of studies ($k = 3$; O'Connor et al. 2004; Tricker et al. 1996; Yates et al. 1999).

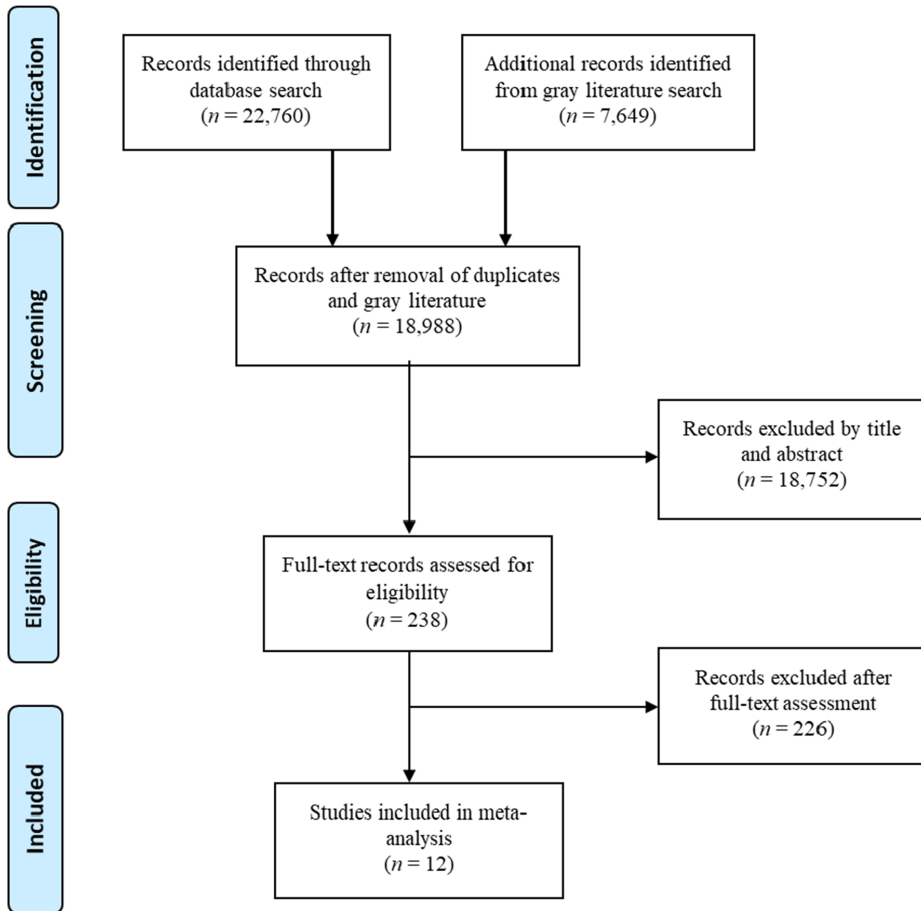


Fig. 1 PRISMA-style flow diagram of the study selection process

Some studies used multiple aggression measures and reported multiple aggression scores (O'Connor et al. 2002, 2004; Panagiotidis et al. 2017; Pope et al. 2000; Su et al. 1993). In these cases, we set the correlation between aggression measures to 0.60 (Diamond and Magaletta 2006; O'Connor et al. 2001) to provide the best estimates of between-study variance and corresponding confidence intervals (Gleser and Olkin 2009; Marín-Martínez and Sánchez-Meca 1999). For crossover studies (O'Connor et al. 2004; Pope et al. 2000; Su et al. 1993; Yates et al. 1999), we used an average correlation of 0.50 between aggression measures over time to provide optimal effect size estimates (Krahe and Möller 2010). Effects were estimated as Hedges' g , where 0.20 is considered small, 0.50 moderate, and 0.80 as large effect sizes, respectively (Hedges and Olkin 2014). For studies

including a passive control group (e.g., no intervention), a placebo group, and a treatment group (Björkqvist et al. 1994), data from the placebo and treatment groups were used to estimate meaningful relative-effect estimates (Karlsson and Bergmark 2015; Magill and Longabaugh 2013). Effect sizes were calculated by pooling post-intervention mean and standard deviations of aggression scores. When mean and standard deviation were not reported or unavailable in the original paper, authors were approached by email (Björkqvist et al. 1994), and asked to provide statistical information (i.e., F and p values) necessary to calculate effect sizes. For the assessment of heterogeneity, we used the Q -statistic and the I^2 index. The latter indicates the proportion of the observed variance that reflects real differences in effect size. It is expressed as a percentage (0–100) with 0% indicating no heterogeneity,

Table 1 Characteristics of randomized controlled trials on the effects of AAS administration on aggression in healthy persons

1st author year	Country	Design	Sample type	N (D/E)	Age range (M±SD)	Groups	AAS	AAS dose	AAS mode	Study duration	Aggression measure	Results
Anderson 1992	UK	Single-blind, PL-controlled, crossover	Healthy males	31	21–41	1: Baseline (<i>n</i> = 31) 1.2: TE (<i>n</i> = 16) 1.3: PL/TE (<i>n</i> = 15)	TE	1: Baseline 1.2: TE-200 mg TE-1 × 8wks 1.3: PL/TE-PL 1 × 4wks ffig by 200 mg TE 1 × 4wks	Injection	16wks	Daily ratings (irritable, ready to fight, easily angered)	No dose effect (<i>p</i> > .05)
Björkqvist 1994	Finland	Double-blind, PL-controlled	Healthy males	27 (3)	21–31 (23.9±)	1: TU (<i>n</i> = 9) pc 2: PL (<i>n</i> = 9) pc 3: Control (<i>n</i> = 9) pc	TU (Panteston®)	40 mg × 1 ×	Oral	≈4.3wks	VAS (SEMC) (irritability, anger) PSAP	PL > TU, and control (<i>p</i> < .02)
Carré 2017	Canada	Double-blind, PL-controlled	Healthy males	114 (7)	18–35 (25.27 ±4.98)	1: TG (<i>n</i> = 57) 2: PL (<i>n</i> = 57)	TG (AndroGel®)	150 mg (pc) × 1 ×	Transdermal (gel)	1 ×	PSAP	TG vs PL: No dose effect (<i>p</i> = 1.1) BSC × (TG vs PL): dose effects (<i>p</i> < .02)
Cueva 2017	UK	Double-blind, PL-controlled, crossover	Healthy males	38	22.4±2.97	1: Baseline (<i>n</i> = 20) 1.2: TE (<i>n</i> = 20) 1.3: PL/TE (<i>n</i> = 18)	T (Testogel™)	100 mg 3 × 34 pc	Transdermal (gel)	3 days	VAS (aggression)	No dose effect (<i>p</i> = .06)
Dreher 2016	Ireland	Double-blind, PL-controlled	Healthy males	40	18–30 (21.25 ±2.97)	1: TU (<i>n</i> = 21) pc 2: PL (<i>n</i> = 19) pc	TE	250 mg	Injection	1 ×	POMS (anger)	No dose effect (<i>p</i> = .43)
O'Connor 2002	UK	Double-blind, PL-controlled	Healthy males	30	19–45 (28.2±)	1: TE wks 0–4.8 (<i>n</i> = 15) 2: PL wks 0–4.8 (<i>n</i> = 15)	TE	200 mg 1 ×/wk × 8wks	Injection	8wks	POMS (anger-hostility) BPAQ	No dose effect (<i>p</i> > .05)
O'Connor 2004	UK	Double-blind, PL-controlled, crossover	Healthy males	24 (4)	22–44 (32.29 ±6.13)	1: TU (<i>n</i> = 13) pc 2: PL (<i>n</i> = 11) pc	TU	1000 mg 1 ×	Injection	28wks	POMS (irritability) BDHI (irritability) BIS-11 POMS (anger-hostility) BPAQ	POMS (anger-hostility): TU wk2 > TU wk0 (<i>p</i> < .05) No other dose effect (<i>p</i> > .05)
Panagiotidis 2017	Germany	Double-blind, PL-controlled	Healthy males	83 (7)	18–35	1: TG (<i>n</i> = 42; age range 18–35; 24.45±3.78) 2: PL (<i>n</i> = 41; age range 18–31; 23.89±3.65)	TG (Testim®)	50 mg × 1 ×	Transdermal (gel)	1 ×	BDHI (irritability) TPP ESR (anger)	TPP × ESR: TG > PL (FAIL condition, <i>p</i> = .041); TG vs PL (GO condition, <i>p</i> = .72) TG × ESR: <i>T_{FAIL}</i> > <i>T_{GO}</i> (<i>p</i> < .001)
Pope 2000	USA	Double-blind, PL-controlled, crossover	Healthy males	53 (T1: 3, T2: 6)	25–49	1: TC (<i>n</i> = 23) 2: PL (30)	TC	1: 150 mg 1 ×/wk × 2wks 2: 300 mg 1 ×/wk × 2wks 3: 600 mg 1 ×/wk × 2 wks	Injection	25wks	PSAP (<i>n</i> = 27) BPAQ	PSAP: TC > PL (<i>p</i> = .03) BPAQ: No dose effect (<i>p</i> = .35)
Su 1993	USA	Double-blind, PL-controlled, crossover	Healthy males	20 (3)	18–42 (27.5 ±5.7)	1: Baseline (<i>n</i> = 20) 2: MT 40 mg (<i>n</i> = 20) 3: MT 240 mg (<i>n</i> = 20) 4: Withdrawal (<i>n</i> = 20)	MT	2: 40 mg-3 ×/d × 3d 3: 240 mg-3 ×/d × 3d	Oral	2wks	VAS (irritability, anger, violent feelings) SCL-90 (hostility)	Irritability: MT 240 mg > Baseline (<i>p</i> < .05) No other dose effect (<i>p</i> > .05)
Tricker 1996	USA	Double-blind, PL-controlled	Healthy males	40 (3)	19–40	1: PL only (<i>n</i> = 10; age: 27±5) 2: TE only (<i>n</i> = 10; age: 26±6)	TE	600 mg 1 ×/wk × 10wks	Injection	30wks	MAI	No dose effect: anger arousal, anger situations, hostile outlook, anger-in, anger-out (<i>p</i> > .05)

Table 1 (continued)

1st author year	Country	Design	Sample type	N (D/E)	Age range (M±SD)	Groups	AAS	AAS dose	AAS mode	Study duration	Aggression measure	Results
Yates 1999	USA	Double-blind, PL-controlled, crossover	Healthy males	32 (11)	21–40	3: PL × ST 3×/wk (n = 9; age: 26±6) 4: TE × ST 3×/wk (n = 11; age: 30±7) 1: PL (n = 32) 1.2: TC 100 (n = 10; age: 27.4±3.3) 1.3: TC 250 (n = 11; age: 27.5±5.5) 1.4: TC 500 (n = 11; age: 30.2±5.9)	TC	1.2: 100 mg 1×/wk × 14wks 1.3: 250 mg 1×/wk × 14wks 1.4: 500 mg 1×/wk × 14wks	Injection	28wks	BDHI (assault)	No dose effect (p = .79)

1×: 1 time, APQ, Aggressive Provocation Questionnaire; BPAQ, Buss-Durkee Hostility Inventory; BPAQ-P, Buss-Perry Aggression Questionnaire-Partner; BSC, Brief Self-Control Scale; D/E, dropouts or excluded; ESR, Emotional Self-Ratings; MAI, Multi-Dimensional Anger Inventory; MT, methyltestosterone; OMI, Observer Mood Inventory; pc, Personal communication; PL, Placebo; POMS, Profile of Mood States; PSAP, Point Subtraction Aggression Paradigm; SCL-90, Symptom Checklist 90; SEMC, Self-Estimated Mood Checklist; ST, strength training; T, testosterone; TC, testosterone cypionate; TE, testosterone enanthate; TG, testosterone gel; TU, testosterone undecanoate; TPP, Technical Provocation Paradigm; YAS, visual analogue scale

25% indicating low heterogeneity, 50% indicating moderate heterogeneity, and 75% suggesting high heterogeneity (Higgins et al. 2003) respectively. Additionally, we used Duval and Tweedie’s (2000) trim and fill method, and Orwin’s (1983) fail-safe *N* to assess publication bias. The trim and fill method (Duval and Tweedie 2000) screens for missing studies and adjusts the effect size by trimming the asymmetric studies and filling a funnel plot symmetrically. Orwin’s (1983) fail-safe *N* quantifies the number of studies required to bring the observed effect size down to a chosen “trivial” estimate (Hedges and Olkin 2014). In the current meta-analysis, we set the “trivial” estimate to *g* of 0.05.

The quality of each included study was assessed using the Cochrane risk of bias tool (Higgins et al. 2003). The protocol for the meta-analysis was pre-registered in PROSPERO (CRD 42019117834). The literature search, coding of variables, and reporting were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) procedure (Moher et al. 2009). The meta-analysis and the meta-regression were performed using the Comprehensive Meta-Analysis version 3.3.070 (Borenstein et al. 2014).

Results

Literature screening and selection

From an initial pool of 30,407 hits, 18,988 records remained after removal of duplicates (*k* = 3772) and gray literature (*k* = 7649) during initial identification and screening. Of this pool, 18,752 were removed after eligibility screening by title and abstract leaving 238 records for further evaluation. After screening the 238 full-text records, 12 studies were finally included. Figure 1 presents the literature search and selection process.

Description of included studies

Of the twelve included studies, publication year ranged from 1992 (Anderson et al. 1992) to 2017 (Carré et al. 2017; Cueva et al. 2017; Panagiotidis et al. 2017). Four of the studies were conducted in the USA (Pope et al. 2000; Su et al. 1993; Tricker et al. 1996; Yates et al. 1999), four in the UK (Anderson et al. 1992; Cueva et al. 2017; O’Connor et al. 2002, 2004), and one each in Germany (Panagiotidis et al. 2017), Finland (Björkqvist et al. 1994), Ireland (Dreher et al. 2016), and Canada (Carré et al. 2017). We received clarification and data from some authors (Björkqvist et al. 1994; Carré et al. 2017; Cueva et al. 2017; Dreher et al. 2016; O’Connor et al. 2004). (See Table 1.)

All the included studies comprised placebo-controlled randomized trials. One of the included studies was single-blinded

(Anderson et al. 1992) and 11 were double-blinded. Additionally, six studies were crossover studies (Anderson et al. 1992; Cueva et al. 2017; O'Connor et al. 2004; Pope et al. 2000; Su et al. 1993; Yates et al. 1999) whereas five were based on a between-subject design (Björkqvist et al. 1994; Carré et al. 2017; Dreher et al. 2016; O'Connor et al. 2002; Panagiotidis et al. 2017; Tricker et al. 1996). The studies included a total of 562 healthy male (females: $n = 0$) participants. Participants' ages ranged from 18 (Su et al. 1993) to 49 (Carré et al. 2017) with a grand mean of 25.83 ($SD = 3.80$).

Testosterone enanthate was administered in four studies (Anderson et al. 1992; Dreher et al. 2016; O'Connor et al. 2002; Tricker et al. 1996) and two studies administered testosterone cypionate (Pope et al. 2000; Yates et al. 1999). In addition, two studies administered testosterone undecanoate (Björkqvist et al. 1994; O'Connor et al. 2004), and three studies administered testosterone gel (Carré et al. 2017; Cueva et al. 2017; Panagiotidis et al. 2017) whereas one study administered methyltestosterone (Su et al. 1993). AAS doses ranged from a one-time application of 50 mg of testosterone gel (Panagiotidis et al. 2017) to a one-time injection of 1000 mg of testosterone undecanoate (O'Connor et al. 2004), and a cumulative injection of 7000 mg of testosterone cypionate over a 14-week period (Yates et al. 1999). When various doses of AAS were used in one study, we used results from the highest dose for calculating the effect size.

Aggression was assessed by self-reports (Anderson et al. 1992; Björkqvist et al. 1994; Carré et al. 2017; Cueva et al. 2017; Dreher et al. 2016; O'Connor et al. 2002, 2004; Panagiotidis et al. 2017; Pope et al. 2000; Su et al. 1993; Tricker et al. 1996; Yates et al. 1999), observer-reports (O'Connor et al. 2004; Tricker et al. 1996; Su et al. 1993;

Yates et al. 1999), and behavioral aggression measures (Carré et al. 2017; Pope et al. 2000). The Buss-Perry Aggression Questionnaire (Buss and Perry 1992) was used in three studies (O'Connor et al. 2002, 2004; Pope et al. 2000), and three studies (O'Connor et al. 2002, 2004; Yates et al. 1999) used the Buss-Durkee Hostility Inventory (Buss and Durkee 1957), two studies (Carré et al. 2017; Pope et al. 2000) used the Point Subtraction Aggression Paradigm (Cherek et al. 1996), and three studies (Dreher et al. 2016; O'Connor et al. 2002, 2004) used the Profile of Mood States (McNair et al. 1992) with two out of these three studies (O'Connor et al. 2002, 2004) additionally using the Aggression Provocation Questionnaire (O'Connor et al. 2001).

Additionally, the Self-Estimated Mood Checklist (Lindman 1985) was used in one study (Björkqvist et al. 1994), and one study (Panagiotidis et al. 2017) used the Technical Provocation Paradigm (Panagiotidis et al. 2017) and emotional self-ratings (Schneider et al. 1994). Moreover, two studies (Cueva et al. 2017; Su et al. 1993) used visual analogue scales (Cline et al. 1992; Norris 1971), one study (Tricker et al. 1996) used the Multi-Dimensional Anger Inventory (Siegel 1986), and one study (Anderson et al. 1992) used daily ratings of irritability, readiness to fight, and being easily angered. 10 studies (Anderson et al. 1992; Carré et al. 2017; Cueva et al. 2017; Dreher et al. 2016; O'Connor et al. 2002, 2004; Panagiotidis et al. 2017; Pope et al. 2000; Tricker et al. 1996; Yates et al. 1999) reported no significant effect of AAS administration on aggression. In addition, one study (Su et al. 1993) found a positive effect of AAS administration on aggression ($p < .05$), whereas one study (Björkqvist et al. 1994) reported a negative effect of AAS administration on aggression ($p < .01$).

Table 2 Mean baseline and post-administration levels of placebo and testosterone for each study (nmol/L)

1st author year	Placebo		Testosterone	
	Baseline	Post-administration	Baseline	Post-administration
Anderson 1992	19.20	33.10	17.70	28.80
Björkqvist 1994	-	-	-	-
Carré 2017	18.38	19.07	19.07	30.16
Cueva 2017	1.04	1.04	.69	10.05
Dreher 2016	20.46	20.44	21.06	66.08
O'Connor 2002	20.10	20.0	21.70	38.42
O'Connor 2004	20.30	20.30	20.70	37.50
Panagiotidis 2017	16.99	15.0	16.62	21.20
Pope 2000	16.30	18.40	17.40	76.00
Su 1993	-	-	-	-
Tricker 1996	18.60	19.40	16.10	76.90
Yates 1999	20.82	19.08	20.82	73.73

Risk of bias

The two authors disagreed once on the random sequence generation dimension for all the included studies yielding a Cohen’s kappa of .58 (Cohen 1988). All studies were evaluated as having a high selection bias as there was no description of the randomization method or concealed allocation process. In addition, all studies were evaluated as having high risks of performance and detection bias as the effectiveness of blinding was not tested. Moreover, all studies had a low risk of attrition bias as there was sufficient reporting and handling of attrition and exclusion. Furthermore, except for one study that did not present means and standard deviations or inferential indices (Björkqvist et al. 1994), we evaluated all studies as having low reporting bias. Figure 2 depicts the risk of bias of the included studies.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Anderson 1992	●	?	●	●	●	●
Björkqvist 1994	●	?	?	?	●	●
Carré 2017	●	?	?	?	●	●
Cueva 2017	●	?	?	?	●	●
Dreher 2016	●	?	?	?	●	●
O’Connor 2002	●	?	?	?	●	●
O’Connor 2004	●	?	?	?	●	●
Panagiotidis 2017	●	?	?	?	●	●
Pope 2000	●	?	?	?	●	●
Su 1993	●	?	?	?	●	●
Tricker 1996	●	?	?	?	●	●
Yates 1999	●	?	?	?	●	●

Fig. 2 Estimated risk of bias of the included studies

Effect of AAS administration on self-reported aggression

Of the twelve included studies, one study (Björkqvist et al. 1994) did not overlap with the 95% CI of the overall pooled effect size. Exclusion of this outlier resulted in a mean and significant random-effects size of $g = 0.171$ (95% CI: 0.029–0.312, $k = 11$, $p = .018$), and there was no significant heterogeneity between the included studies ($I^2 = 0.000$, $Q = 8.891$, $p = .542$). The effect sizes and associated 95% confidence intervals are presented in Fig. 3.

The overall random-effects of AAS administration on self-reported aggression, including the outlier (Björkqvist et al. 1994), was not significant ($g = 0.081$, 95% CI: -0.111–0.273, $p = .408$). (See Supplementary Figure 1.) When adjusting for publication bias using Duval and Tweedie’s trim and fill method, the overall result ($k = 12$) turned out non-significant ($g = 0.170$, 95% CI: 0.029–0.312, $p = .890$). (See Supplementary Figure 2.) Results from Orwin’s fail-safe N analysis indicated that 27 studies with an effect size of zero would be needed to bring Hedges’ g below 0.05.

Effect of long-term AAS administration on self-reported aggression

The random-effects of administering AAS over longer periods (3 days to 14 weeks) on self-reported aggression under a random-effects model was $g = 0.100$ (95% CI: -0.079–0.278, $p = .273$). There was no significant heterogeneity across studies in terms of effect sizes ($I^2 = 5.286$, $Q = 6.335$, $p = .321$). (See Fig. 4.)

Effect of acute AAS administration on self-reported aggression

Under a fixed-effect model, the effect of acute administration of AAS on self-reported aggression was $g = 0.291$ (95% CI: 0.014–0.524, $p = .014$, $Q = .867$, $p = .833$). (See Fig. 5.)

Effect of AAS dose on self-reported aggression

AAS dose (mg) was not associated with self-reported aggression in a random-effects meta-regression model ($B = 0.000$, $SE = 0.000$ (95% CI: -0.000–0.000), $p = .096$).

Effect of high-dose AAS administration on self-reported aggression

The mean effect of higher doses (over 500 mg) of AAS on self-reported aggression under a fixed-effect model was non-significant ($g = 0.191$; 95% CI: -0.007–0.388, $p = .059$, $Q = 1.399$, $p = .844$). (See Fig. 6.)

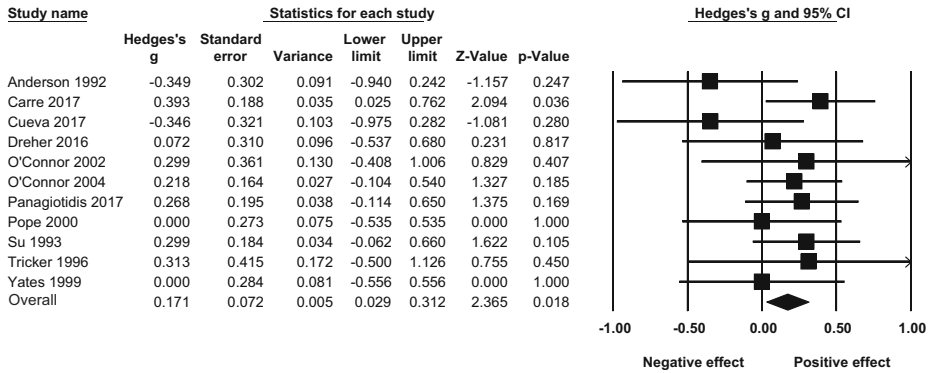


Fig. 3 The effect (random-effects model) of AAS administration on self-reported aggression

Effect of AAS administration on observer-reported aggression

The overall fixed-effect of AAS administration on aggression based on observer ratings resulted in an effect size of $g = 0.157$ (95% CI: $-0.026-0.581$, $p = .469$, $Q = .249$, $p = .833$). The effect sizes and associated 95% confidence intervals for each study are presented in Fig. 7.

Discussion

The present systematic review and meta-analysis of eleven studies (Anderson et al. 1992; Carré et al. 2017; Cueva et al. 2017; Dreher et al. 2016; O'Connor et al. 2002, 2004; Panagiotidis et al. 2017; Pope et al. 2000; Su et al. 1993; Tricker et al. 1996; Yates et al. 1999), after excluding an outlier (Björkqvist et al. 1994), indicates that AAS administration is associated with an increase in self-reported aggression, albeit small, among healthy males in RCTs. This finding is consistent with the results of a recent meta-analysis

(Geniole et al. 2020) indicating that testosterone administration has a small and positive correlation with aggression in males. Relatedly, our finding that acute AAS administration has a positive effect on self-reported aggression is consistent with evidence that acute increases in testosterone have a positive correlation with aggression (Geniole et al. 2020).

The present study is the first comprehensive systematic review and meta-analytic investigation of the effect of AAS administration and aggression in healthy males in RCTs. However, our results should be interpreted with caution. Firstly, a meta-regression examining dosage as a moderator of the identified effect of AAS on self-reported aggression turned out not significant. Similarly, we did neither detect an effect of AAS administration on observer-reported aggression nor for the effects of long-term (3 days to 14 weeks) and high-dose AAS administration on self-reported aggression. Also, as noted previously, only healthy males were examined in the included RCTs and the duration and doses used in the twelve RCTs deviate from the prolonged use of high-dose cycles consisting of the ingestion of supraphysiologic doses of different types of AAS per week over several months (Kanayama

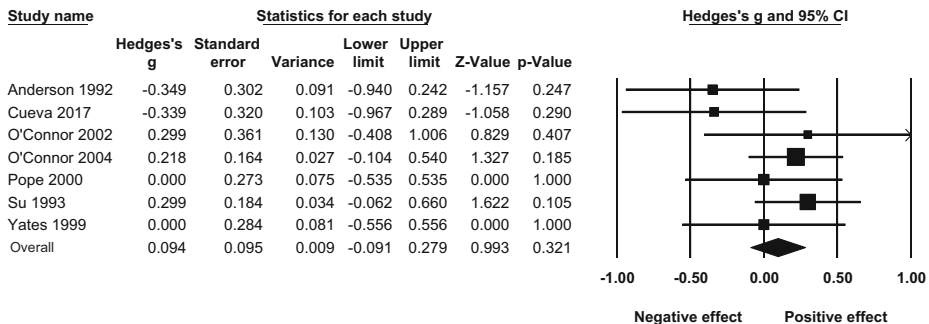


Fig. 4 The effect (random-effects model) of administering AAS over longer periods on self-reported aggression

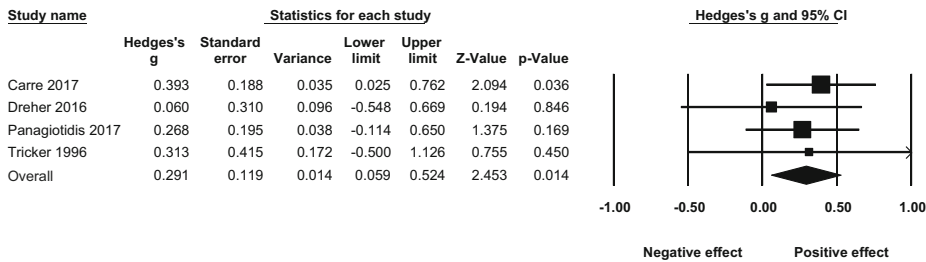


Fig. 5 The effect (fixed-effect model) of acute AAS administration on self-reported aggression

et al. 2013) often reported by users in ecologically valid settings. In one study, the reported weekly AAS dose ranged from 125 to 7000 (mean = 1278) mg per week over an average of 9.1 years (Bjørnebekk et al. 2017). In another recent study, it was shown that an AAS cycle usually comprises the ingestion of five different AAS with an average dose of 901 mg per week for a typical duration of 13 weeks (Smit et al. 2020b). In the present meta-analysis, the highest dose administered was a one-time injection of 1000 mg of testosterone undecanoate (O'Connor et al. 2004) and a cumulative injection of 7000 mg of testosterone cypionate over a 14-week period (Yates et al. 1999). Inferably, AAS doses and duration of administration in the RCTs included in our meta-analysis are far lower than the actual doses reported by AAS users (Bjørnebekk et al. 2017; Kanayama et al. 2013).

Similarly, besides the administration of methyltestosterone in one study (Su et al. 1993), fluoxymesterone, oxymetholone, and trenbolone that are anecdotally associated with increased aggression in humans (Barker 1987; Llewellyn 2011) were not administered in the RCTs included in the present review. Moreover, testosterone undecanoate administered in two studies (Björkqvist et al. 1994; O'Connor et al. 2004) is a depot with a very gradual decay and long half-life leading to relatively stable testosterone levels over a prolonged period of time (Hirschhäuser et al. 1975). Hence, discrepancies in AAS doses, type, duration of use, and half-life between the AAS in the RCTs and naturalistic contexts should be noted when interpreting our findings.

In addition, evidence from cross-sectional studies indicates that polypharmacy and stacking (Sagoe et al. 2015; Salinas et al. 2019) may account for increased aggression among AAS users (Lundholm et al. 2015). The absence of polypharmacy in the RCTs included in our meta-analysis may also explain the discrepancy between findings from RCTs and those reported in more ecologically valid contexts. Other potential confounding factors include small sample sizes and lack of a priori power analyses, diversity in aggression measures, risk of bias (selection, performance, and detection biases), diversity in route of administering AAS (injecting, transdermally), diversity in time gap between AAS administration, incomplete data reporting, and sampling of only males in included RCTs.

Moreover, the inclusion of only healthy volunteers in the RCTs may have precluded vulnerable subjects from participating which may have led to the underestimation of the effects of AAS administration on aggression. Sampling is important with evidence that testosterone increases aggression in men with certain personality profiles especially among those with fewer cytosine-adenine-guanine repeats in exon 1 of the androgen receptor gene (Geniolo et al. 2019). The importance of sampling is further evidenced in that, apart from bodybuilders and competitive athletes, a large portion of non-experimental research linking AAS use with aggression has been conducted among subgroups associated with aggression such as drug users, offenders, and prisoners (Lundholm et al.

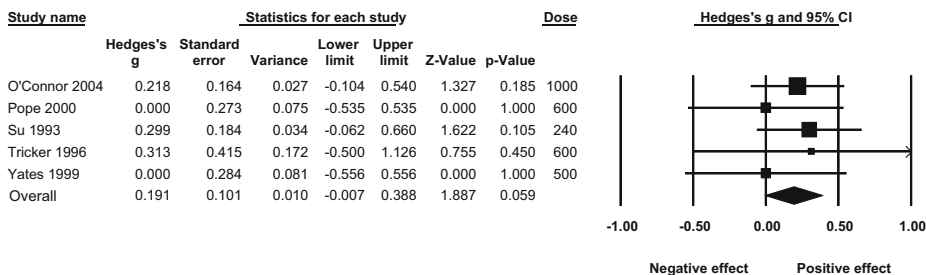


Fig. 6 The effect (fixed-effect model) of administering higher (over 500 mg) doses of AAS on self-reported aggression

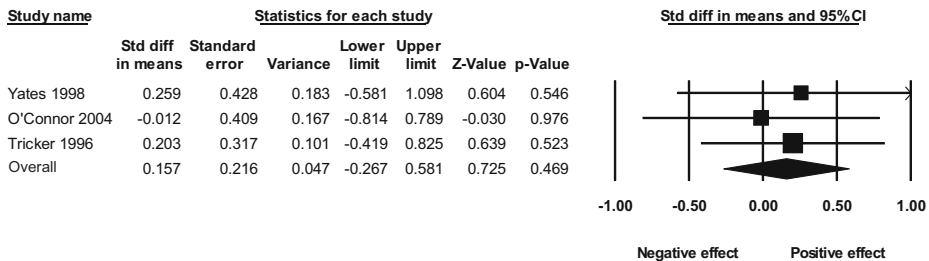


Fig. 7 The effect (fixed-effect model) of AAS administration on observer-reported aggression

2010; Pope et al. 1996), as well as policemen, doormen, and nightclub bouncers (Hoberman 2017; Midgley et al. 2001). Future researchers considering the aforementioned factors may conduct more ecologically valid RCTs (e.g., by using dosages and duration of use similar to those by real AAS users) to better elucidate the effect of AAS administration on aggression in humans. Furthermore, more studies should explore factors of AAS administration (e.g., type of AAS, duration of use, premorbid functioning, and genetics) that might moderate the effects of AAS on aggression.

Conclusions

The present systematic review and meta-analysis provide evidence for an increase, although small, in self-reported aggression in healthy males following AAS administration in RCTs. Moreover, when restricting the analysis to the effects of acute AAS administration on self-reported aggression, we found a significant effect. We also identified important limitations of the RCTs on issues such as non-ecological doses, lack of personality and polypharmacy controls, small sample sizes, risk of bias, short study duration, and the inclusion of only healthy males. While future RCTs adjusting for the above factors may contribute better to contemporary understanding of the effect of AAS administration on aggression in humans, the present study provides an important foundation for addressing this important public health issue. As the appreciation of the heterogeneity of AAS use matures, there is a need to identify the role that AAS plays in aggression and violence and what may be attributed to the set and setting of their use.

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Declarations

Conflict of interest The authors declare no competing interests.

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Aggression and psychological distress in male and female anabolic-androgenic steroid users: A multigroup latent class analysis

Running head: Aggression and distress in AAS users

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ABSTRACT

The relationship between anabolic-androgenic steroid (AAS) use and aggression and psychological distress requires further elucidation. To our knowledge, no previous study has examined whether the patterns of aggression and psychological distress are the same in male and female AAS users by multigroup latent class analysis (MLCA). We therefore conducted a MLCA to identify discrete subgroups of aggression and psychological distress in AAS users, and used measurement invariance to examine whether the identified subgroups can be applied to both sexes. We also examined the relationship between sex and subgroup belongingness. The sample comprised 206 AAS users (females = 58.30%) aged 14 to 56 (mean = 26.86, $SD = 7.12$ years). They completed questionnaires assessing demographics, AAS use, aggression, and psychological distress. Based on the MLCA, five subgroups were identified: high aggression moderate distress users (HAMoD: 07.63%), moderate aggression distress users (18.64%), moderate direct aggression-mild indirect aggression moderate distress users (22.95%), mild direct aggression-moderate indirect aggression-distress users (11.71%), and low aggression mild distress users (LAMiD: 39.06%). Although a homogenous five-class solution was the best model for both sexes, sex was significantly associated with the probability of subgroup membership. In particular, members of the HAMoD subgroup were more likely to be male whereas members of the LAMiD subgroup were more likely to be female. Our study provides novel empirical evidence of the idiosyncratic patterns of aggression and psychological distress among male and female AAS users.

Keywords: aggression, anabolic-androgenic steroids, multigroup latent class analysis, sex, psychological distress

INTRODUCTION

Anabolic-androgenic steroids (AAS) comprise testosterone and its synthetic derivatives. These drugs are used for treatment of insufficient testosterone production and cachexia associated with chronic diseases and advancing age (Ali and Garcia, 2014; Kicman, 2008). Due to its anabolic effects, AAS have typically been used by elite athletes and bodybuilders primarily to increase muscle mass and enhance strength. Further, AAS use has spread into the general population over the last four decades (Sagoe and Pallesen, 2018). The global lifetime prevalence of AAS use (Sagoe et al., 2014a) is estimated at 3.3% with a higher prevalence among males (6.4%) compared to females (1.6%).

Users often ingest supra-physiological doses of AAS for years. Despite experiencing various aesthetic and performance benefits (Cheung and Grossmann, 2018; Sagoe et al., 2014b), users also often report adverse physiological and psychological effects (Baggish et al., 2017; Bensoussan and Anderson, 2019; Christou et al., 2017; Cunningham et al., 2013; Hauger et al., 2019a, 2019b; Kaufman et al., 2019). The most well-known psychological adverse effect of AAS use among the general population is lack of impulse control, hostility, and high levels of aggressive and violent behavior, sometimes referred to as “roid rage” or “steroid rage” (Pope and Katz, 1987; Tragger, 1988). In line with this, numerous studies have indicated that AAS use is associated with aggression (Jenssen and Johannessen, 2015; Perry et al., 2005; Sagoe et al., 2016; Værøy, 2013) or increases in aggression (Panagiotidis et al., 2017; Pope et al., 2000; Wagels et al., 2018), although experimental and longitudinal studies present contrasting evidence (Carré et al., 2017; Chegeni et al., 2019; O'Connor et al., 2002). From these inconsistent results, it is not clear whether all AAS users experience aggression and psychological distress upon use and whether there are unobserved patterns of aggression and psychological distress among AAS users.

Although characteristics of substance users as well as side-effects associated with different substances mainly are described at an aggregated level, identifying subgroups of such users and their behavioral outcomes can facilitate identification of at-risk individuals and groups most sensitive to the negative psychological consequences of AAS use, as well as the development of targeted interventions (Babor and Caetano, 2006; Lanza and Rhoades, 2013). In this regard, several studies have examined subgroups of substance users (Krauss et al., 2017; Shin et al., 2010). These studies have mainly focused on alcohol and tobacco use (Evans-Polce et al., 2016; Morean et al., 2016). Patterns of risk and protective factors for behavioral outcomes of substance use have also been previously examined (Syvertsen et al., 2010).

Subgroups of AAS (Christiansen et al., 2017; Sagoe, 2014; Zahnow et al., 2018) and appearance- and performance-enhancing drug (APED) users (Hildebrandt et al., 2007) based on users' approach to risk and effectiveness of AAS and use patterns have been identified in some previous studies. However, although aggression and psychological distress are major behavioral outcomes associated with AAS use (Cunningham et al., 2013; Havnes et al., 2019; Pagonis et al., 2006) as previously indicated, no previous study has examined subgroups of AAS users based on their aggression and psychological distress profile. Indeed, different APEDs are associated with different behavioral outcomes and it is important to examine these unique outcomes (Hildebrandt et al., 2007). A multigroup latent class analysis (MLCA; Lazarsfeld and Henry, 1968) is superior to traditional categorization of subgroups using cut-off points (Berzofsky et al., 2008). Hence, we conducted a MLCA to assess physical aggression, verbal aggression, anger, and hostility and psychological distress patterns in male and female AAS users.

Moreover, AAS use is predominantly a male practice and AAS use among females is an understudied area (Sagoe et al., 2014a; Sagoe and Pallesen, 2018). Relatedly, the few

studies that have examined the side effects of AAS use among females are based on small samples (Abrahin et al., 2017; Börjesson et al., 2016; Grogan et al., 2006; Havnes et al., 2020; Ip et al., 2010). In addition, males and females tend to use different doses and types of AAS and believe that the doses and the types they choose is best fitting to their sex (Abrahin et al., 2017; Santos, 2014). More importantly, females are an important group in clinical practice and policy making on AAS use. Thus, information about patterns of aggression and psychological distress in AAS-using females is important. Accordingly, we included female AAS users in the current study to identify their patterns of aggression and psychological distress and to examine subgroups of female and male AAS users. We also investigated whether there are unobserved sex differences in the identified patterns.

MATERIALS AND METHODS

Participants

Participants comprised 206 current AAS-using bodybuilders (females = 58.30%) with a history of at least six months' regular AAS use prior to data collection. Age of participants ranged from 14 to 56 ($M = 26.89$, $SD = 7.12$) years. Other participant characteristics are presented in Table 1.

Insert Table 1 about here

Measures

Demographics

The questionnaire assessed demographic factors including age, sex, weight, height, educational level, marriage, and job status.

Sports and Weight Training

We assessed participants' main involvement in sports and exercise as well as and total number of years of regular weight training. We also asked participants how many times per week (number of days and hours) they trained with weights.

AAS Use

Current AAS use was assessed with the question “Do you currently use anabolic-androgenic steroids?” (yes/no). In verifying AAS use, participants specified the AAS they used (see Table 1). For the assessment of AAS use duration, participants also indicated how long (years) they had been using AAS regularly.

Aggression

We used the Short-Form Buss-Perry Aggression Questionnaire (BPAQ-SF; Diamond and Magaletta, 2006; Samani, 2008) to assess aggression. Four items represent physical aggression (e.g., “I have trouble controlling my temper”), three items assess verbal aggression (e.g., “I often find myself disagreeing with people”), three items reflect hostility (e.g., “Other people always seem to get the breaks”), and two items measure anger (e.g., “Sometimes I fly off the handle for no good reason”). Items are answered on a 5-point Likert-type scale ranging from 1 (*Very unlike me*) to 5 (*Very like me*). In the present study, Cronbach’s α for physical aggression, verbal aggression, hostility, and anger were .73, .70, .77, and .69 respectively.

Psychological Distress

We assessed symptoms of psychological distress (anxiety and depression) using the Hospital Anxiety and Depression Scale (HADS; Montazeri et al., 2003; Zigmond and Snaith, 1983). HADS contains seven items reflecting anxiety symptoms (HADS-A; e.g., “I feel restless as I have to be on the move”) and seven items reflecting depressive symptoms (HADS-D; e.g., “I have lost interest in my appearance”) experienced over the last week. Items are scored on a 4-point scale (0–3). We computed a composite score of anxiety and depression to indicate psychological distress in general, adhering to previous studies that have shown superior factor loadings of one general factor (Bjelland et al., 2002; Kjærgaard et al., 2014). Scores from HADS utilizing the general factor range from 0 to 56. In the present study, Cronbach’s α for psychological distress was .82.

Procedure

Eligibility criteria for participation were being a current: (1) weightlifter and (2) regular AAS user for at least six months. Participants were recruited from training centers and sports supplement stores in Tehran, Iran. Data was collected via personal meetings at the training centers and supplement stores. All participants provided oral consent, participation was voluntary and anonymous, and participants could withdraw from participation. Upon participants' consent, a trained research assistant handed paper questionnaires to participants for completion. Clarification about the questionnaire was provided when necessary. No incentive or compensation was provided for participation. Data was collected in June 2019. The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from Alzahra University in Tehran, Iran.

Statistical Analysis

Descriptive statistics were used to determine characteristics of the sample. Characteristics of the sample was determined in terms of descriptive statistics as means and standard deviations for interval and ratio level variables and by percentages for nominal level variables. The major goal of the current study was to examine patterns of aggression and psychological distress in male and female AAS users, and to investigate whether the identified patterns can be applied to both sexes. First, we conducted a Latent Class Analysis (LCA; Bakk and Vermunt, 2016; Collins and Lanza, 2010) to examine discrete patterns of direct aggression (i.e., physical and verbal aggression), indirect aggression (i.e., anger and hostility), and psychological distress for the entire sample. In the context of present study, the aforementioned indicators were used to estimate latent classes of current AAS users. The Bayesian Information Criterion (BIC; Schwarz, 1978) is the most commonly used fit criteria to select the optimal number of latent classes (Collins and Lanza, 2010; Nylund et al., 2007). Models with lower values of information criteria have a better fit to the data (Kankaraš et al.,

2010). A common approach is therefore to select the model with a number of latent classes which shows the lowest BIC (Hagenaars, 1990; McCutcheon, 1987). The likelihood-ratio chi-square (L^2) is a descriptive measure for assessing model fit and when L^2 is significant it shows that the model does not fit the data. Entropy R^2 and total proportion of adjacent classification error were used as indicators of the quality of the classification.

Measurement invariance is required to determine whether the identified latent classes can be applied to both sexes (Kankaraš et al., 2010). Thus, after selecting a latent class model for the entire sample, we tested for measurement invariance across sex in order to make a valid comparison across subgroups of male and female AAS users (Clogg and Goodman, 1985; McCutcheon, 1987). When comparing latent classes across groups, different levels of homogeneity (i.e., measurement invariance) can occur, each of which involves restricting specific sets of model parameters to be equivalent in all groups. There are three prototypical models that differ in the levels of measurement invariance (Clogg and Goodman, 1985). First is the homogeneous model which assumes that the latent classes have the same structure in each group. In this case effects of the group variable on the indicator variables are completely mediated by the latent classes. Hence, the homogeneous model imposes restrictions on the measurement model without deteriorating the fit with the data (Figure 1a).

Second is the partially homogeneous model where some of the model parameters are restricted to be equal in all groups. For example, when differences in answers of participants with different sexes are not associated with differences in a latent class, direct effects occur. Here, the goal is to examine whether the group variable has a direct effect on the indicator variables (Figure 1b). In addition, the heterogeneous model assumes that the latent classes have different structures in each group. In this unrestrictive model, the group variable has three sets of effects including effect on latent classes, direct effect on indicator variables, and interaction effects with latent classes on indicators. Hence, a heterogeneous model lacks any

comparability of results across groups as all measurement model parameters are group-specific (Figure 1c).

To test measurement invariance, we conducted homogeneous, partially homogeneous, and heterogeneous multigroup latent class analysis (MLCA) with sex as the grouping variable. Moreover, to relax the assumption of measurement invariance, we assumed that some, but not all, indicators are invariant across sex. We added the direct effect of the grouping variable on each indicator (in the partially homogeneous model). The goal of this step is to check the invariance of each indicator. See Figure 1 for details. A MLCA approach is flexible in the sense that not all latent classes need to be equivalent in order to validly compare results across groups.

Insert Figure 1 about here

Next, for comparing and choosing the best model for the data, we followed a model comparison procedure where difference in likelihood-ratio chi-square (L^2) with a difference in degrees of freedom is used to determine which model is most appropriate. We calculated the difference in L^2 and in degrees of freedom between consecutive nested models. The unrestricted heterogeneous model served as the baseline for this comparison. When moving from the homogenous model to the unrestricted heterogeneous model, if the difference in L^2 between two consecutive nested models (i.e., one model is obtained from a general model by imposing complex and decreasing homogeneity on the former) is significant, the model with more heterogeneity and less degrees of freedom fits the data best (Magidson and Vermunt, 2002). Finally, class proportions for each group were examined. Here, participants were assigned to latent classes based on the likelihood of belonging to a class using the proportional assignment rule (Goodman, 2007; Magidson and Vermunt, 2002). We used the walt test to examine the relationship between sex and class membership. Descriptive analyses

were conducted using RStudio version 1.1.463 (RStudio, Inc). The MLCA was performed using advanced LatentGOLD 5.1 (Vermunt and Magidson, 2016).

RESULTS

Sample Description

The average height and weight of female users were 165.11 ($SD = 5.91$) and 62.06 ($SD = 10.41$) respectively. Male AAS users' average weight and height were 180.46 ($SD = 6.09$) and 84.64 ($SD = 16.23$) respectively. Female and male AAS users trained, on average, 4.37 ($SD = 3.38$) and 6.19 ($SD = 5.85$) hours per week at the gym. The average AAS use duration was 1.51 ($SD = .66$) years for males and 1.19 ($SD = .43$) years for females. Oxandrolone (Anavar) (males = 57, females = 55), testosterone (males = 66, females = 48), stanozolol (Winstrol) (males = 96, females = 40), Dianabol (methandrostenolone) (males = 96, females = 33), and Anadrol (oxymetholone) (males = 39, females = 23) were the most used types of AAS among both sexes. See Table 1 for other participant characteristics.

Patterns of Latent Classes and Measurement Invariance

Fit statistics for the latent classes are presented in Table 2. A 5-class solution was the best model as evident by the lowest BIC (4326.81). The squared log-likelihood (L^2) was 2220.11 ($p = 0.000$), the total proportion of adjacent classification errors was 0.02, and entropy R^2 was .94.

Insert Table 2 about here

As the next step, considering the 5-class solution from the initial LCA, we conducted a MLCA to assess measurement invariance. Table 3 presents results of the consecutive nested models. When comparing these nested models, we found that sequentially adding direct effects of sex on classes and the interaction between sex and classes did not lead to a significant improvement of fit. Indeed the ΔL^2 indicated a deterioration of fit. Hence, the

model comparison procedure indicated that the homogeneous model fit was better than that of all other models. Hence, sex did not cause measurement variance. From Table 3, we can thus conclude that patterns of aggression and psychological distress are not dependent on the sex of AAS users.

Insert Table 3 about here

We taxonomized the patterns of the five latent classes on four risk categories: low, mild, moderate, and high. Accordingly, class 1 (high aggression moderate distress users: HAMoD; 7.63%) was characterized by the highest levels of direct (i.e., physical and verbal aggression), indirect (i.e., anger and hostility), and moderate psychological distress. Class 2 (moderate aggression distress users: MoAD; 18.64%) comprised moderate levels of direct and indirect aggression and psychological distress. Class 3 (moderate direct aggression-mild indirect aggression moderate distress users: ModA-MiiA MoD; 11.71%) were characterized by moderate levels of physical and verbal aggression, mild levels of anger and hostility, and moderate psychological distress. Class 4 (mild direct aggression-moderate indirect aggression-distress users: MidA-MoiAD; 11.62%) displayed mild levels of physical and verbal aggression, moderate levels of anger and hostility as well as psychological distress. Class 5 (low aggression mild distress users: LAMiD; 39.06%) were characterized by lowest levels of all the indicators of aggression and mild psychological distress. Figure 2 presents the patterns of aggression and psychological distress for the 5-class model.

Insert Figure 2 about here

In Table 4, we report the class proportions obtained from the selected model. It can be seen that there was an inverse proportional sex distribution of the subgroups. Specifically, the proportion of male AAS users in class 1 (HAMoD) was 91.67% while the proportion of female users was 08.33%. Also, class 2 (MoAD) consisted of 80.42% males and 19.58%

females. The third class (ModA-MiiA-MoD) included 32.46% of male AAS users and 67.54% of female AAS users. Class 4 (MidA-MoiAD) consisted of 30.00% of male AAS users and 70.00% of female AAS users. Finally, the proportion of male users in the fifth class (LAMiD) was 10.51% and the proportion of female users was 89.49%. Table 4 indicates results from Wald test. From Table 4, sex was significantly related to class membership (Wald = 31.04, $p < .001$) with members of class 1 (HAMoD) more likely to be male ($z = -5.02$, $p < .001$) whereas members of class 5 (LAMiD) were more likely to be female ($z = 3.51$, $p < .001$).

Insert Table 4 about here

DISCUSSION

The present study examined discrete patterns of AAS male and female users based on measures of aggression and psychological distress using a multigroup latent class analysis. We also examined whether the identified patterns are applicable to both sexes. Five latent classes offered the best explanation for the patterns of physical aggression, verbal aggression, anger, hostility, and psychological distress: high aggression moderate distress (7.63%), low aggression mild distress (39.06%), moderate aggression distress (18.64%), moderate direct aggression-mild indirect aggression moderate distress (22.95%), and mild direct aggression-moderate indirect aggression-distress (11.71%). Altogether, the proportional distribution of the identified subgroups indicates that while majority of AAS users are characterized by low to moderate aggression and psychological distress, about 8% display high aggression with mild psychological distress. Moreover, the proportional distribution denotes an idiosyncratic pattern of aggression and psychological distress in the current AAS-using sample, in line with previous indication from a study of APED users (Hildebrandt et al., 2014). The distribution is also in line with findings from previous studies in which AAS use had higher associations with increased hostility, irritability, and anger rather than direct aggression (Hildebrandt et al.,

2014; Panagiotidis et al., 2017). The observed subgroups of AAS users with different profiles of aggression and psychological distress in the current study adds support to a previous systematic review suggesting that aggression and psychological distress are linked to AAS use but not in all subsets of AAS users (Trenton and Currier, 2005).

Furthermore, results from the MLCA indicates that a homogenous model is most appropriate when determining male and female AAS users' direct and indirect aggression and psychological distress profiles. Inferably, AAS users' belongingness to specific subgroups is not sex-determined and the patterns of aggression and psychological distress identified in the present study is applicable to both males and females. Relatedly, the inverse proportional sex distribution of the subgroups, with the highly aggressive subgroup having significantly higher proportions of males whereas the low aggression subgroup comprise of significantly higher proportions of females, indicates that a higher proportion of males (compared to females) are at an elevated risk of aggression and psychological distress. This finding can also be explained by evidence of earlier AAS use initiation, more extensive use (e.g., higher weekly doses and higher number of AAS per cycle) as well as a higher prevalence of stacking, polypharmacy and pyramiding in males compared to females (Ip et al., 2010). Importantly, the present finding of an inverse proportional sex distribution of the subgroups is consistent with evidence from a recent meta-analysis of experimental studies showing that the association between endogenous testosterone levels as well as testosterone administration and aggression are stronger and significant in males but not females (Geniole et al., 2019).

The current study's findings can inform preventive as well as harm reduction and treatment interventions on AAS use, and aggression and psychological distress. Preventive interventions on AAS use incorporating education about the potential for aggressive behavior and psychological distress may be beneficial in reducing motivation and intention for AAS initiation (Bates et al., 2021; Petróczi et al., 2014; Sagoe et al., 2016). Similarly, it is

important that harm reduction and treatment interventions for AAS use is extended into the amelioration of aggression and psychological distress (Bates et al., 2019, 2021; Pope and Kanayama, 2021). In this regard, the homogenous gender model identified in this study underlines the indispensability of female AAS users in such policy making particularly in relation to the tendency for aggression and psychological distress. Furthermore, there is a need for more refined approaches to treatment and harm reduction in which the importance of AAS users' different profiles of aggression and psychological distress are taken into consideration.

The present findings should be interpreted in the context of limitations such as our reliance on self-reports which can be problematic for assessing substance use (Hickman et al., 2002), and our inability to draw causal inferences due to the cross-sectional survey design. In the current study the average length of AAS use was 1.33 ($SD = .56$) years which equals to, at least, two cycles of AAS use (Hildebrandt et al., 2007). However, we do not know whether the participants were "on cycle" or "off cycle" when participating in the data collection. Moreover, the most popular AAS used by both sexes were oxandrolone/Anavar, testosterone, stanozolol/Winstrol, Dianabol/methandrostenolone, and Anadrol/oxymetholone in line with evidence from previous studies (Abrahin et al., 2017; Gruber and Pope, 2000). From these most frequently used types of AAS, only Anadrol (oxymetholone) is anecdotally associated with increased aggression in humans (Barker, 1987; Llewellyn, 2011). Hence, it is also plausible that factors such as particular AAS, AAS use method (e.g., 'blast and cruise', 'blitz-cycles', 'stacking') and polypharmacy (Hildebrandt et al., 2007; Lundholm et al., 2015) as well as personality (Hauger et al., 2021), AAS dependence and cognition (Hauger et al., 2019b), and premorbidity such as structural brain abnormalities (Bjørnebekk et al., 2017; Hauger et al., 2019a) account for the differences between the subgroups identified in the present study and further studies are encouraged to explore these.

Despite the abovementioned limitations, the current study has some notable strengths. First, to our knowledge, the current study represents a novel approach in examining discrete subgroups of aggression and psychological distress among male and female AAS users in particular. Another strength is our use of MLCA in the identification of subgroups and role of sex as this method is empirically superior to traditional categorization using cut-off points (Berzofsky et al., 2008). In addition, the preponderance of AAS research so far has been conducted largely on male samples in Western countries (Sagoe et al., 2014b; Sagoe and Pallesen, 2018). Further research using longitudinal designs may elucidate transitions between latent classes. An examination of the psychosocial correlates of AAS users' belongingness to the subgroups identified in the present study may also be interesting. Finally, it could be of interest to replicate these subgroups and investigate the AAS types associated with members of each subgroup.

CONCLUSION

Using MLCA, we investigated the patterns of male and female AAS users' aggression and psychological distress and whether the identified patterns can be applied to both sexes. We identified five discrete patterns of direct and indirect aggression and psychological distress with about 8% displaying the highest levels of aggression and mild psychological distress. Our findings also indicate that patterns of aggression and psychological distress are applicable to both male and female AAS users. Here, members of the high aggression and moderate psychological distress subgroup are more likely to be male whereas members of the low, mild, and/or moderate aggression and psychological distress subgroup are more likely to be female. Our study provides pioneering empirical evidence of the unique patterns of aggression and psychological distress among male and female AAS users. Our findings can be useful for preventive, harm reduction and treatment interventions on AAS use, and aggression and psychological distress.

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TABLE 1.
Sample characteristics.

Variable	Overall (<i>N</i> = 206)		Male (<i>n</i> = 86)	Female (<i>n</i> = 120)
	Range	Mean (<i>SD</i>)	Mean (<i>SD</i>)	Mean (<i>SD</i>)
Age (years)	14–56	26.89 (7.12)	26.69 (6.72)	27.04 (7.44)
Height (cm)	154–192	171.54 (9.66)	180.46 (6.09)	165.11 (5.91)
Weight (kg)	45–170	71.53 (17.23)	84.64 (16.23)	62.06 (10.41)
Weight training				
Total years	1–36	3.28 (4.02)	3.52 (4.96)	3.08 (3.04)
Days per week	1–7	3.40 (1.49)	3.97 (1.62)	2.97 (1.23)
Hours per week	1–20	5.12 (4.66)	6.19 (5.85)	4.37 (3.38)
AAS use duration (years)	1–3	1.33 (.56)	1.51 (.66)	1.19 (.43)
		<i>N</i> (%)	<i>n</i> (%)	<i>n</i> (%)
Highest education				
High School		12 (5.80)	5 (5.80)	7 (5.80)
Diploma		35 (17.00)	16 (18.60)	19 (15.80)
Technician		20 (9.7)	8 (9.30)	12 (10.00)
Bachelor		92 (44.70)	39 (45.30)	53 (44.20)
Master		34 (16.5)	14 (16.30)	20 (16.70)
PhD		10 (4.9)	1 (1.2)	9 (7.50)
Marriage status				
Single		153 (74.30)	67 (77.90)	86 (71.70)
Married		52 (25.20)	18 (20.90)	34 (28.30)
Work status				
Full time		58 (28.20)	30 (34.90)	28 (23.30)
Part time		28 (13.60)	7 (8.10)	21 (17.50)
Self-employed		38 (18.40)	24 (27.90)	14 (11.70)
Unemployed		34 (16.50)	8 (9.3)	26 (21.70)
Student		40 (19.40)	14 (16.30)	26 (21.70)
Sports involvement				
Competitive sport		6 (2.90)	4 (4.70)	2 (1.70)
Recreational sport		34 (16.50)	17 (19.80)	17 (14.20)
Competitive bodybuilding		30 (14.60)	10 (11.60)	20 (16.70)
Recreational bodybuilding		105 (51.00)	52 (60.50)	53 (44.20)
		<i>N</i>	<i>n</i>	<i>n</i>
AAS type used ^a				
Anadrol (Oxymetholone)		62	39	23
Anavar (Oxandrolone)		112	57	55
Deca-Durabolin (Nandrolone decanoate)		47	30	17
Depo-Testosterone		7	6	1
Dianabol (Methandrostenolone)		71	38	33
Durabolin		7	2	5
Equipoise (Boldenone)		12	8	4
Finajet (Trenbolone)		12	9	3
Maxibolim (Ethylestrenol)		2	2	0
Methyltestosterone		4	4	0
Primobolan		9	4	5
Stanozolol (Winstrol)		136	96	40
Steroid cocktail		3	1	2
Sustanon		44	21	23
Testosterone		114	66	48

Percentages may not add up to 100% due to missing data on the respective items.

TABLE 2.

Fit statistics for the latent class analysis.

Model	BIC (LL)	N par	L^2	ACE (%)
1-class	4857.99	75	2878.33	0.00
2-class	4438.13	81	2426.71	0.01
3-class	4349.63	87	2306.45	0.02
4-class	4338.65	93	2263.71	0.03
5-class	4326.81	99	2220.11	0.02
6-class	4330.37	105	2191.91	0.03

BIC: Bayesian Information Criteria. N par: Number of parameters in the model. L^2 : Squared log-likelihood. ACE: Adjacent Classification Error.

TABLE 3.

Fit statistics of the estimated five-class multigroup latent class models

Model	BIC (LL)	L^2	df	Comparison	ΔL^2	<i>Sig. result</i>
Homogeneous model (HM)	4326.81	2220.11	100	—	—	—
Adding direct effect of sex on one indicator at a time						
Physical aggression (PA)	4408.85	2500.22	88	HM vs. PA	-148.40	Deterioration
Verbal aggression (VA)	4417.60	2445.45	76	HM vs. VA	-145.99	Deterioration
Anger (A)	4412.08	2397.58	68	HM vs. A	-144.70	Deterioration
Hostility (H)	4369.70	2291.68	56	HM vs. H	-127.40	Deterioration
Partially homogeneous model (PHM) with all direct effects included	4411.33	2190.40	30	HM vs. PHM	29.71	Deterioration
Heterogeneous model (HeM)	2008.66	2315.42	75	HM vs. HeM	-90.65	Deterioration

BIC: Bayesian Information Criteria. N par: Number of parameters in the model. L^2 : Squared log-likelihood. ΔL^2 : difference in L^2 between two consecutive nested model.

TABLE 4.

Proportions of male and female AAS users in latent classes of aggression and psychological distress

Sex	HAMoD (%)	MoAD (%)	ModA-MiiA- MoD (%)	MidA-MoiAD (%)	LAMiD (%)
Male	91.67	80.42	32.46	30.00	10.51
Female	8.33	19.58	67.54	70.00	89.49
Total	07.36	18.64	22.95	11.71	39.06
Wald test§	-5.02*	-0.52	1.19	1.76	3.51*

HAMoD: high aggression moderate distress users (07.63%). MoAD: moderate aggression distress users (18.64%). ModA-MiiA MoD: moderate direct aggression-mild indirect aggression moderate distress users (22.95%). MidA-MioAD: mild direct aggression-moderate indirect aggression-distress users (11.71%). LAMiD: low aggression mild distress users (39.06%).

§Wald test: 31.04, $p < .001$; female = 1, male = 0; * $p < .001$

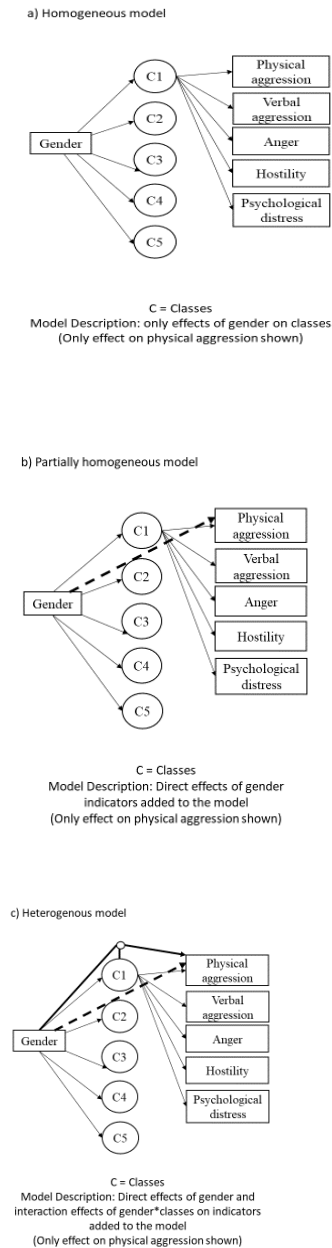


FIGURE 1. Three types of multiple group latent class models

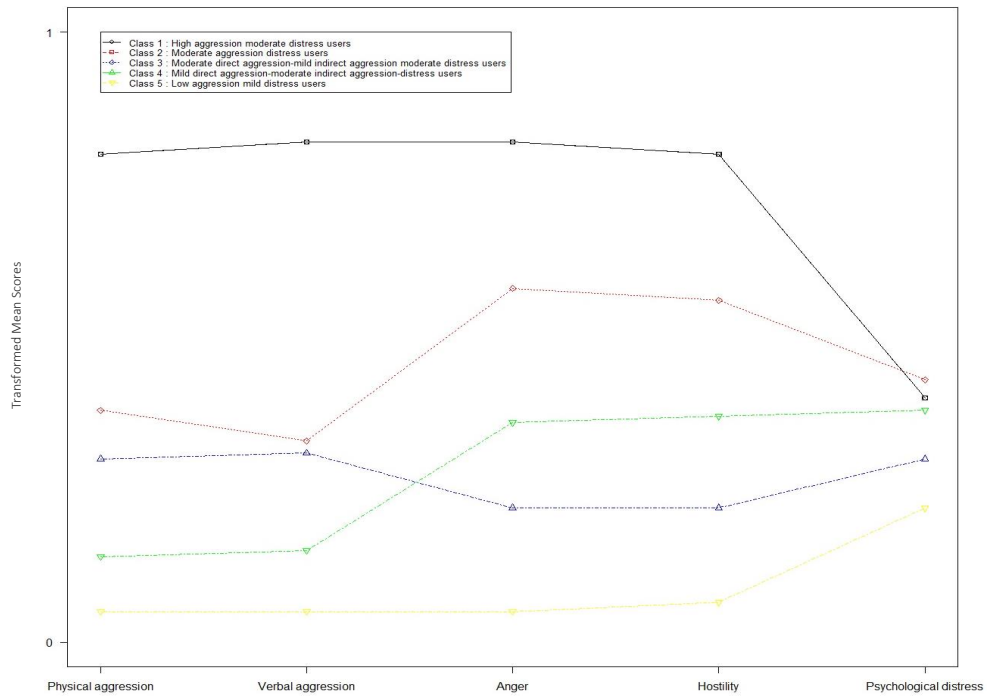


FIGURE 2. Patterns of aggression and psychological distress in male and female AAS users.

Doctoral Theses at The Faculty of Psychology,
University of Bergen

1980	Allen, Hugh M., Dr. philos.	Parent-offspring interactions in willow grouse (<i>Lagopus L. Lagopus</i>).
1981	Myhrer, Trond, Dr. philos.	Behavioral Studies after selective disruption of hippocampal inputs in albino rats.
1982	Svebak, Sven, Dr. philos.	The significance of motivation for task-induced tonic physiological changes.
1983	Myhre, Grete, Dr. philos.	The Biopsychology of behavior in captive Willow ptarmigan.
	Eide, Rolf, Dr. philos.	PSYCHOSOCIAL FACTORS AND INDICES OF HEALTH RISKS. The relationship of psychosocial conditions to subjective complaints, arterial blood pressure, serum cholesterol, serum triglycerides and urinary catecholamines in middle aged populations in Western Norway.
	Værnes, Ragnar J., Dr. philos.	Neuropsychological effects of diving.
1984	Kolstad, Arnulf, Dr. philos.	Til diskusjonen om sammenhengen mellom sosiale forhold og psykiske strukturer. En epidemiologisk undersøkelse blant barn og unge.
	Løberg, Tor, Dr. philos.	Neuropsychological assessment in alcohol dependence.
1985	Hellesnes, Tore, Dr. philos.	Læring og problemløsning. En studie av den perseptuelle analysens betydning for verbal læring.
	Håland, Wenche, Dr. philos.	Psykoterapi: relasjon, utviklingsprosess og effekt.
1986	Hagtvatn, Knut A., Dr. philos.	The construct of test anxiety: Conceptual and methodological issues.
	Jellestad, Finn K., Dr. philos.	Effects of neuron specific amygdala lesions on fear-motivated behavior in rats.
1987	Aarø, Leif E., Dr. philos.	Health behaviour and socioeconomic Status. A survey among the adult population in Norway.
	Underlid, Kjell, Dr. philos.	Arbeidsløse i psykososialt perspektiv.
	Laberg, Jon C., Dr. philos.	Expectancy and classical conditioning in alcoholics' craving.
	Vollmer, Fred, Dr. philos.	Essays on explanation in psychology.
	Ellertsen, Bjørn, Dr. philos.	Migraine and tension headache: Psychophysiology, personality and therapy.
1988	Kaufmann, Astrid, Dr. philos.	Antisocial atferd hos ungdom. En studie av psykologiske determinanter.

	Mykletun, Reidar J., Dr. philos.	Teacher stress: personality, work-load and health.
	Havik, Odd E., Dr. philos.	After the myocardial infarction: A medical and psychological study with special emphasis on perceived illness.
1989	Bråten, Stein, Dr. philos.	Menneskedyaden. En teoretisk tese om sinnets dialogiske natur med informasjons- og utviklingspsykologiske implikasjoner sammenholdt med utvalgte spedbarnsstudier.
	Wold, Bente, Dr. psychol.	Lifestyles and physical activity. A theoretical and empirical analysis of socialization among children and adolescents.
1990	Flaten, Magne A., Dr. psychol.	The role of habituation and learning in reflex modification.
1991	Alsaker, Françoise D., Dr. philos.	Global negative self-evaluations in early adolescence.
	Kraft, Pål, Dr. philos.	AIDS prevention in Norway. Empirical studies on diffusion of knowledge, public opinion, and sexual behaviour.
	Endresen, Inger M., Dr. philos.	Psychoimmunological stress markers in working life.
	Faleide, Asbjørn O., Dr. philos.	Asthma and allergy in childhood. Psychosocial and psychotherapeutic problems.
1992	Dalen, Knut, Dr. philos.	Hemispheric asymmetry and the Dual-Task Paradigm: An experimental approach.
	Bø, Inge B., Dr. philos.	Ungdoms sosiale økologi. En undersøkelse av 14-16 åringers sosiale nettverk.
	Nivison, Mary E., Dr. philos.	The relationship between noise as an experimental and environmental stressor, physiological changes and psychological factors.
	Torgersen, Anne M., Dr. philos.	Genetic and environmental influence on temperamental behaviour. A longitudinal study of twins from infancy to adolescence.
1993	Larsen, Svein, Dr. philos.	Cultural background and problem drinking.
	Nordhus, Inger Hilde, Dr. philos.	Family caregiving. A community psychological study with special emphasis on clinical interventions.
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	Solheim, Ragnar, Dr. philos.	Spesifikke lærevansker. Diskrepanskriteriet anvendt i seleksjonsmetodikk.
	Johnsen, Bjørn Helge, Dr. psychol.	Brain asymmetry and facial emotional expressions: Conditioning experiments.
1994	Tønnessen, Finn E., Dr. philos.	The etiology of Dyslexia.
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	Johannessen, Birte F., Dr. philos.	Det flytende kjønn. Om lederskap, politikk og identitet.
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	Aas, Henrik N., Dr. psychol.	Alcohol expectancies and socialization: Adolescents learning to drink.
	Bjørkly, Stål, Dr. psychol.	Diagnosis and prediction of intra-institutional aggressive behaviour in psychotic patients
1996	Anderssen, Norman, Dr. psychol.	Physical activity of young people in a health perspective: Stability, change and social influences.
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	Einarsen, Ståle, Dr. psychol.	Bullying and harassment at work: epidemiological and psychosocial aspects.
1997	Knivsberg, Ann-Mari, Dr. philos.	Behavioural abnormalities and childhood psychopathology: Urinary peptide patterns as a potential tool in diagnosis and remediation.
	Eide, Arne H., Dr. philos.	Adolescent drug use in Zimbabwe. Cultural orientation in a global-local perspective and use of psychoactive substances among secondary school students.
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	Binder, Per-Einar, Dr. psychol.	Individet og den meningsbærende andre. En teoretisk undersøkelse av de mellommenneskelige forutsetningene for psykisk liv og utvikling med utgangspunkt i Donald Winnicotts teori.
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	Engelsen, Birthe Kari, Dr. psychol.	Measurement of the eating problem construct.
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	Kallestad, Jan Helge, Dr. philos.	Teachers, schools and implementation of the Olweus Bullying Prevention Program.
H	Ofte, Sonja Helgesen, Dr. psychol.	Right-left discrimination in adults and children.
	Netland, Marit, Dr. psychol.	Exposure to political violence. The need to estimate our estimations.
	Diseth, Åge, Dr. psychol.	Approaches to learning: Validity and prediction of academic performance.
	Bjuland, Raymond, Dr. philos.	Problem solving in geometry. Reasoning processes of student teachers working in small groups: A dialogical approach.
2003 V	Arefjord, Kjersti, Dr. psychol.	After the myocardial infarction – the wives' view. Short- and long-term adjustment in wives of myocardial infarction patients.
	Ingjaldsson, Jón Þorvaldur, Dr. psychol.	Unconscious Processes and Vagal Activity in Alcohol Dependency.
	Holden, Børge, Dr. philos.	Følger av atferdsanalytiske forklaringer for atferdsanalysens tilnærming til utforming av behandling.
	Holsen, Ingrid, Dr. philos.	Depressed mood from adolescence to 'emerging adulthood'. Course and longitudinal influences of body image and parent-adolescent relationship.
	Hammar, Åsa Karin, Dr. psychol.	Major depression and cognitive dysfunction- An experimental study of the cognitive effort hypothesis.
	Sprugevica, Ieva, Dr. philos.	The impact of enabling skills on early reading acquisition.
	Gabrielsen, Egil, Dr. philos.	LESE FOR LIVET. Lesekompetansen i den norske voksenbefolkningen sett i lys av visjonen om en enhetsskole.
H	Hansen, Anita Lill, Dr. psychol.	The influence of heart rate variability in the regulation of attentional and memory processes.
	Dyregrov, Kari, Dr. philos.	The loss of child by suicide, SIDS, and accidents: Consequences, needs and provisions of help.
2004 V	Torsheim, Torbjørn, Dr. psychol.	Student role strain and subjective health complaints: Individual, contextual, and longitudinal perspectives.

	Haugland, Bente Storm Mowatt Dr. psychol.	Parental alcohol abuse. Family functioning and child adjustment.
	Milde, Anne Marita, Dr. psychol.	Ulcerative colitis and the role of stress. Animal studies of psychobiological factors in relationship to experimentally induced colitis.
	Stornes, Tor, Dr. philos.	Socio-moral behaviour in sport. An investigation of perceptions of sportspersonship in handball related to important factors of socio-moral influence.
	Mæhle, Magne, Dr. philos.	Re-inventing the child in family therapy: An investigation of the relevance and applicability of theory and research in child development for family therapy involving children.
	Kobbeltvedt, Therese, Dr. psychol.	Risk and feelings: A field approach.
2004 H	Thomsen, Tormod, Dr. psychol.	Localization of attention in the brain.
	Løberg, Else-Marie, Dr. psychol.	Functional laterality and attention modulation in schizophrenia: Effects of clinical variables.
	Kyrkjebø, Jane Mikkelsen, Dr. philos.	Learning to improve: Integrating continuous quality improvement learning into nursing education.
	Laumann, Karin, Dr. psychol.	Restorative and stress-reducing effects of natural environments: Experiential, behavioural and cardiovascular indices.
	Holgersen, Helge, PhD	Mellom oss - Essay i relasjonell psykoanalyse.
2005 V	Hetland, Hilde, Dr. psychol.	Leading to the extraordinary? Antecedents and outcomes of transformational leadership.
	Iversen, Anette Christine, Dr. philos.	Social differences in health behaviour: the motivational role of perceived control and coping.
2005 H	Mathisen, Gro Ellen, PhD	Climates for creativity and innovation: Definitions, measurement, predictors and consequences.
	Sævi, Tone, Dr. philos.	Seeing disability pedagogically – The lived experience of disability in the pedagogical encounter.
	Wium, Nora, PhD	Intrapersonal factors, family and school norms: combined and interactive influence on adolescent smoking behaviour.
	Kanagaratnam, Pushpa, PhD	Subjective and objective correlates of Posttraumatic Stress in immigrants/refugees exposed to political violence.
	Larsen, Torill M. B. , PhD	Evaluating principals` and teachers` implementation of Second Step. A case study of four Norwegian primary schools.
	Bancila, Delia, PhD	Psychosocial stress and distress among Romanian adolescents and adults.
2006 V	Hillestad, Torgeir Martin, Dr. philos.	Normalitet og avvik. Forutsetninger for et objektivt psykopatologisk avviksbegrep. En psykologisk, sosial, erkjennelsesteoretisk og teoriehistorisk framstilling.

	Nordanger, Dag Øystein, Dr. psychol.	Psychosocial discourses and responses to political violence in post-war Tigray, Ethiopia.
	Rimol, Lars Morten, PhD	Behavioral and fMRI studies of auditory laterality and speech sound processing.
	Krumsvik, Rune Johan, Dr. philos.	ICT in the school. ICT-initiated school development in lower secondary school.
	Norman, Elisabeth, Dr. psychol.	Gut feelings and unconscious thought: An exploration of fringe consciousness in implicit cognition.
	Israel, K Pravin, Dr. psychol.	Parent involvement in the mental health care of children and adolescents. Empirical studies from clinical care setting.
	Glasø, Lars, PhD	Affects and emotional regulation in leader-subordinate relationships.
	Knutsen, Ketil, Dr. philos.	HISTORIER UNGDOM LEVER – En studie av hvordan ungdommer bruker historie for å gjøre livet meningsfullt.
	Matthiesen, Stig Berge, PhD	Bullying at work. Antecedents and outcomes.
2006	Gramstad, Arne, PhD	Neuropsychological assessment of cognitive and emotional functioning in patients with epilepsy.
H	Bendixen, Mons, PhD	Antisocial behaviour in early adolescence: Methodological and substantive issues.
	Mrumbi, Khalifa Maulid, PhD	Parental illness and loss to HIV/AIDS as experienced by AIDS orphans aged between 12-17 years from Temeke District, Dar es Salaam, Tanzania: A study of the children's psychosocial health and coping responses.
	Hetland, Jørn, Dr. psychol.	The nature of subjective health complaints in adolescence: Dimensionality, stability, and psychosocial predictors
	Kakoko, Deodatus Conatus Vitalis, PhD	Voluntary HIV counselling and testing service uptake among primary school teachers in Mwanza, Tanzania: assessment of socio-demographic, psychosocial and socio-cognitive aspects
	Mykletun, Arnstein, Dr. psychol.	Mortality and work-related disability as long-term consequences of anxiety and depression: Historical cohort designs based on the HUNT-2 study
	Sivertsen, Børge, PhD	Insomnia in older adults. Consequences, assessment and treatment.
2007	Singhammer, John, Dr. philos.	Social conditions from before birth to early adulthood – the influence on health and health behaviour
V	Janvin, Carmen Ani Cristea, PhD	Cognitive impairment in patients with Parkinson's disease: profiles and implications for prognosis
	Braarud, Hanne Cecilie, Dr. psychol.	Infant regulation of distress: A longitudinal study of transactions between mothers and infants
	Tveito, Torill Helene, PhD	Sick Leave and Subjective Health Complaints

	Magnussen, Liv Heide, PhD	Returning disability pensioners with back pain to work
	Thuen, Elin Marie, Dr.philos.	Learning environment, students' coping styles and emotional and behavioural problems. A study of Norwegian secondary school students.
	Solberg, Ole Asbjørn, PhD	Peacekeeping warriors – A longitudinal study of Norwegian peacekeepers in Kosovo
2007	Søreide, Gunn Elisabeth, Dr.philos.	Narrative construction of teacher identity
H	Svensen, Erling, PhD	WORK & HEALTH. Cognitive Activation Theory of Stress applied in an organisational setting.
	Øverland, Simon Nygaard, PhD	Mental health and impairment in disability benefits. Studies applying linkages between health surveys and administrative registries.
	Eichele, Tom, PhD	Electrophysiological and Hemodynamic Correlates of Expectancy in Target Processing
	Børhaug, Kjetil, Dr.philos.	Oppseding til demokrati. Ein studie av politisk oppseding i norsk skule.
	Eikeland, Thorleif, Dr.philos.	Om å vokse opp på barnehjem og på sykehus. En undersøkelse av barnehjemsbarns opplevelser på barnehjem sammenholdt med sanatoriebarns beskrivelse av langvarige sykehusopphold – og et forsøk på forklaring.
	Wadel, Carl Cato, Dr.philos.	Medarbeidersamhandling og medarbeiderledelse i en lagbasert organisasjon
	Vinje, Hege Forbech, PhD	Thriving despite adversity: Job engagement and self-care among community nurses
	Noort, Maurits van den, PhD	Working memory capacity and foreign language acquisition
2008	Breivik, Kyrre, Dr.psychol.	The Adjustment of Children and Adolescents in Different Post-Divorce Family Structures. A Norwegian Study of Risks and Mechanisms.
V	Johnsen, Grethe E., PhD	Memory impairment in patients with posttraumatic stress disorder
	Sætrevik, Bjørn, PhD	Cognitive Control in Auditory Processing
	Carvalho, Susana Fonseca, PhD	Prevention of bullying in schools: an ecological model
2008	Brønnick, Kolbjørn Selvåg	Attentional dysfunction in dementia associated with Parkinson's disease.
H	Posserud, Maj-Britt Rocio	Epidemiology of autism spectrum disorders
	Haug, Ellen	Multilevel correlates of physical activity in the school setting
	Skjerve, Arvid	Assessing mild dementia – a study of brief cognitive tests.

	Kjønniksen, Lise	The association between adolescent experiences in physical activity and leisure time physical activity in adulthood: a ten year longitudinal study
	Gundersen, Hilde	The effects of alcohol and expectancy on brain function
	Omvik, Siri	Insomnia – a night and day problem
2009 V	Molde, Helge	Pathological gambling: prevalence, mechanisms and treatment outcome.
	Foss, Else	Den omsorgsfulle væremåte. En studie av voksnes væremåte i forhold til barn i barnehagen.
	Westrheim, Kariane	Education in a Political Context: A study of Knowledge Processes and Learning Sites in the PKK.
	Wehling, Eike	Cognitive and olfactory changes in aging
	Wangberg, Silje C.	Internet based interventions to support health behaviours: The role of self-efficacy.
	Nielsen, Morten B.	Methodological issues in research on workplace bullying. Operationalisations, measurements and samples.
	Sandu, Anca Larisa	MRI measures of brain volume and cortical complexity in clinical groups and during development.
	Guribye, Eugene	Refugees and mental health interventions
	Sørensen, Lin	Emotional problems in inattentive children – effects on cognitive control functions.
	Tjomsland, Hege E.	Health promotion with teachers. Evaluation of the Norwegian Network of Health Promoting Schools: Quantitative and qualitative analyses of predisposing, reinforcing and enabling conditions related to teacher participation and program sustainability.
	Helleve, Ingrid	Productive interactions in ICT supported communities of learners
2009 H	Skorpen, Aina Øye, Christine	Dagliglivet i en psykiatrisk institusjon: En analyse av miljøterapeutiske praksiser
	Andreassen, Cecilie Schou	WORKAHOLISM – Antecedents and Outcomes
	Stang, Ingun	Being in the same boat: An empowerment intervention in breast cancer self-help groups
	Sequeira, Sarah Dorothee Dos Santos	The effects of background noise on asymmetrical speech perception
	Kleiven, Jo, dr.philos.	The Lillehammer scales: Measuring common motives for vacation and leisure behavior
	Jónsdóttir, Guðrún	Dubito ergo sum? Ni jenter møter naturfaglig kunnskap.
	Hove, Oddbjørn	Mental health disorders in adults with intellectual disabilities - Methods of assessment and prevalence of mental health disorders and problem behaviour
	Wageningen, Heidi Karin van	The role of glutamate on brain function

	Bjørkvik, Jofrid	God nok? Selvaktelse og interpersonlig fungering hos pasienter innen psykisk helsevern: Forholdet til diagnoser, symptomer og behandlingsutbytte
	Andersson, Martin	A study of attention control in children and elderly using a forced-attention dichotic listening paradigm
	Almås, Aslaug Grov	Teachers in the Digital Network Society: Visions and Realities. A study of teachers' experiences with the use of ICT in teaching and learning.
	Ulvik, Marit	Lærerutdanning som danning? Tre stemmer i diskusjonen
2010	Skår, Randi	Læringsprosesser i sykepleieres profesjonsutøvelse. En studie av sykepleieres læringserfaringer.
V	Roald, Knut	Kvalitetsvurdering som organisasjonslæring mellom skole og skoleeigar
	Lunde, Linn-Heidi	Chronic pain in older adults. Consequences, assessment and treatment.
	Danielsen, Anne Grete	Perceived psychosocial support, students' self-reported academic initiative and perceived life satisfaction
	Hysing, Mari	Mental health in children with chronic illness
	Olsen, Olav Kjellevoid	Are good leaders moral leaders? The relationship between effective military operational leadership and morals
	Riese, Hanne	Friendship and learning. Entrepreneurship education through mini-enterprises.
	Holthe, Asle	Evaluating the implementation of the Norwegian guidelines for healthy school meals: A case study involving three secondary schools
H	Hauge, Lars Johan	Environmental antecedents of workplace bullying: A multi-design approach
	Bjørkelo, Brita	Whistleblowing at work: Antecedents and consequences
	Reme, Silje Endresen	Common Complaints – Common Cure? Psychiatric comorbidity and predictors of treatment outcome in low back pain and irritable bowel syndrome
	Helland, Wenche Andersen	Communication difficulties in children identified with psychiatric problems
	Beneventi, Harald	Neuronal correlates of working memory in dyslexia
	Thygesen, Elin	Subjective health and coping in care-dependent old persons living at home
	Aanes, Mette Marthinussen	Poor social relationships as a threat to belongingness needs. Interpersonal stress and subjective health complaints: Mediating and moderating factors.
	Anker, Morten Gustav	Client directed outcome informed couple therapy

	Bull, Torill	Combining employment and child care: The subjective well-being of single women in Scandinavia and in Southern Europe
	Viiig, Nina Grieg	Tilrettelegging for læreres deltakelse i helsefremmende arbeid. En kvalitativ og kvantitativ analyse av sammenhengen mellom organisatoriske forhold og læreres deltakelse i utvikling og implementering av Europeisk Nettverk av Helsefremmende Skoler i Norge
	Wolff, Katharina	To know or not to know? Attitudes towards receiving genetic information among patients and the general public.
	Ogden, Terje, dr.philos.	Familiebasert behandling av alvorlige atferdsproblemer blant barn og ungdom. Evaluering og implementering av evidensbaserte behandlingsprogrammer i Norge.
	Solberg, Mona Elin	Self-reported bullying and victimisation at school: Prevalence, overlap and psychosocial adjustment.
2011	Bye, Hege Høivik	Self-presentation in job interviews. Individual and cultural differences in applicant self-presentation during job interviews and hiring managers' evaluation
V	Notelaers, Guy	Workplace bullying. A risk control perspective.
	Moltu, Christian	Being a therapist in difficult therapeutic impasses. A hermeneutic phenomenological analysis of skilled psychotherapists' experiences, needs, and strategies in difficult therapies ending well.
	Myrseth, Helga	Pathological Gambling - Treatment and Personality Factors
	Schanche, Elisabeth	From self-criticism to self-compassion. An empirical investigation of hypothesized change processes in the Affect Phobia Treatment Model of short-term dynamic psychotherapy for patients with Cluster C personality disorders.
	Våpenstad, Eystein Victor, dr.philos.	Det tempererte nærvær. En teoretisk undersøkelse av psykoterapeutens subjektivitet i psykoanalyse og psykoanalytisk psykoterapi.
	Haukebø, Kristin	Cognitive, behavioral and neural correlates of dental and intra-oral injection phobia. Results from one treatment and one fMRI study of randomized, controlled design.
	Harris, Anette	Adaptation and health in extreme and isolated environments. From 78°N to 75°S.
	Bjørknes, Ragnhild	Parent Management Training-Oregon Model: intervention effects on maternal practice and child behavior in ethnic minority families
	Mamen, Asgeir	Aspects of using physical training in patients with substance dependence and additional mental distress
	Espevik, Roar	Expert teams: Do shared mental models of team members make a difference
	Haara, Frode Olav	Unveiling teachers' reasons for choosing practical activities in mathematics teaching

2011 H	Hauge, Hans Abraham	How can employee empowerment be made conducive to both employee health and organisation performance? An empirical investigation of a tailor-made approach to organisation learning in a municipal public service organisation.
	Melkevik, Ole Rogstad	Screen-based sedentary behaviours: pastimes for the poor, inactive and overweight? A cross-national survey of children and adolescents in 39 countries.
	Vøllestad, Jon	Mindfulness-based treatment for anxiety disorders. A quantitative review of the evidence, results from a randomized controlled trial, and a qualitative exploration of patient experiences.
	Tolo, Astrid	Hvordan blir lærerkompetanse konstruert? En kvalitativ studie av PPU-studenters kunnskapsutvikling.
	Saus, Evelyn-Rose	Training effectiveness: Situation awareness training in simulators
	Nordgreen, Tine	Internet-based self-help for social anxiety disorder and panic disorder. Factors associated with effect and use of self-help.
	Munkvold, Linda Helen	Oppositional Defiant Disorder: Informant discrepancies, gender differences, co-occurring mental health problems and neurocognitive function.
	Christiansen, Øivin	Når barn plasseres utenfor hjemmet: beslutninger, forløp og relasjoner. Under barnevernets (ved)tak.
	Brunborg, Geir Scott	Conditionability and Reinforcement Sensitivity in Gambling Behaviour
	Hystad, Sigurd William	Measuring Psychological Resiliency: Validation of an Adapted Norwegian Hardiness Scale
2012 V	Roness, Dag	Hvorfor bli lærer? Motivasjon for utdanning og utøving.
	Fjermestad, Krister Westlye	The therapeutic alliance in cognitive behavioural therapy for youth anxiety disorders
	Jenssen, Eirik Sørnes	Tilpasset opplæring i norsk skole: politikeres, skolelederes og læreres handlingsvalg
	Saksvik-Lehouillier, Ingvild	Shift work tolerance and adaptation to shift work among offshore workers and nurses
	Johansen, Venke Frederike	Når det intime blir offentlig. Om kvinners åpenhet om brystkreft og om markedsføring av brystkreftsaken.
	Herheim, Rune	Pupils collaborating in pairs at a computer in mathematics learning: investigating verbal communication patterns and qualities
	Vie, Tina Løkke	Cognitive appraisal, emotions and subjective health complaints among victims of workplace bullying: A stress-theoretical approach
	Jones, Lise Øen	Effects of reading skills, spelling skills and accompanying efficacy beliefs on participation in education. A study in Norwegian prisons.

2012 H	Danielsen, Yngvild Sørebo	Childhood obesity – characteristics and treatment. Psychological perspectives.
	Horverak, Jøri Gytre	Sense or sensibility in hiring processes. Interviewee and interviewer characteristics as antecedents of immigrant applicants' employment probabilities. An experimental approach.
	Jøsendal, Ola	Development and evaluation of BE smokeFREE, a school-based smoking prevention program
	Osnes, Berge	Temporal and Posterior Frontal Involvement in Auditory Speech Perception
	Drageset, Sigrunn	Psychological distress, coping and social support in the diagnostic and preoperative phase of breast cancer
	Aasland, Merethe Schanke	Destructive leadership: Conceptualization, measurement, prevalence and outcomes
	Bakibinga, Pauline	The experience of job engagement and self-care among Ugandan nurses and midwives
	Skogen, Jens Christoffer	Foetal and early origins of old age health. Linkage between birth records and the old age cohort of the Hordaland Health Study (HUSK)
	Leveresen, Ingrid	Adolescents' leisure activity participation and their life satisfaction: The role of demographic characteristics and psychological processes
	Hanss, Daniel	Explaining sustainable consumption: Findings from cross-sectional and intervention approaches
Rød, Per Arne	Barn i klem mellom foreldrekonflikter og samfunnmessig beskyttelse	
2013 V	Mentzoni, Rune Aune	Structural Characteristics in Gambling
	Knudsen, Ann Kristin	Long-term sickness absence and disability pension award as consequences of common mental disorders. Epidemiological studies using a population-based health survey and official ill health benefit registries.
	Strand, Mari	Emotional information processing in recurrent MDD
	Veseth, Marius	Recovery in bipolar disorder. A reflexive-collaborative exploration of the lived experiences of healing and growth when battling a severe mental illness
	Mæland, Silje	Sick leave for patients with severe subjective health complaints. Challenges in general practice.
	Mjaaland, Thera	At the frontiers of change? Women and girls' pursuit of education in north-western Tigray, Ethiopia
	Odéen, Magnus	Coping at work. The role of knowledge and coping expectancies in health and sick leave.
	Hynninen, Kia Minna Johanna	Anxiety, depression and sleep disturbance in chronic obstructive pulmonary disease (COPD). Associations, prevalence and effect of psychological treatment.

	Flo, Elisabeth	Sleep and health in shift working nurses
	Aasen, Elin Margrethe	From paternalism to patient participation? The older patients undergoing hemodialysis, their next of kin and the nurses: a discursive perspective on perception of patient participation in dialysis units
	Ekornås, Belinda	Emotional and Behavioural Problems in Children: Self-perception, peer relationships, and motor abilities
	Corbin, J. Hope	North-South Partnerships for Health: Key Factors for Partnership Success from the Perspective of the KIWAKKUKI
	Birkeland, Marianne Skogbrott	Development of global self-esteem: The transition from adolescence to adulthood
2013	Gianella-Malca, Camila	Challenges in Implementing the Colombian Constitutional Court's Health-Care System Ruling of 2008
H	Hovland, Anders	Panic disorder – Treatment outcomes and psychophysiological concomitants
	Mortensen, Øystein	The transition to parenthood – Couple relationships put to the test
	Årdal, Guro	Major Depressive Disorder – a Ten Year Follow-up Study. Inhibition, Information Processing and Health Related Quality of Life
	Johansen, Rino Bandlitz	The impact of military identity on performance in the Norwegian armed forces
	Bøe, Tormod	Socioeconomic Status and Mental Health in Children and Adolescents
2014	Nordmo, Ivar	Gjennom nåløyet – studenters læringserfaringer i psykologutdanningen
V	Dovran, Anders	Childhood Trauma and Mental Health Problems in Adult Life
	Hegelstad, Wenche ten Velden	Early Detection and Intervention in Psychosis: A Long-Term Perspective
	Urheim, Ragnar	Forståelse av pasientaggresjon og forklaringer på nedgang i voldsrate ved Regional sikkerhetsavdeling, Sandviken sykehus
	Kinn, Liv Grethe	Round-Trips to Work. Qualitative studies of how persons with severe mental illness experience work integration.
	Rød, Anne Marie Kinn	Consequences of social defeat stress for behaviour and sleep. Short-term and long-term assessments in rats.
	Nygård, Merethe	Schizophrenia – Cognitive Function, Brain Abnormalities, and Cannabis Use
	Tjora, Tore	Smoking from adolescence through adulthood: the role of family, friends, depression and socioeconomic status. Predictors of smoking from age 13 to 30 in the "The Norwegian Longitudinal Health Behaviour Study" (NLHB)
	Vangsnes, Vigdis	The Dramaturgy and Didactics of Computer Gaming. A Study of a Medium in the Educational Context of Kindergartens.

	Nordahl, Kristin Berg	Early Father-Child Interaction in a Father-Friendly Context: Gender Differences, Child Outcomes, and Protective Factors related to Fathers' Parenting Behaviors with One-year-olds
2014	Sandvik, Asle Makoto	Psychopathy – the heterogeneity of the construct
H	Skotheim, Siv	Maternal emotional distress and early mother-infant interaction: Psychological, social and nutritional contributions
	Halleland, Helene Barone	Executive Functioning in adult Attention Deficit Hyperactivity Disorder (ADHD). From basic mechanisms to functional outcome.
	Halvorsen, Kirsti Vindal	Partnerskap i lærerutdanning, sett fra et økologisk perspektiv
	Solbue, Vibeke	Dialogen som visker ut kategorier. En studie av hvilke erfaringer innvandrerdommer og norskfødte med innvandrereforeldre har med videregående skole. Hva forteller ungdommenes erfaringer om videregående skoles håndtering av etniske ulikheter?
	Kvalevaag, Anne Lise	Fathers' mental health and child development. The predictive value of fathers' psychological distress during pregnancy for the social, emotional and behavioural development of their children
	Sandal, Ann Karin	Ungdom og utdanningsval. Om elevar sine opplevingar av val og overgangsprossessar.
	Haug, Thomas	Predictors and moderators of treatment outcome from high- and low-intensity cognitive behavioral therapy for anxiety disorders. Association between patient and process factors, and the outcome from guided self-help, stepped care, and face-to-face cognitive behavioral therapy.
	Sjølie, Hege	Experiences of Members of a Crisis Resolution Home Treatment Team. Personal history, professional role and emotional support in a CRHT team.
	Falkenberg, Liv Eggset	Neuronal underpinnings of healthy and dysfunctional cognitive control
	Mrdalj, Jelena	The early life condition. Importance for sleep, circadian rhythmicity, behaviour and response to later life challenges
	Hesjedal, Elisabeth	Tverrprofesjonelt samarbeid mellom skule og barnevern: Kva kan støtte utsette barn og unge?
2015	Hauken, May Aasebø	« <i>The cancer treatment was only half the work!</i> » A Mixed-Method Study of Rehabilitation among Young Adult Cancer Survivors
V	Ryland, Hilde Katrin	Social functioning and mental health in children: the influence of chronic illness and intellectual function
	Rønsen, Anne Kristin	Vurdering som profesjonskompetanse. Refleksjonsbasert utvikling av læreres kompetanse i formativ vurdering

	Hoff, Helge Andreas	Thinking about Symptoms of Psychopathy in Norway: Content Validation of the Comprehensive Assessment of Psychopathic Personality (CAPP) Model in a Norwegian Setting
	Schmid, Marit Therese	Executive Functioning in recurrent- and first episode Major Depressive Disorder. Longitudinal studies
	Sand, Liv	Body Image Distortion and Eating Disturbances in Children and Adolescents
	Matanda, Dennis Juma	Child physical growth and care practices in Kenya: Evidence from Demographic and Health Surveys
	Amugsi, Dickson Abanimi	Child care practices, resources for care, and nutritional outcomes in Ghana: Findings from Demographic and Health Surveys
	Jakobsen, Hilde	The good beating: Social norms supporting men's partner violence in Tanzania
	Sagoe, Dominic	Nonmedical anabolic-androgenic steroid use: Prevalence, attitudes, and social perception
	Eide, Helene Marie Kjærgård	Narrating the relationship between leadership and learning outcomes. A study of public narratives in the Norwegian educational sector.
2015	Wubs, Annegreet Gera	Intimate partner violence among adolescents in South Africa and Tanzania
H	Hjelmervik, Helene Susanne	Sex and sex-hormonal effects on brain organization of fronto-parietal networks
	Dahl, Berit Misund	The meaning of professional identity in public health nursing
	Røykenes, Kari	Testangst hos sykepleierstudenter: «Alternativ behandling»
	Bless, Josef Johann	The smartphone as a research tool in psychology. Assessment of language lateralization and training of auditory attention.
	Løvvik, Camilla Margrethe Sigvaldsen	Common mental disorders and work participation – the role of return-to-work expectations
	Lehmann, Stine	Mental Disorders in Foster Children: A Study of Prevalence, Comorbidity, and Risk Factors
	Knapstad, Marit	Psychological factors in long-term sickness absence: the role of shame and social support. Epidemiological studies based on the Health Assets Project.
2016	Kvestad, Ingrid	Biological risks and neurodevelopment in young North Indian children
V	Sælør, Knut Tore	Hinderløyper, halmstrå og hengende snører. En kvalitativ studie av håp innenfor psykisk helse- og rusfeltet.
	Mellingen, Sonja	Alkoholbruk, partilfredshet og samlivsstatus. Før, inn i, og etter svangerskapet – korrelerer eller konsekvenser?
	Thun, Eirunn	Shift work: negative consequences and protective factors

	Hilt, Line Torbjørnsen	The borderlands of educational inclusion. Analyses of inclusion and exclusion processes for minority language students
	Havnen, Audun	Treatment of obsessive-compulsive disorder and the importance of assessing clinical effectiveness
	Slåtten, Hilde	Gay-related name-calling among young adolescents. Exploring the importance of the context.
	Ree, Eline	Staying at work. The role of expectancies and beliefs in health and workplace interventions.
	Morken, Frøydis	Reading and writing processing in dyslexia
2016	Løvoll, Helga Synnevåg	Inside the outdoor experience. On the distinction between pleasant and interesting feelings and their implication in the motivational process.
H	Hjeltnes, Aslak	Facing social fears: An investigation of mindfulness-based stress reduction for young adults with social anxiety disorder
	Øyeflaten, Irene Larsen	Long-term sick leave and work rehabilitation. Prognostic factors for return to work.
	Henriksen, Roger Ekeberg	Social relationships, stress and infection risk in mother and child
	Johnsen, Iren	«Only a friend» - The bereavement process of young adults who have lost a friend to a traumatic death. A mixed methods study.
	Helle, Siri	Cannabis use in non-affective psychoses: Relationship to age at onset, cognitive functioning and social cognition
	Glambek, Mats	Workplace bullying and expulsion in working life. A representative study addressing prospective associations and explanatory conditions.
	Oanes, Camilla Jensen	Tilbakemelding i terapi. På hvilke måter opplever terapeuter at tilbakemeldingsprosedyrer kan virke inn på terapeutiske praksiser?
	Reknes, Iselin	Exposure to workplace bullying among nurses: Health outcomes and individual coping
	Chimhutu, Victor	Results-Based Financing (RBF) in the health sector of a low-income country. From agenda setting to implementation: The case of Tanzania
	Ness, Ingunn Johanne	The Room of Opportunity. Understanding how knowledge and ideas are constructed in multidisciplinary groups working with developing innovative ideas.
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