The use of performance enhancers by otherwise healthy individuals may influence their overall well-being for better; or possibly, as a result of unintended side effects, for worse. It could also influence an individual’s insurance status; but it is very challenging for insurers to make an accurate risk assessment.

Medical enhancement, the use of pharmaceutical agents to enhance performance, may be physical or cognitive enhancement or both. Performance-enhancing drugs or enhancers are commonly drugs approved to treat medical conditions; or alternatively they are used ‘off-label’ to improve performance or appearance.

Modern pharmacy has made significant contributions to society through medical innovations and drug development. Early discoveries, such as insulin and penicillin, contributed to the emergence of a huge pharmaceutical industry. Drug research and development has focused primarily on treatments for diseases, with exceptions, notably oral contraceptives in 1960. More recently we have seen the increasing medicalisation of conditions, such as anxiety or minor skin complaints, which would previously be seen as within the normal remit of human circumstance. This trend has evolved into the use of pharmaceuticals for enhancement, in the absence of disease and without a medical condition.

Performance-enhancing drugs are commonly associated in competitive sports. Doping, the use of performance-enhancing drugs in sports, is banned by the majority of sports governing bodies. Anti-doping campaigns have intensified over the recent years with coordinated eradication campaigns; the founding of the World Anti-Doping Agency (WADA) in 1999; and more reliable testing methods. As testing has improved, however, many believe that the ability to cheat the tests has also improved. It is tacitly acknowledged that doping may continue to thrive in certain sports; and that some athletes consider enhancers necessary to perform at an elite level.

Use of enhancers may be even more common in sports without doping controls and in recreational sports. Additionally, pharmaceutical enhancement for non-athletic purposes is increasingly found in the wider population. The pursuit of improved performance in academia, business and social environments has led to this increase. This may have been driven by competitive pressures; the relative performance of peers; and the perceived efficacy and safety of marketed drugs.

Population surveys suggest use of drug enhancement, particularly for cognitive performance, is gaining acceptance. Reasons for the use of enhancers are various: they include increased concentration; reduced fatigue; improved physical performance; competitive advantage; and improved appearance by increased muscle mass and decreased body fat. Use of performance enhancing drugs among insurance applicants and policy holders may influence their health and well-being.

Neuroenhancement drugs
Cognitive enhancing drugs, also called ‘smart drugs’ or ‘nootropics’, include amphetamine, methylenedate, modafanil and caffeine. Use in normal healthy individuals is reportedly increasing with a prevalence reported in the range of 5% to 35% (Smith and Farah, 2011). Although improved cognitive abilities with the use of stimulants have been reported, available data is limited. Benefits are most consistently reported in clinical populations; while evidence for benefit in healthy individuals is mixed. Some studies report enhancement with improved memory and possibly executive functions; but others report impairment or detrimental effects. (Smith and Farah, 2011)

Amphetamines have been used for medical and non-medical reasons for almost 100 years, including enhancing alertness in military settings, treating depression and for athletic competition. More recently, amphetamines and methylphenidate, both common treatments for attention-deficit hyperactivity disorder (ADHD), have been extensively used off-label to increase...
alertness, energy or concentration in healthy individuals. This has especially been the case with university students, in a trend dubbed ‘academic doping’. The adverse effects of amphetamine and methylphenidate are similar and include insomnia, nervousness, rare cases of psychosis, anorexia, elevations in blood pressure, sudden cardiac death, and addiction potential.

Modafinil, a novel stimulant approved for use in the treatment of excessive daytime sleepiness associated with narcolepsy, sleep apnea and shift work sleep disorder, has been used non-medically by military personnel to manage fatigue and increasingly is used in academic and business settings. Modafinil may be better tolerated than amphetamines but may still cause anorexia, elevations in blood pressure and tachycardia.

Caffeine, the most widely used stimulant, is known to increase mental alertness, energy, and the ability to concentrate. Its use as a cognitive enhancer is widespread, including use of caffeine-containing energy drinks. Caffeine’s cognitive enhancing effects are likely indirect through its action on arousal mood and concentration (Nehlig, 2010). It also has analgesic properties and has been associated with possible decreased risk of type 2 diabetes, Parkinson’s disease, Alzheimer’s disease, certain cancers and even all-cause mortality in some studies (Lopez-Garcia et al., 2008). Risks include headache, anxiety, tremors, insomnia, depression, possible substance misuse, elevated blood pressure and potentially coronary or arrhythmic events.

Androgens and other hormones
Anabolic androgenic steroids (AAS) are synthetic analogs of the naturally occurring hormone testosterone known for their anabolic (muscle-building) and androgenic (masculising) effects. Their primary clinical use is as androgen replacement therapy in men with a testosterone deficiency. Other clinical uses may include treatment for delayed puberty, muscle-wasting associated with chronic disease and occasionally other conditions. More commonly, AAS use is associated with competitive athletes and is a major focus of anti-doping campaigns. While use in elite athletes is often highly publicised, most use occurs in recreational athletes, body builders and non-athletes, with estimated use in one percent of the population (Sjöqvist et al. 2008)

The frequency of adverse effects of AAS use in healthy individuals is not clearly identified. Risks may be underestimated in the medical literature due to under-reporting of illicit use. Equally, use could be overestimated given an anti-doping environment or due to other factors such as combination drugs or adverse training effects without established causality.

Cardiovascular adverse effects, including hypertension, left ventricular hypertrophy, myocardial ischemia, arrhythmias, thromboembolism and blood lipid abnormalities, have been reported (Angel et al. 2012, Urhausen et al. 2004 D’Andrea et al., 2007). AAS have been associated with psychiatric abnormalities including disorders of mood and aggressive behaviour. Associations between AAS use and risky behaviours including illicit drug use, alcohol or opioid misuse, drinking and driving, or violent or criminal activities have been reported (McCabe et al. 2007, Buckman et al 2009). Oral synthetic 17-alpha-alkylated androgens have been associated with liver toxicity including elevated liver enzymes, cholestatic jaundice, and peliosis hepatitis. Cases of hepatocellular adenomas or carcinomas have been reported with long-term use (Gorayski et al. 2008). Increased risk of benign prostatic hypertrophy and prostate cancer with AAS use has been suggested but not conclusively proven and tendon rupture has also been reported. Additionally, AAS users may use other substances to gain muscle mass, lose fat mass or to otherwise enhance physical appearance with added adverse effects.

Despite being marketed as anabolic steroids, androstenedione and dehydroepiandrosterone (DHEA), androgen precursors, have not been shown to increase testosterone levels, strength or performance. Adverse effects include increases in serum levels of oestrogen and lutening hormone (LH) which are of unknown significance, and negative effects on serum lipids have been reported.

Human growth hormone (HGH), relatively common as enhancer for athletes, increases lean body mass but has no demonstrated beneficial effect on strength or exercise capacity in trained athletes (Liu 2008). HGH was evaluated in a randomised controlled trial with recreational athletes. HGH significantly increased lean body mass and decreased fat mass in both men and women; and increased sprint capacity in men also administered testosterone (Meinhardt et al., 2010). Adverse effects are significant, including insulin resistance, diabetes, soft tissue edema, hypertension, cardiomegaly, myopathy, and carpal tunnel syndrome. Cases of Creutzfeldt-Jakob disease, a fatal neurodegenerative disease, have been associated with the use of cadaveric human HGH.

Other performance enhancing drugs
The list of drugs considered enhancers continues to expand as available drugs, developed and approved for disease entities, are being used as enhancers. Antidepressants, anxiolytics, antipsychotics, and certain anticonvulsants may improve mood and anxiety when used by individuals without any diagnosed condition. Similarly, oral hypoglycemics, antihypertensives and particularly cholesterol lowering HMG-CoA reductase inhibitors (statins) may be used in cardiovascular risk factor prevention outside of thresholds for recommended treatment guidelines.

Beta blockers, a class of medications approved for treatment of several cardiovascular and other conditions, may be used to reduce performance anxiety or tremors in normal or anxious individuals. They are banned for specific sports that require steadiness such as archery, gymnastics and shooting. Beta blockers slow the heart rate, decrease hand tremor and help reduce anxiety. They may be used for performance anxiety associated with presentations or presentations or block the heart rate, decrease tension and improve performance.
speeches, despite lack of evidence of effectiveness. Another apparently common practice with limited evidence of effectiveness is the use of beta blockers to enhance surgeons’ performance by decreasing anxiety and tremor, although this has not been correlated with patient outcomes (Elman et al. 1998). Adverse effects of beta blockers with short-term use include bradycardia, increased airway resistance, and decreased endurance.

Creatine, one of the most common nutritional supplements, has been shown to enhance short duration, high intensity exercise such as sprinting, with no apparent benefit for endurance sports. It is heavily advertised for sports and is not presently a banned substance by WADA. Adverse effects of creatine include weight gain, with reports of acute interstitial nephritis and possible renal failure.

**Implications for insurance underwriting**

Performance enhancing drug use is widespread in the general population and also likely in life and health insurance groups. Insurance applicants and policy holder groups are diverse, healthier than the general population and with characteristics that may fit with performance enhancing drug use: highly motivated, well-educated, well-informed, successful, employed, and competitive.

Reasons for performance enhancing drug use have common themes: improvement or maintenance of function, health or wellness promotion, and competitive advantage. The wealth of promotional information related to enhancers and the dearth of evidence-based recommendations relevant to benefits and risks serve to translate wishful thinking into widespread and not always sensible use of these drugs. Individual wellness initiatives are generally welcome by insurance companies; although they may be misguided through inadequate information.

For insurance underwriting, the types, names and dosages of enhancers and prescriber details are relevant for risk assessment. Applicants using enhancers frequently take multiple enhancers and may or may not fully disclose all drugs; while others may not consider supplements to be relevant and inadvertently omit them. Applicants may obtain enhancers from alternate sources without informing their doctor, so medical records do not include this information. Dosage of enhancers is also important as these dosages are sometimes higher than recommended medical dosages and may contribute to adverse events. Route of administration may also be important, particularly with the potentially hazardous injection practices of AAS, and potentially other unsafe or unapproved routes.

The method of procuring of enhancer drugs may be relevant in terms of the overall medical care of the applicant. An applicant who obtains an enhancer from their doctor is more likely to have adequate follow-up, and early recognition of adverse effects; whereas an applicant whose source of the drug is a trainer or through internet sales is less likely to have adequate follow-up. Physician prescribed medications are most likely legitimate prescriptions with proper manufacture and quality controls, whereas other sources could potentially be less reliable in terms of quality.

Regulatory issues may be relevant for insurance underwriting. Some enhancers may be illegal in some markets. For enhancers obtained from an illegal source, an applicant may be less likely to disclose drug use on an application and unlikely to tell their doctor. The source of the drug, particularly if not through legitimate prescription and licensed pharmacies, may also be important. Some drugs may be diverted from veterinary manufacture. Others from illegal sources may be without quality assurances and may contain an incorrect amount of the enhancer, harmful contaminants or undisclosed active ingredients. The risks associated with obtaining the drug illegally and nondisclosure are relevant for risk assessment.

Risk assessment may be challenging even with the applicant’s list of types, names and dosages of enhancers. Indications, usage guidelines and safety information for several drugs used as enhancers are available but developed specifically for drug use to treat a particular condition. Evidence-based research and guidelines for use as enhancers are limited or unavailable. Additionally, studies of the long term effects of enhancers are limited or unavailable, particularly at older ages.

Co-existing medical conditions and prescribed medications are relevant to an underwriting assessment with enhancers. Enhancers may exacerbate a condition or interact with prescription medications. The prescribing doctor may not be aware of the enhancer or the potential interactions. Some enhancers may worsen psychiatric conditions, lower seizure threshold in susceptible individuals or promote tumour growth. Enhancers may be part of an overall drug-centric approach to medical conditions and the level of adherence to recommended treatment including non-drug treatments may be helpful in the overall assessment.

Motivation to use enhancers may be relevant to insurance underwriting. An individual could be engaged in several positive behaviours and lifestyle choices that may translate into a longer, healthier life. The individual may have a pattern of healthy lifestyle and has gradually incorporated enhancers into their daily regimen, possibly as part of fitness goals or anti-aging efforts. In contrast, an individual may have an undisclosed or occult illness that prompted lifestyle changes and various treatments to counter, for example, muscle wasting associated with disease or frailty in an older applicant.

An overall underwriting risk assessment is valuable to identify the risk appetite of the applicant and any associated risk-taking behaviors. Use of enhancers may be associated with use of other drugs, alcohol misuse or substance or illicit drug misuse. Additional risk-taking behaviours may be identified with information related to occupations or avocations, including sports associated with significant injury potential or potentially criminal activity, particularly where legitimate drugs sources are not identified. Sports demanding maximal exertion may increase risk for sudden adverse events, particularly with enhancers with cardiovascular risk, such as stimulants.

Performance-enhancing drug use in insurance applicants adds to the complexities of underwriting risk assessment. The concept that enhancers may contribute to a shift from a disease model, in which a drug is used to treat a condition or disease, to a health model, in which a drug is used to enhance

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health or possibly in some instances, prevent a condition is an interesting one. However, pharmaceutical companies will likely continue to focus on drug development for recognized medical conditions rather than invest in the development of enhancers or lifestyle drugs. With both healthy and unhealthy applicants using medications, and at times the same medications, the ability to differentiate these groups in an underwriting setting becomes more challenging. Evidence supporting use of performance enhancing drugs is limited and despite the connotations of the term 'enhancer', drug use in the healthy may or may not equate with health.

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