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Health and social responses to problems associated with the use of performance- and image-enhancing drugs

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Health and social responses to drug problems: a European guide

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Health and social responses to problems associated with the use of performance- and image-enhancing drugs

A background paper for the updated European Responses Guide

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What are performance- and image-enhancing drugs?

Performance- and image-enhancing drugs (PIEDs) include a wide range of drugs across various pharmacological categories and are subject to different legal controls and medicinal regulation across European countries. Their common feature is the function of their use: the alteration of physical performance or appearance. In the main, PIEDs are substances that are taken to promote muscularity. Users of these drugs may also use them together with other ancillary drugs to mitigate side effects or to further alter appearance, for example weight loss products, such as dinitrophenol, or skin-tanning injections like melanotan II. PIEDs form part of a wider category of substance use, often referred to as human enhancement drugs (HEDs) (Evans-Brown et al., 2012, McVeigh et al., 2012, Brennan et al., 2013, Chatwin et al., 2017, Van de Ven et al., 2019; see Table 1).

Table 1: Categories of HEDs (PIEDs specifically are shown in the shaded area)

	Category	Examples
A	Musculature	Anabolic steroids Human growth hormone Human chorionic gonadotrophin
B	Weight loss	Sibutramine Clenbuterol Dinitrophenol
C	Skin and hair	Melanotan II
		Mercury Latisse
D	Sexual performance	Sildenafil Bremelanotide Yohimbine
E	Cognitive function	Methylphenidate Modafinil Piracetam
F	Mood and behaviour	Fluoxetine Beta blockers Diazepam

In Table 1, PIEDs are those substances used to: A) enhance the structure and function of muscle, B) reduce weight, and C) change the appearance of the skin (Van de Ven et al., 2019). In addition to PIEDs, HEDs include substances taken to enhance or improve sexual performance (category D), cognitive functioning (E) or mood and behaviour (F).

Drugs within these other categories of HEDs, together with additional prescription drugs, may also be used in the self-directed treatment of side effects of PIEDs (e.g. sildenafil for anabolic steroid induced erectile dysfunction, common among anabolic-androgenic steroids (AAS) users (Horwitz et al., 2019)) or for additional enhancement purposes (e.g. insulin for potential anabolic properties (Anderson et al., 2018)). While delineation between the drugs is inexact, the motivations for use provide a clearer demarcation. For example, melanotan II is commonly used for its skin-tanning properties but is also used for its perceived sexual enhancement effects (McVeigh et al., 2012, Van de Ven et al., 2019); human growth hormone and growth hormone releasing peptides have been used to enhance muscularity and also to promote weight loss (Evans-Brown and McVeigh, 2009, Granado et al., 2010, Van Hout and Hearne, 2016). Most commonly, the literature and the media refer to PIED use as anabolic steroid use and, in broad terms, PIED users can be considered as those using AAS and associated drugs.

The use of PIEDs is by no means a new phenomenon and while attention during the 20th century was largely restricted to professional/elite athletes, PIED use has moved beyond the sporting arena and is now predominantly found among non-elite, recreational gym users (Evans-Brown et al., 2012, McVeigh et al., 2012, Coomber et al., 2014, Hanley Santos and Coomber, 2017, McVeigh and Begley, 2017, Salinas et al., 2019, Van de Ven et al., 2019). While the focus of research and the identification of the extent of PIED use has focused primarily on Northern Europe, North America and Australia, there is a growing body of evidence that PIED use and in particular the use of anabolic steroids is a global phenomenon (Sagoe et al., 2014, Zahnow et al., 2017, Sagoe and Pallesen, 2018).

This paper provides an overview of the main issues associated with the use of PIEDs in Europe and the responses developed to address these. However, the evidence on these topics is limited and what there is mainly relates to the use of these substances, in particular AAS, by gym users. Information on use of other types of PIED, user groups and environments is included where available, but the paper primarily focuses on the AAS-using population.

Box 1: Brief overview of the development of the use of PIEDs in the general population

Since the 1990s, there has been growing evidence related to PIED use within the general population. The use of AAS within the gym culture was established in parts of the United States by the 1970s, having first been introduced by elite and avant-garde bodybuilders from the late 1950s and 1960s (Hoberman, 1992, Yesalis, 1993, Hoberman and Yesalis, 1995, Hoberman, 2001, Evans-Brown et al., 2012). By the late 1980s, widespread AAS had been identified among young males in the general population of the United States with reported prevalence estimates ranging between 3% and 12% (Buckley, 1988, Yesalis et al., 1993). Subsequent surveys in Canada (Melia et al., 1996), Australia (Handelsman and Gupta, 1997) and Sweden (Nilsson, 1995) identified anabolic steroid use among adolescent males. By the 1990s, the use of PIEDs within gyms was well established within the United Kingdom (Korkia and Stimson, 1993, Lenehan et al., 1996).

More recently, surveys of the general population in the United Kingdom have shown an increase in AAS prevalence during the 2010s (Home Office, 2019), with findings supported by extensive targeted research and surveillance (Begley et al., 2017, McVeigh and Begley, 2017, Hope and Iversen, 2019). Studies across Europe have identified AAS use within the general population, e.g. Austria (Blank et al., 2017), Ireland (Jennings et al., 2014), Italy (Pacifici et al., 2016), the Netherlands (Stubbe et al., 2014), Nordic countries (Sagoe, Torsheim et al., 2015), Poland (Gwizdek et al., 2018), Spain (Calatayud et al., 2019) and Sweden (Leifman et al., 2011, Molero et al., 2017).

Use of specific PIEDs

AAS are synthetic derivatives of the hormone testosterone and the most commonly reported PIED within the gym environment (Begley et al., 2017). Lifetime prevalence of AAS use has been estimated as 3.8% in Europe (Sagoe et al., 2014), among the highest levels globally (Sagoe and Pallesen, 2018). The anabolic component of these drugs is related to protein building in skeletal muscle and bone while the androgenic effects of these drugs are associated with masculinisation, essential reproductive function and the development of secondary male characteristics (Kochakian, 1975, Kicman, 2008). They are administered via various routes but are predominantly used orally or via intramuscular injection. They have been shown to increase muscle size and strength (Bahrke and Yesalis, 2004) and are reported to have a range of other perceived benefits including increased energy, sex drive and youthfulness (Begley et al., 2017).

Human growth hormone has been used by athletes for over 30 years (Holt et al., 2009). Once restricted to elite sport and bodybuilders, it is now readily available on the illicit market (Begley et al., 2017) and no longer cost-prohibitive to the general public due to advances in technology, communication and transport (Evans-Brown and McVeigh, 2009, Brennan et al., 2011). While there is scant evidence regarding its effectiveness as a doping agent within competitive sport

(Holt, 2009), it is used for both its anabolic and lipolytic (fat-reducing) actions (Holt et al., 2009). There is little evidence regarding adverse effects (Evans-Brown and McVeigh, 2009, Holt et al., 2009); however, concern has been raised regarding carpal tunnel syndrome, renal damage, cardiovascular damage, and other symptoms associated with acromegaly (Hintz, 2004, Pope et al., 2014, Anderson et al., 2018, Davani-Davari et al., 2019).

Synthetic peptide hormones have become a significant part of the PIED illicit market since around 2010, including substances such as CJC-1295 (Henninge et al., 2010, Van Hout and Hearne, 2016), GHRP-2 (Thomas et al., 2010), GHRP-6 (Krug et al., 2014), hexarelin (Thomas et al., 2011) and a variety of forms of insulin-like growth factor-1 (IGF-1) (Evans-Brown et al., 2012). These drugs are often described as either promoting the release of or being related to growth hormone (Llewellyn, 2017). While little is known of the specific risks associated with each substance, if they are effective, harms would be expected to be similar to those associated with the use of human growth hormone. In addition, adulteration, mislabelling and incorrect strengths have been reported in products available on the illicit market (Kimergård et al., 2014, Stensballe et al., 2015).

The use of ancillary drugs to combat the adverse effects of AAS is well established in the PIED communities within the gym environment (Korkia and Stimson, 1997). A range of ancillary drugs may be used to treat or prevent the adverse effects of AAS, such as tamoxifen (for gynaecomastia), human chorionic gonadotrophin (testicular shutdown), diuretics (water retention), sildenafil (erectile dysfunction) and isotretinoin (acne) (Evans-Brown et al., 2012, Llewellyn, 2017). Weight loss or fat burners are also used, including 2,4-dinitrophenol (DNP) (Hoxha and Petroczi, 2015, McVeigh et al., 2017) and clenbuterol (Huckins and Lemons, 2013, Spiller et al., 2013).

It is important to note that drugs used to combat the adverse effects of AAS are also used by groups of individuals independently of AAS use for their pharmacological effects. This is particularly true of weight loss agents such as DNP (Petroczi et al., 2015, Ainsworth et al., 2018) and clenbuterol (Milano et al., 2018, Tester et al., 2020). Similarly, while melanotan II (an injectable skin-tanning agent) was initially used by AAS users (Evans-Brown, Dawson et al., 2009), its use has been adopted by other populations (Van Hout and Brennan, 2014, Begley et al., 2017). Conversely, the people who use skin-lightening products (Scarpa and Guerci, 1987, Lartey et al., 2017) including corticosteroids, hydroquinone, mercury, or dermal fillers and botulinum (Botox) (Brennan et al., 2018) remain a group of HED users who, while they may be considered PIED users, have not been identified as part of the AAS-using communities and we have little relevant data about them (Evans-Brown et al., 2012).

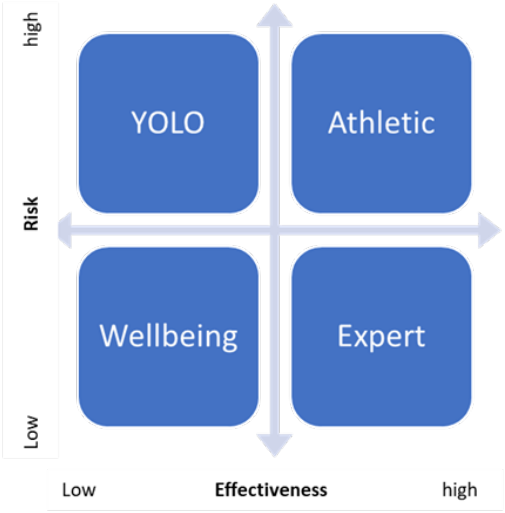
The use of a range of licit and illicit substances among some PIED-using populations is common (Sagoe, McVeigh et al., 2015). Research has shown cocaine use in the previous year approaching 40% (Hope et al., 2013), with consumption in some cases at very high dosages

(Salinas et al., 2019). High levels of AAS use among those attending treatment for drug problems is now recognised as a significant issue in a number of countries (Al-Falasi et al., 2009, Skarberg, 2009, Nokleby, 2013, Molero et al., 2017).

Populations and environments

The vast majority of PIED use data relates to AAS use within the gym environment. All the available information/studies indicate that most AAS users are male but female use does occur, in relatively small numbers. AAS use can have profound and lasting effects (see Table 2) (Jespersen, 2013, Nokleby, 2013, Onakomaiya and Henderson, 2016). While much of the media attention regarding AAS and the 'body beautiful' has a focus on young men, there are increasing numbers of older men using AAS. A recent survey of 684 PIED users recruited from gyms and needle and syringe programmes (NSPs) in the UK indicated that there were similar proportions of men aged 40 years and over (20%) as there were under the age of 25 years (21%) (Begley et al., 2017), emphasising that users of PIEDs are not a homogenous group.

Figure 1: Typology of AAS user from Christiansen et al. (2016)



Building on the categorisations of PIED users conducted in the 1990s (Lenehan et al., 1996, Dawson, 2001, Evans-Brown et al., 2012), we now have a more detailed appreciation of the varied typologies of users (Christiansen et al., 2016, Zahnow et al., 2018), ranging from chaotic and hedonistic use through to measured and conservative use for muscular gains. Based on qualitative interviews, Christiansen et al. (2016) developed the categories of user and visual depiction based on both risk and effectiveness of use shown in Figure 1. The categories were termed as YOLO ('you only live once'), athletic, wellbeing, and expert types based on both effectiveness and risk associated with AAS use. Cluster analysis of 611 male AAS users recruited from gyms and NSPs in the United Kingdom demonstrated a similar distribution of categories of users.

The use of AAS and associated PIEDs is higher among groups with specific characteristics such as professions where size or strength is an asset (Humphrey et al., 2008, Waterhouse, 2014, Hoberman, 2015, Turvey and Crowder, 2015). The use of PIEDs has also been highlighted among men who have sex with men (Ip et al., 2019) and those within the criminal justice system (Klötz et al., 2006, Klötz, 2008, Klötz et al., 2010, Lundholm et al., 2010, Hope et al., 2013, Lundholm et al., 2013, Lundholm et al., 2015). While for the majority of PIED users sport is not the main motivation for use, it does appear to be one contributory factor for a significant minority (Begley et al., 2017).

Problems associated with PIED use

The majority of research literature related to harms associated with PIED use centres on the use of AAS (Pope et al., 2014). The harms that have been identified as associated with the use of the main types of PIEDs and other HEDs that may be used to counteract these problems are summarised in the appendix to this report. However, much of the data is derived from case reports/series and cross-sectional study designs that are observational in nature, and in some cases causality is far from clear.

With respect to AAS, some of the most commonly reported effects are due to the hormone imbalance caused by the administration of exogenous testosterone (in the form of AAS), including acne, acceleration of male pattern baldness and gynaecomastia, and the effects of cessation of use resulting in hypogonadism and low testosterone (Kanayama et al., 2018). There is now compelling evidence regarding the development of dependence to AAS in some individuals (Kanayama et al., 2010, Pope et al., 2010, Kanayama and Pope, 2013, Hauger et al., 2019). While there remains debate regarding the role of AAS in aggression (Pope et al., 2000, Ambar and Chiavegatto, 2009, Oberlander and Henderson, 2012, Hildebrandt et al., 2014, Li et al., 2014, Sagoe et al., 2016, Chegeni et al., 2019), AAS appear to have a profound cognitive and emotional effect on some individuals (see Table 2).

Table 2: Examples of harms associated with the use of anabolic steroids

Physical

- Cardiovascular disease
- Hypertension
- Impaired lipid metabolism
- Damaged cardiac structure and function
- Insulin resistance
- Haematological disorders
- Musculoskeletal damage
- Testicular atrophy and impaired testosterone production
- Acne, hirsutism and male pattern baldness
- Changes to cerebral cortex

Psychological and behavioural

- Aggression
- Depression
- Dependence
- Anxiety and mood swings
- Impaired memory and cognitive function

Additional concerns

- Young people and normal maturation
- Females and virilisation including hirsutism and deepening of the voice
- Amenorrhoea/anovulation, clitoral enlargement, atrophy of breast tissue
- Injecting injury and transmission of blood-borne viruses

Adapted from ACMD (2010a, 2010b)

Long-term AAS use associated with cardiovascular risk related to myocardial dysfunction and accelerated coronary atherosclerosis is well established (Kuipers et al., 1991, Hartgens et al., 1996, Angell et al., 2012, Pope et al., 2014, Baggish et al., 2017). Long-term high-dosage AAS are also associated with structural changes to the brain (Bjornebekk et al., 2017, Westlye et al., 2017, Bjornebekk et al., 2019, Kaufman et al., 2019), impaired memory and changes to cognition (Bjornebekk et al., 2019, Hauger et al., 2019).

In recent years, worrying evidence in relation to blood-borne viruses has emerged in the United Kingdom. Evidence from public health surveillance indicates that between 1% and 2% of PIED injectors are HIV positive, a similar rate to levels observed in illicit drug users in the United Kingdom (Hope et al., 2013, Hope et al., 2016, McVeigh et al., 2016). Furthermore, one in 20 people who inject PIEDs have antibodies to the hepatitis C virus (HCV), indicating that they have been infected with HCV, with many of those who had only injected PIEDs being unaware of their hepatitis status (Hope et al., 2017). Blood-borne virus infections are likely to be related to a combination of risky injecting practices (including prior psychoactive drug injecting) and sexual behaviours (Hope and Iversen, 2019), with high levels of secondary distribution of injecting equipment (33% of the 467 participants) identified as a possible barrier to the dissemination of targeted harm reduction advice (Glass et al., 2018). There is no evidence to identify whether the situation in the United Kingdom is replicated across Europe, with information on HIV among PIED users globally restricted to rare case reports (Sklarek et al., 1984, Scott and Scott Jr., 1989, Henrion et al., 1992, Varriale et al., 1999). That said, the occurrence of injection site infection and tissue damage is well documented in this group (Hope et al., 2010, Driscoll et al., 2011, Fernandes-Flores et al., 2011, Banke et al., 2012, Pai et al., 2013).

The main alternative route of AAS administration is orally, which is associated with liver damage, in some cases life-threatening conditions (Schwingel et al., 2015, Stepien et al., 2015, Bond et al., 2016, Li et al., 2018, Niedfeldt, 2018, Smit, Nuijens et al., 2019).

Harm can also be directly attributed to the illicit nature of production and supply of PIEDs, with contamination of illicitly manufactured PIEDs (Evans-Brown et al., 2009, Graham et al., 2009, Pai et al., 2013, Breindahl et al., 2015) contributing to bacterial and fungal infections (Hope et al., 2010).

Different sources of supply and factors associated with this

In addition to providing a large market of consumers, the United Kingdom plays an important role as a transit hub in the global illicit trade of PIEDs (Antonopoulos and Hall, 2016, Hall and Antonopoulos, 2019). Both the internet and the gym owner/manager (Salinas et al., 2019) play a pivotal role in the potentially highly lucrative PIED illicit market (Forrest, 2019). However, much of the market could be described as ‘social supply’ or ‘minimally commercial supply’ (Coomber et al., 2018, Coomber and Salinas, 2019). The AAS/PIED market has been described as being decentralised, flexible, without hierarchies, and open to new traders within the gym/bodybuilding culture (Antonopoulos and Hall, 2016).

The availability of illicitly produced PIEDs is a long-standing, well-documented issue across Europe (Musshoff et al., 1997, Evans-Brown, Kimergård et al., 2009, Graham et al., 2009). However, with low-cost manufacturing capacity in countries such as China and India, the globalisation of free trade and the development of communication and transport networks, there has been an increase in the availability of illicitly manufactured PIEDs (Evans-Brown et al.,

2012). Counterfeit and 'underground laboratory' products are not restricted to AAS but include peptide hormones (Kimergård et al., 2014, Breindahl et al., 2015, Stensballe et al., 2015), ancillary drugs (Evans-Brown et al., 2014) and contaminated supplements (Geyer et al., 2008, Thomas et al., 2010, Abbate et al., 2014, Rocha et al., 2016). This has led to speculation that legitimately produced PIEDs are rarely available (Kimergård and McVeigh, 2014).

Responses to PIED use

Legal responses

While sporting sanctions in relation to PIED use or doping are well established and harmonised across Europe, there are significant differences in the role that National Anti-Doping Organizations (NADOs) take in relation to recreational sport or PIED use (Backhouse et al., 2014). In countries such as Denmark and Sweden and the Flemish community of Belgium, the NADOs have extended their roles beyond elite and competitive sport to implement drug testing of recreational weight trainers with removal of gym memberships to eradicate use within participating gyms.

Criminal law in relation to possession and supply of PIEDs depends on the specific substance and varies greatly between European countries. For example, in Norway the use of doping substances is illegal (Tangen and Møller, 2019), with Germany also introducing the criminalisation of 'doping' with jail terms of up to three years for athletes found guilty (Van de Ven, 2016). In the United Kingdom, the majority of PIEDs are controlled under the Misuse of Drugs Act 1971, making it an offence to produce, supply or possess with intent to supply AAS and associated drugs but not an offence to possess for personal use (ACMD, 2010a; ACMD, 2010b).

Research conducted in 2012 indicates that for many of the countries that had implemented specific PIED legislation (in relation to doping substances and offences), they still predominantly relied on general drug control legislation for prosecutions (Houlihan and Garcia, 2012). Drug control legislation relating to both possession offences and supply offences vary between the countries of Europe (Backhouse et al., 2014).

Prevention

There is a paucity of evidence related to the response to problems associated with PIED use across Europe. Recent reviews of drug prevention across Europe have found that there is little evidence of effectiveness of interventions for PIED users outside competitive or elite sport. While some behaviour change interventions exist, they are predominantly school-based and sport-focused, often hampered by brief or imprecise descriptions of intervention content, lack of behavioural outcome measures, and short-term follow-up times (Bates et al., 2017). An EU study of doping prevention in recreational sport across Europe concluded that while most Member States felt that effective prevention of doping in recreational sport was important, studies examining the effects of anti-doping education programmes were rare (Backhouse et al., 2014).

Recent work has called for multi-layered interventions that recognise the variation and complexity of PIED use in multiple settings targeting relevant ages and levels and types of risk (Bates and Backhouse, 2019). Furthermore, policies need to be developed based on rigorous scientific evidence in order to tackle the current dopogenic environment that is stimulating PIED use (Backhouse et al., 2017). In the United Kingdom, the National Institute for Health and Care Excellence (NICE, 2017) guidance on targeted drug prevention concluded that PIED users may be less likely to present to services because they may not identify as drug users and because no evidence of effective interventions to reduce this form of drug use had been identified.

Since 2008, a Swedish national anti-doping network involving several key stakeholders engaged in doping prevention in society has disseminated 100% Pure Hard Training (100% PHT), a community-based programme aimed at reducing doping use among recreational gym-goers. Developed by STAD (a research and development unit within the Stockholm region and the Karolinska Institute), the collaboration between stakeholders (gym staff, gym owners, police authorities, and municipal as well as regional prevention coordinators) includes training of gym staff and improved enforcement and policy work. So far, more than 500 gyms, located in more than 100 of Sweden's 290 municipalities, have implemented the prevention programme. A process and effect evaluation of 100% PHT is currently being conducted (Molero et al., 2016).

The Erasmus+ Sport project — Doping E-learning Tools (DELTS), a partnership of agencies from Finland, Greece, United Kingdom, Lithuania, the Netherlands and Australia — was a two-year project (2018-2019) aimed at improving prevention materials and health education in the field of PIEDs. Three e-learning tools were evaluated, one aimed at healthcare providers and two aimed at the fitness industry. A standardised evaluation methodology evaluated the accessibility and usability of the tools, with materials being shown to increase knowledge related to PIEDs among diverse groups of professionals. The survey and interviews found that all tools were regarded as clear and easy to use. The other main outcome of the project was the implementation of a best practice data bank to collate material on PIED harm reduction, prevention, educational information, and medical information (DELTS, date unknown).

Treatment cessation support and harm reduction

Information regarding structured treatment or structured support for the cessation of PIEDs is limited. There are numerous case reports of the treatment of either physical or psychological adverse effects of PIED use; however, there is scant evidence related to ongoing treatment and support within structured services. Much of the literature related to treatment and psychiatric support of those with AAS dependence is from the United States in the 1990s (Hays et al., 1990, Giannini et al., 1991, Brower, 1992, Corcoran and Longo, 1992, Kanayama et al., 2010). There are also published accounts regarding the treatment of androgen-induced hypogonadism and the recovery of normal testicular activity (Scally and Hodge, 2001, Rahnema et al., 2014, Anawalt, 2019). The role of the primary care physician in the treatment and care of PIED users has been

highlighted, including identification, assessment and treatment of AAS use and the management of AAS related problems (Dawson, 2001, Brooks et al., 2016, Casavant and Griffith, 2017). The United Kingdom's Department of Health now recognises PIEDs within their clinical guidelines on drug misuse and dependence, but acknowledge that there is little evidence to draw on (Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group, 2017) with these conclusions being supported by the Swedish National Institute for Public Health (2010).

In the United Kingdom, NICE has provided guidance on the provision of needle and syringes for PIED users who inject, recognising the increasing numbers of individuals attending NSPs (McVeigh et al., 2003, Kimergård and McVeigh, 2014), and the existence of new drugs (IGF-1 and analogues) and new client groups (melanotan II users) (NICE, 2014). However, evidence of the effectiveness of blood-borne virus transmission prevention or reduction of other drug-related risk behaviours is limited (Bates et al., 2013).

Also in the United Kingdom, Public Health England (2015) and the Advisory Council on the Misuse of Drugs (ACMD, 2010a, ACMD, 2010b) have recognised the practice of several services in the community and in prison. While services have evolved over time and in some cases have closed, they were considered appropriate models of delivery. Engagement with PIED users largely takes place within NSPs, often attached to community drug teams. Together with the provision of appropriate injecting equipment and safer injecting advice, some services provide comprehensive health monitoring (including regular blood tests), psychological interventions and referrals to specialist services. In addition to drug agency-based services, some pharmacies have provided interventions and outreach within the gym environment and have been shown to be successful at engaging with PIED users. However, there is scarce evidence on treating dependence, managing withdrawal, or initiating behaviour change in users in any settings (Bates et al., 2019, Harvey et al., 2019), with PIED users more likely to manage their own adverse drug effects (Zahnow et al., 2017) and seeking health information from their peers or via websites (Tighe et al., 2017, Harvey et al., 2019).

NICE (2014) also highlighted the Bridge Project as an example of harm reduction in the community and within the prison environment. Based on feedback from NSP users and local bodybuilders and powerlifters, one gym was prioritised as having significant problems with injecting-related litter and high-risk behaviour by attendees. Issues included needle re-use, people starting injecting at a young age, and people injecting each other, sometimes injecting several people with the same needle. Outreach work consists of a weekly drop-in session at the gym where, besides needle and syringe provision, advice is offered to gym members on nutrition and weight training. Regular work with this gym has led to relationships being developed with key gym staff and members, who in turn now refer people to the Bridge Project.

A drug worker, with specialist knowledge of PIED use, attends a local prison on a weekly basis and prisoners are encouraged to speak to them on any substance use issues, including PIEDs. A drug worker also provides a session where inmates can attend a PIED training session, focusing on harm reduction. Alongside the training, prisoners are offered an additional gym session, supervised by gym staff, and a personal trainer. There is a similar scheme offered in a neighbouring prison, where one-off training sessions are provided in partnership with the prison staff.

In the Netherlands the possession, production and supply of AAS and other PIEDs is not a priority within law enforcement or in public policy (Van de Ven, 2016). The AAS clinic in Haarlem is located centrally in the Netherlands and saw approximately 180 clients, referred by general practitioners across the Netherlands, during a five-year period. Detailed assessments and investigations were conducted and a wide range of AAS associated conditions reported and details of treatment provided, together with some intervention outcomes. This service is unusual as it describes the presentation of AAS users referred to the specialist clinic, and while standardised reporting was not utilised, the papers provide a description of interventions provided and some limited outcomes (Smit and de Ronde, 2018, Smit, de Hon et al., 2019)

In Norway, the possession or use of AAS and other PIEDs is illegal. However, treatment for those with health problems related to previous or present use of AAS and other doping agents is publicly available, with users having the same rights as other patients (Nesvaag and Lie, 2010, Ministry of Health, 2012). The use of AAS and other PIEDs has been identified as being common among those in drug treatment (Nokleby, 2013), although it still remains unrecognised in many individual cases (Havnes et al., 2020). To complement the structured drug treatment system and overcome barriers to service engagement, a dedicated telephone support service together with purposeful marketing through social media has been developed. Over a four-year period, 232 AAS users and 60 next of kin contacted the information service and received an hour-long information session with healthcare personnel (Havnes et al., 2019).

What are the likely future developments/opportunities and challenges in this area and what are the implications for drug policy and practice in Europe?

Research is needed to better understand the variety of drugs that are described under the umbrella term of PIEDs. New drugs continue to (re)emerge and there is little data on those that have never been through rigorous clinical trials (e.g. the majority of the available AAS) or are yet to be fully developed for the pharmaceutical market (e.g. many growth hormone promoters and selective androgen receptor modulators). There is also only limited (but concerning) information on those substances that have been withdrawn due to identified harms (e.g. the weight loss product 2,4-dinitrophenol).

Estimating the prevalence of PIED use remains problematic, with the clandestine nature of illicit use hampering primary research, and the reluctance of many PIED users to present to health

services together with low numbers in contact with the criminal justice system being a barrier to indirect methods of prevalence calculation. While the gym environment offers a means of access to a section of PIED consumers, there is evidence as to the heterogeneity of the population of users. Recent studies in Europe have shown diverse characteristics of PIED users, both in relation to their demographic characteristics and the diversity of motivations for use (Christiansen et al., 2016, Begley et al., 2017, Zahnow et al., 2018). While PIED users will predominantly use drugs to increase size and strength, their underlying motivations can be multifaceted, such as related to appearance, occupational stature, anti-ageing and sporting ability (Begley et al., 2017), with influencing factors, as with any substance use, that are complex, relating to the individual and their social network together with wider factors at institutional, community and societal levels (Bates et al., 2019a).

The diversity in the populations is evident in the risk behaviours among some groups of PIED users. While research related to blood-borne viruses is largely limited to the United Kingdom (Hope et al., 2013, Hope et al., 2017), other concerns associated with risk behaviours related to psychoactive drug use and incarceration have been highlighted in Scandinavian studies (Skarberg and Engstrom, 2007, Skarberg, 2009, Klötz et al., 2010, Nokleby, 2013, Christoffersen et al., 2019). However, it is clear that some of the most influential members of the online PIED communities do not associate themselves with, or even recognise, these characteristics or risk behaviours and that the resulting health-related messages alienate them and act as a barrier to drug treatment or harm reduction service engagement (Underwood, 2019). Many PIED users would welcome the opportunity to engage with health-related services if they felt they were appropriate (Griffiths et al., 2016, Tighe et al., 2017, Zahnow et al., 2017). Successful inclusion of influential online figures within the community and those within the gym environments (Salinas et al., 2019) frequented by PIED users may be the key to successful engagement with at least some of the wider drug-using populations (McVeigh, 2019).

For those individuals using PIEDs who are not part of the gym community, for instance those using weight loss drugs (e.g. 2,4-dinitrophenol, rimonabant, sibutramine, ephedrine, clenbuterol, thyroxine), skin-tanning products (e.g. melanotan II), skin-lightening products (e.g. corticosteroids, hydroquinone, mercury), or dermal fillers and botulinum, the challenges are even greater (Evans-Brown et al., 2012).

Globally, there is a dearth of evidence regarding interventions to address the use of PIEDs. Published work is largely descriptive, with little focus on outcomes relating to the prevention or cessation of PIED use, or the treatment, management or reduction of the associated harms. Evidence is urgently required to support the development of effective services for users and of evidence-based guidance and interventions to respond to users in a range of healthcare settings (Bates et al., 2019).

This paper has focused on PIED users, a sub-category of the wider population of human enhancement drug users. PIED users largely engage in the gym culture and, in the main, use AAS and associated drugs. In addition to the relative size of this population, an estimated 3.8% of adult Europeans having used AAS (Sagoe et al., 2014), this population has a broader influence on the general population. PIED users have been at the forefront of the introduction (or re-introduction) of several drugs which have then diffused to the wider population. Gamma-hydroxybutyrate (GHB) had long been established within the anabolic steroid using community for its perceived growth hormone promoting properties (Duchaine, 1989) before its widespread adoption within the nightlife environment or as a drug of concern in relation to 'chemsex'. Melanotan II, a sunless tanning agent, was used by bodybuilders and identified within NSPs (Evans-Brown, Dawson et al., 2009, Evans-Brown et al., 2012) prior to its adoption by the wider population (Brennan et al., 2016). Dinitrophenol, the most potent of weight loss agents (Evans-Brown et al., 2012), was first identified over a century ago (Barral, 1916) but rediscovered within bodybuilding circles in the 1980s (Duchaine, 1989, Llewellyn, 2017) and has latterly been associated with several deaths of both young men and women attempting to manage their weight (Petroczi et al., 2015, McVeigh et al., 2017).

Over the last three decades, PIED users have been forerunners in the use of these drugs prior to their diffusion to the wider population, and as such, the users may be considered a sentinel population in future drug trends. While there is increasing evidence in relation to the long-term effects of the more established drugs such as AAS, there remains little evidence relating to emerging peptide hormones. Furthermore, while concerning evidence relating to blood-borne virus prevalence among PIED users has been established in the United Kingdom, there remains uncertainty as to whether this phenomenon is unique or is mirrored across Europe. Recent systematic reviews have revealed the paucity of evidence in relation to drug prevention and harm reduction or in the support of cessation and relapse prevention. Research has to date been relatively small-scale, providing scant evidence to inform a pan-European response to the issues associated with this form of drug use.

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Appendix: Examples of harms associated with the main types of performance and image enhancement drugs (shaded area) and other human enhancement drugs

Category	Example	Examples of associated harms
Musculature	Anabolic-androgenic steroids	Cardiovascular effects (including cardiomyopathy, polycythaemia, hypertension, atherosclerosis); endocrine abnormalities — hypogonadism, aromatisation leading to gynaecomastia (males), virilisation leading to changes in genitalia, deepening of the voice, increased hair (women); psychiatric changes (depression, dependence, aggression, mania); hepatic abnormalities; cognitive and brain changes (structural changes and cognitive impairment); renal damage; immunosuppression; dermatological changes (severe acne).
	Human growth hormones	Cardiovascular effects (cardiomyopathy, hypertension); clinical features of acromegaly — endocrine disorders (diabetes); changes in bone structure (carpal tunnel syndrome, enlargement of hands, feet, forehead, jaw); thickening of skin; potential increased risk/acceleration of cancers.
	Human chorionic gonadotrophin	Used to stimulate testosterone production, similar to anabolic steroids; aromatisation and longer-term disruption to normal hypothalamic-pituitary-testicular function.
Weight loss	Sibutramine	Myocardial infarction or cerebrovascular events (in those with underlying cardiovascular disease).
	Clenbuterol	Cardiovascular effects (hypertrophy, hypertension, tachycardia, atrial fibrillation); anxiety.
	Dinitrophenol	Metabolic poison; fatalities due to hyperthermia; cataracts.
Skin and hair	Melanotan II	Nausea and vomiting; abnormal pigmentation; spontaneous erections; hypertension.
	Mercury	Renal damage; gastrointestinal disturbance; neurotoxicity affecting central nervous system.
	Latisse	Hyperpigmentation of eyelids; darkening of iris; conjunctivitis.
Sexual performance	Sildenafil	Headaches; nausea; hot flushes; temporary distortion of peripheral vision.
	Bremelanotide	Hot flushes; nausea; skin irritation; fatigue.
	Yohimbine	Intoxication associated with anxiety, hypertension, atrial fibrillation and seizures.
Cognitive function	Methylphenidate	Anxiety; headaches; sleep disturbance; nausea.
	Modafinil	Anxiety; headaches; sleep disturbance; nausea.
	Piracetam	Limited evidence of adverse effects.
Mood and behaviour	Fluoxetine	Sexual dysfunction; discontinuation syndrome (including insomnia, fatigue, dizziness, headaches and depression).
	Beta blockers	Weight gain; fatigue; sleep disturbance; cold extremities.
	Diazepam	Sedation; confusion; dependence.