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Research paper

The pharmaceuticalisation of 'healthy' ageing: Testosterone enhancement for longevity

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ABSTRACT

The United Nations estimates that the world's population will reach 8.5 billion by 2030, and the populations of most countries are expected to grow older. This is case for many developed countries, including Australia, the United Kingdom, Canada, the United States of America, and member states of the European Union. Older cohorts will comprise a larger proportion of overall populations, driven in part by our increases in life expectancy. An ageing population poses challenges for governments; notably, older people tend to have multiple, chronic health conditions which can place a burden of health budgets. At the same time, we are witnessing a shift in how we respond to the health needs of our populations, with global drug policy acknowledging that some substances are contributing to increased morbidity and mortality (e.g. opioids) while others may have beneficial therapeutic effects (e.g. psylocibin, cannabis). There is general agreement that as men age their levels of testosterone decrease, and there is some evidence to suggest that there have been population-level declines in testosterone which are not associated with age. Anecdotally, testosterone is accessed by men seeking to self-medicate in the belief that they are experiencing low testosterone levels. There has also been a rise in anti-ageing clinics in the United States, providing access to testosterone replacement therapy (TRT). The non-medical use of testosterone can result in a number of adverse health events, including complications from the use of black market or underground products. Placing testosterone under a new prescribing regime may address some of these concerns, but is society ready for this change, and if so, what would this regime look like? This paper will explore the issue of how society responds to enhancement for longevity, or how we increasingly use pharmaceuticals to address and prevent illness, with a specific focus on testosterone and testosterone deficiency.

The United Nations estimates that the world's population will reach 8.5 billion by 2030, an increase from 7.7 billion people in 2019 (United Nations Department of Economic and Social Affairs Population Division, 2019). This population growth is accompanied by the ageing of populations in most countries largely due to advances in medicine and public health that reduce mortality, especially in children, but also due to declining fertility (United Nations Department of Economic and Social Affairs Population Division, 2019). Governments in many developed parts of the world, including Australia, the United Kingdom, the United States, Canada, and the European Union member states will have populations with a larger median age and higher proportions aged 65 years and over. Already in 2015, the median age for Australia, the US, and the UK was 37.2, 37.6, and 40.2 years, respectively (United Nations Department of Economic and Social Affairs Population Division, 2017), an increase from 35.4, 35.2, and 37.6 years in 2000, respectively (Ritchie, 2019). In 2015, it was estimated that 8.5% of the world's population was aged 65 years and over, and this is expected to increase to 12% in 2030 and 16.7% in 2050 (He, Goodkind, & Kowal, 2016). The demographic shift is good news for longevity and overall population health, but it signals the need to revisit social and health infrastructure that was designed for a younger population with a shorter lifespan.

The ageing population presents significant policy challenges. First, given lower fertility rates, some countries do not have enough people entering the workforce to replace the older generation and fund their retirement. Second, existing social support systems may experience fi-

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nancial stress if older generations do not have sufficient personal funds to support their own retirement. Third, as people age, they tend to have multiple, chronic conditions, which require support from government health budgets. Thus, continuously increasing life expectancy and stable healthy or disability-free periods highlight the emergence of a "longevity trap" (von Zglinicki et al., 2016). Indeed, while we are expanding the lifespan, we are not only expanding the *healthy* lifespan but also the length of chronic disease. The World Health Organisation estimates that 71% of global deaths in 2016 were due to non-communicable diseases, with cardiovascular diseases the leading cause (World Health Organisation, 2018). Subsequently, there is growing focus on ensuring good quality of life later in life (Sinclair, 2019). As Blackburn and Epel (2017) write: "*Ageing and death are immutable facts of life, but how we live until our last day is not.*" Over the last three decades, a number of possible solutions regarding how to deal with the ageing population have been proposed. These include the emergence of commercial and clinical anti-ageing movements aimed at extending the time customers and patients can live without or delay the common morbidities of ageing (e.g. wrinkling of the skin, hardening of the arteries, memory loss, muscle loss and visual impairment) (Robert H. Binstock, Fishman, & Johnson, 2006). In this commentary, we focus on the use of testosterone to repair, reverse, or slow the undesirable signs and conditions of ageing, with a particular focus on men. It will explore the issue of how society responds to enhancement for longevity, or how we increasingly use pharmaceuticals to address and prevent illness, with a specific focus on testosterone and testosterone deficiency.

The case of testosterone

Anabolic-androgenic steroids (AAS) are a group of hormones that possess both anabolic properties, which causes muscle growth and fat loss, and androgenic properties, which causes such masculinising effects as voice deepening and facial hair growth. Of this group, testosterone was first synthesised in 1935, followed by a number of other synthetic variations (see Kanayama and Pope (2018) and Nieschlag and Nieschlag (2017) for detailed histories). Testosterone is used as a treatment for a number of medical conditions, such as the use of hormone replacement therapy for men with hypogonadism (Barbonetti, D'Andrea, & Francavilla, 2020). They are also prescribed for conditions such as hereditary angioedema, anaemia, breast cancer in women, infertility in men, and weight loss/muscle wasting (Llewellyn, 2017).

There is general agreement that as men age their levels of testosterone decrease (Andersson et al., 2007; Travison, Araujo, Hall, & McKinlay, 2009, 2007). Additionally, there is some evidence to suggest that there have been population-level declines in testosterone which are not associated with age but rather other factors such as obesity (Wang et al., 2011). Other studies have pointed to generational declines in testosterone levels which are not attributed to health or lifestyle changes (Travison et al., 2007). Low testosterone can contribute to ill-health during male ageing such as insulin resistance and metabolic syndrome, atherosclerosis and vascular disease, and with increased incidence of diabetes, cardiovascular events and mortality (Yeap, Araujo, & Wittert, 2012). From a medical perspective, maintaining appropriate levels of testosterone in men is therefore essential to good health.

The increasing focus on anti-ageing is not simple the result of an ageing population, as gaining control over ageing has been a human ambition since early civilization (Gruman, 2003). People are constantly exposed to an idealised image of beauty via advertisements and social media, and this image often equates beauty with a youthful appearance (Brown & Knight, 2015). As a consequence, men and women are increasingly using licit and illicit substances as a 'cure' for this ageing process. This also includes the use of testosterone, which has been used non-medically for several decades in bodybuilding, fitness, and sporting populations for its muscle building properties (Bahrke & Yesalis, 2002). As with many substances, the motivations for non-medical steroid use are more nuanced than the literature would suggest. Within the literature, non-medical steroid use appears to relate broadly to performance and image enhancing purposes, with researching linking use in this context with striving to achieve a muscular body that is seen as a visible sign of masculinity (Cranswick, Richardson, Littlewood, & Tod,). However, some consumers have reported that initial use stemmed from the belief that they had low levels of testosterone, which negatively impacted their lives (see Underwood, van de Ven, & Dunn,); for instance, the experience of mental health issues such as depression was attributed to low testosterone levels, with some participants indicating that without self-medicating with testosterone they would have committed suicide. Some consumers have reported seeking medical advice regarding low testosterone, but being denied prescriptions because of its scheduling that restricts the conditions for which doctors can prescribe it (see Underwood et al., under review). Healthy ranges of testosterone vary significantly (e.g. from 300 ng/dl to 1000–1200 ng/d). As such, what constitutes 'healthy' testosterone levels in terms of how one 'feels' will vary dramatically amongst individuals. Yet, accessing testosterone as a medical treatment requires a diagnosis of low-T (<300), despite how one 'feels'. Subsequently, while there is limited research exploring this specific behaviour, it does suggest that some consumers are resorting to the black market to self-medicate in the hopes of improving their quality of life, which requires users to take risks in accessing and using these drugs (Fincoeur, Van de Ven, & Mulrooney, 2015; van de Ven & Mulrooney, 2017).

The rise of anti-ageing

Modern society places a high value on appearance and youth. Whole markets have emerged to sell products for aesthetic purposes with the underlying intention to help people age their best (Koenraadt & van de Ven, 2018; Van Hout & McVeigh, 2020). While it may be tempting to mock the fitness industry or the latest 'super-fruit', the reality is that if we are to live longer, we should also seek to live healthier. This approach benefits individuals but also eases the socio-economic burden of an ageing and unhealthy population. Thus, as we are living longer and extending the 'lifespan', we must also seek to ensure that we live functional lives (i.e. the 'healthspan') (Fleming, 2019).

It is increasingly common to define ageing as a health problem. However, the range of physical and cognitive decline and deficits that we tacitly accept as an inescapable part of old age render it difficult to distinguish disease from 'normal functioning' for that stage of life (McGee, 2020). For example, according to Rattan (2018) "ageing starts after the end of the natural lifespan of a species, termed 'essential lifespan', and is characterised by a progressive loss of physical function and fitness that culminates in death of an individual" (Rattan, 2018). Similarly, de Grey (2005) defines ageing as "the lifelong accumulation of various intrinsic side effects of normal metabolic processes, which ultimately reach an abundance that disrupts metabolism and causes severe dysfunction of tissues and the whole organism" (de Grey, 2005). Healthy ageing from this perspective seems a misnomer, or a contradiction in terms, and anti-ageing becomes the only way to prolong health near the end of or, indeed, throughout the lifespan.

While there has been some pushback to its use (Lee, 2017), the term 'anti-ageing' has become embedded in our vernacular, with a multitude of interventions promising to reverse ageing and its effects. These interventions range from cosmetics, hair dye, cosmetic surgery, exercise programs, and nutritional regimens to the use of supplements and 'anti-ageing *medicine*'. Following this trend is a significant rise in commercial 'anti-ageing' clinics, particularly in the United States (Mykytyn, 2006). In some countries these clinics are situated within the sports medicine domain. The association between anti-ageing and sports is no coincidence given a number of therapeutic substances, including cannabis, are banned in professional sport in part due to their beneficial performance enhancement effects. Depending on the jurisdiction, many of these anti-ageing and performance enhancement substances are also scheduled substances available only by prescription from a medical practitioner for

a diagnosed health condition. This is the case for anabolic-androgenic steroids (AAS), including testosterone.

The tight regulation of substances with multiple purposes such as testosterone has contributed to significant debates around appropriate uses of medicines and the necessity of medical intervention (see Flatt, Settersten, Ponsaran and Fishman (2013) (Micans, 2005)). Support for the use of medicines with enhancement effects can fall within the purview of 'preventative medicine' that concurrently prevents disease and reduces future health costs that might be related to ageing (Binstock, 2004). Under preventative medicine, medicines with enhancement effects would be accessed through healthcare professionals, as is the status quo. Others argue that enhancement drugs have a role outside traditional medicine (i.e. curing or preventing disease) to facilitate living an 'optimal life' (Mykytyn, 2006). This view raises the question of whether optimizing life extends the goals of medicine and, with it, the regulation of drugs or is another endeavour entirely.

Can regulation accommodate the various uses of testosterone?

Testosterone is a prime case study to illustrate the regulatory gap between medicine and life optimization. Testosterone treats medical issues associated with low testosterone levels as well as helps to prevent and overcome age-related decline in energy and libido, issues that might warrant a prescription from a doctor. Testosterone also simply allows individuals to 'feel' younger (Katz & Gish, 2015) and aids in achieving desired physical and cosmetic enhancements. The current regulatory landscape makes no provision for this latter use, which has two complex consequences. First, it draws what appears to be an arbitrary bright line between the anti-ageing uses of testosterone that are acceptable and unacceptable. Second, it refers those who wish to access testosterone outside accepted medical indications to the black market. Both of these consequences merit further analysis as a first step to considering whether it is appropriate to revise regulation to include the anti-ageing use of testosterone for an "optimal life".

There are several complexities associated with prescribing testosterone that limit the flexibility of the current medical model. First, the medical model is based on quantification of what constitutes a testosterone deficit and, in turn, a calculable and consistent measure of the dose that ought to be prescribed. It is unclear how such a calculus would be applied to attaining an 'optimal life'. Second, expanding the medical model would involve redefining what constitutes good health in older age and developing techniques to measure how healthy a person is (Micans, 2005). Some theorists define health negatively as a condition free from disease (Bess, 2010). Others, such as the World Health Organisation, define health positively by considering "a state of complete physical, mental and social well-being". Neither definition seems to capture the nuances of relative health in older age. Reiner (2010) bypasses the need to define health outright by proposing 'restoration' as a more appropriate term for describing the use of substances aimed at attaining an optimal life. The term holds promise insofar as an optimal life is determined individually, not medically. Even where we have medical thresholds (e.g. testosterone levels), subjective feelings of well-being often come into play (Underwood et al., under review). Without more progressive ideas about health in older age and how testosterone can contribute to an optimal life, it would be impossible to instate consistent medical practice and regulation. This consistency is necessary to delimit the responsibility of medical professionals but also ensure beneficial, evidence-based, and fair care for patients.

Even a medical model inclusive of testosterone prescription for 'optimal life' anti-ageing uses will have limitations on who is allowed access. Ultimately, groups of people who would like access to testosterone for cosmetic enhancement or consume it in doses that exceed medical indications (e.g. bodybuilders, athletes etc.) will be excluded from the medical and anti-ageing models turning to the black market. The medical and ethics justification for such exclusions are unclear. The individual and social risks associated with consuming drugs like testosterone is relatively low, especially in contrast to the consumption of other (legal) substances such as tobacco or alcohol (van Amsterdam, Nutt, Phillips, & van den Brink, 2015), or even risky leisurely pursuits such as playing sports. However, the quality of underground AAS is not guaranteed. As a result, the extant literature suggests that the risk associated with the consumption of AAS derives from their clandestine nature. Furthermore, studies show that underground AAS products are commonly under-dosed, sometimes over-dosed, frequently contain or are replaced by another active steroid ingredient (Graham et al., 2009; Tircova, Bosakova, & Kozlik, 2019), and are often produced in unhygienic conditions. People who access testosterone via the black market, regardless of motive, generally use higher doses than therapeutically described (Pope et al., 2014). This evidence suggests that a regulatory model for testosterone that excludes currently 'unacceptable' anti-ageing and enhancement uses could be encouraging the black market and risky behaviour increasing the potential harm to individuals.

A prescription regime is not the only option, nor perhaps the most ideal given the multiple uses of testosterone and its low risk profile when accessed through legitimate channels. An over the counter (OTC) model for certain enhancement drugs, including testosterone, might be an option. Not only would such an approach help mitigate issues around access and quality, but it would also help negate the ethical and legal issues faced by medical practitioners under a prescription model. Such a shift would encourage dialogue between users and medical professionals about testosterone use and would relieve doctors of a potentially burdensome gatekeeping duty. An over the counter model may seem a radical suggestion given the current discourse on the use of enhancement drugs is driven in large part by anti-doping concerns. However, it does align with recent developments and proposals on how to approach the consumption of drugs from a policy perspective. For instance, one can consider the trajectory of cannabis consumption in Canada from illegal and criminalised, to a medical model, and then to its latest iteration in which cannabis is legal, decriminalised and supplied by governments. One primary rationale for this increasingly liberal approach was to remove the trade of such substances from organised supply networks and to supply consumers with a safe and regulated alternative (Ingram, 2016). Notably, the decriminalisation of other 'harder' drugs has been enacted or proposed from various governments around the world, with increasing acknowledgement of the harms associated with prohibition and savings, in term of both economics and human suffering, brought about by a harm reduction model (Bures, 2019).

The above discussion has focused on OTC access to testosterone for the purposes of anti-ageing, and we acknowledge that moving to this model can have consequences for testosterone use for other purposes. Broader access to testosterone may facilitate use amongst those for whom the legal status acts as a barrier to use (Dunn, Mazanov, & Sitharthan, 2009). There is some evidence of an increase in AAS use amongst young men, who may be experiencing harms but not seeking medical help (Van de Ven et al., 2018); easier access to steroids may see an uptake amongst this group. Furthermore, an OTC model may reinforce ideals that society has regarding beauty and ageing. By making a substance accessible, we may also be supporting the expectation that individuals ought to be trying to attain that ideal.

A cautionary note about 'anti-ageing quackery'

Anti-ageing is a billion dollar industry (Weintraub, 2010). However, many purported anti-ageing products (including supplements) lack evidence regarding their effectiveness but are nonetheless widely promoted and sold. Indeed, as outlined by Mykytyn (2006) "anti-ageing medicine is a broad term that may comprise groups selling remedies over the Internet, companies touting the 'anti-ageing'-ness of their products, practitioners who work outside of scientific medicine, and practitioners of anti-ageing medicine in clinics who believe that their work is strictly scientific." For example, the use of growth hormone (GH) as an anti-ageing agent has attracted much interest, however, the long-term safety and

efficacy of GH use for anti-ageing has not been demonstrated (Bartke, 2019; Subramanian, Mat Yusoff, Esa, Zakaria, & Ponnampalam, 2018). Yet, in the United States, human GH in anti-ageing clinics is often administered to patients (Perls, 2004). The nutritional and sport supplement industry suffers from the same abundance of unfounded claims of benefit (Peeling, Binnie, Goods, Sim, & Burke, 2018). In some cases, excessive and prolonged use may even lead to adverse health effects (Kennedy, 2018; Razzaque, 2018). The dearth of efficacy evidence for many advertised anti-ageing 'treatments' with the market- and consumer-driven underpinnings of the anti-ageing industry are likely to fuel scepticism about the necessity to revisit the regulation of certain substances. It is conceivable that an OTC model of regulation for testosterone could fuel anti-ageing quackery and experimentation that, at best, is innocuous and, at worst, causes serious health problems. Nevertheless, as Flatt et al. (2013) note, "the reality is that strong consumer markets have arisen around successful ageing and "successful living": markets that are founded on the belief that it is possible, acceptable, and even necessary to intervene into the ageing process in order to optimise ageing experiences".

Conclusion

Over the next decades, nations will be adapting funding and infrastructure to support the health and flourishing of their ageing populations. This commentary intended to initiate a dialogue about including the adaptation of regulation of substances that could help sustain health later in life. Many of these, like testosterone, are existing substances with established safety and efficacy profiles, strict medical indications, yet documented uses outside of traditional medicine (often labelled enhancement). It is imperative that the regulatory legacy of such substances as 'medical' not be used to preclude an honest examination of whether their current regulation is fit for purpose amidst major demographic and conceptual changes around ageing (Dunn, McKay, & van de Ven, 2019).

In the case of testosterone, two mammoth tasks lay ahead in rethinking its regulation for anti-ageing. First, the enthusiasm for using substances like testosterone for anti-ageing purposes will need empirical support. Part of that evidence will be studies of the groups using testosterone and their motives. The other part will be producing rigorous scientific evidence of their efficacy. This evidence will provide the basis for considering whether the benefit conferred by testosterone warrants the difficult ethical discussions and red tape involved in reforming regulation. Second is the exploration of options for reforming the regulation of testosterone. This commentary presented the advantages and challenges of prescription and OTC models of regulation, but, as we have seen with policy changes with other substances such as cannabis, there are other options (Caulkins et al., 2015). Liberal options will have to ethically justify any potential harm, small as it may be and the potential for inequalities in access. Options that are more restrictive will have to ethically justify the restriction of access to substances that could promote health in the ageing population. Willingness of scientists, both medical and social, as well as regulators to discuss the fraught topic of substance regulation will signal a first and necessary step to considering how we might better support those at the top of the population pyramid.

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References

Andersson, A. M., Jensen, T. K., Juul, A., Petersen, J. H., Jorgensen, T., & Skakkebaek, N. E. (2007). Secular decline in male testosterone and sex hormone binding globulin serum levels in Danish population surveys. *Journal of Clinical Endocrinology and Metabolism, 92*(12), 4696–4705. 10.1210/jc.2006-2633.

Bahrke, M. S., & Yesalis, C. E. (2002). *Performance-enhancing substances in sport and exercise*. Champaign, Illinois: Human Kinetics.

Barbonetti, A., D'Andrea, S., & Francavilla, S. (2020). Testosterone replacement therapy. *Andrology*. 10.1111/andr.12774.

Bartke, A. (2019). Growth hormone and aging: Updated review. *World Journal of Men's Health, 37*(1), 19–30. Retrieved from http://synapse.koreamed.org/doix.php?id=10.5534%2Fwjmh.180018.

Bess, M. (2010). Enhanced humans versus "normal people": Elusive definitions. *Journal of Medicine and Philosophy, 35*(6), 641–655. 10.1093/jmp/jhq053.

Binstock, R. H. (2004). Anti-aging medicine and research: A realm of conflict and profound societal implications. *Journals of Gerontology. Series A, Biological Sciences and Medical Science, 59*(6), B523–B533. 10.1093/gerona/59.6.b523.

Binstock, R. H., Fishman, J. R., & Johnson, T. E. (2006). Twenty-four- anti-aging medicine and science: social implications. In R. H. Binstock, L. K. George, S. J. Cutler, J. Hendricks, & J. H. Schulz (Eds.), *Handbook of Aging and the Social Sciences (Sixth Edition)* (pp. 436–455). Burlington: Academic Press.

Blackburn, E., & Epel, E. (2017). *The telomere effect*. London: Orion Spring.

Brown, A., & Knight, T. (2015). Shifts in media images of women appearance and social status from 1960 to 2010: A content analysis of beauty advertisements in two Australian magazines. *Journal of Aging Studies, 35*, 74–83. 10.1016/j.jaging.2015.08.003.

Bures, B. (2019). Is Canada About To Decriminalize All Drugs? *Yahoo Finance.*. Retrieved from https://finance.yahoo.com/news/canada-decriminalize-drugs-194052524.html.

Caulkins, J. P., Kilmer, B., Kleiman, M. A. R., MacCoun, R. J., Midgette, G., Oglesby, P., et al. (2015). *Options and issues regarding marijuana legalization*. RAND Corporation. Retrieved from California.

Cranswick, I., Richardson, D., Littlewood, M., & Tod, D. 2020. "Oh take some man-up pills": A life-history study of muscles,masculinity, and the threat of injury. *Performance Enhancement & Health*.

de Grey, A. D. N. J. (2005). Resistance to debate on how to postpone ageing is delaying progress and costing lives. *EMBO Reports, 6*(S1), S49–S53. 10.1038/sj.embor.7400399.

Dunn, M., Mazanov, J., & Sitharthan, G. (2009). Predicting future anabolic-androgenic steroid use intentions with current substance use: Findings from an Internet-based survey. *Clinical Journal of Sport Medicine, 19*(3), 222–227.

Dunn, M., McKay, F. H., & van de Ven, K. (2019). There's a (drug policy) storm coming. *Performance Enhancement & Health, 6*(3), 95–97. 10.1016/j.peh.2019.05.001.

Fincoeur, B., Van de Ven, K., & Mulrooney, K. J. (2015). The symbiotic evolution of anti–doping and supply chains of doping substances: How criminal networks may benefit from anti-doping policy. *Trends in Organized Crime, 18*(3), 229–250.

Flatt, M. A., Settersten, R. A., Jr., Ponsaran, R., & Fishman, J. R. (2013). Are "anti-aging medicine" and "successful aging" two sides of the same coin? Views of anti-aging practitioners. *THE journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 68*(6), 944–955. 10.1093/geronb/gbt086.

Fleming, A. (2019). *The science of senolytics: How a new pill could spell the end of ageing.* The guardian 2 September 2019. The Guardian. Retrieved from https://www.theguardian.com/science/2019/sep/02/the-science-of-senolytics-how-a-new-pill-could-spell-the-end-of-ageing .

Graham, M. R., Ryan, P., Baker, J. S., Davies, B., Thomas, N. E., & Cooper, S. M. (2009). Counterfeiting in performance- and image-enhancing drugs. *Drug Testing and Analysis, 1*(3), 135–142. 10.1002/dta.30.

Gruman, G. J. (2003). *A history of ideas about the prolongation of life*. New York: Springer Publishing Company.

He, W., Goodkind, D., & Kowal, P. (2016). *U.S. census bureau, international population reports, P95/16-1, an aging world*. US Department of Commerce. Retrieved from Washington, D.C.

Ingram, C. (2016). *Justin trudeau may have made the best case for legal pot ever*. International Drug Policy Consortium. Retrieved from https://idpc.net/alerts/2016/06/justin-trudeau-may-have-made-the-best-case-for-legal-pot-ever?setlang=zh.

Kanayama, G., & Pope, H. G., Jr. (2018). History and epidemiology of anabolic androgens in athletes and non-athletes. *Molecular and Cellular Endocrinology, 464*, 4–13. 10.1016/j.mce.2017.02.039.

Katz, S., & Gish, J. (2015). Aging in the biosocial order: Repairing time and cosmetic rejuvenation in a Medical Spa Clinic. *Sociological Quarterly, 56*(1), 40–61. 10.1111/tsq.12080.

Kennedy, M. (2018). The vitamin epidemic: What is the evidence for harm or value? *Internal Medicine Journal, 48*(8), 901–907. 10.1111/imj.13976.

Koenraadt, R., & van de Ven, K. (2018). The Internet and lifestyle drugs: An analysis of demographic characteristics, methods, and motives of online purchasers of illicit lifestyle drugs in the Netherlands. *Drugs: Education, Prevention and Policy, 25*(4), 345–355.

Lee, M. (2017). Allure magazine will no longer use the term "Anti-Aging". *Allure*. Retrieved from https://www.allure.com/story/allure-magazine-phasing-out-the-word-anti-aging.

Llewellyn, W. (2017). *Anabolics* (11th Ed.). Jupiter, Florida: Molecular Nutrition LLC.

McGee, A. (2020). Using the therapy and enhancement distinction in law and policy. *Bioethics, 34*(1), 70–80. 10.1111/bioe.12662.

Micans, P. (2005). The need for anti-aging medicine: The challenges faced to incorporate preventative medicine into the clinic and into society. *Annals of the New York Academy of Sciences, 1057*, 545–562. 10.1196/annals.1356.042.

Mykytyn, C. E. (2006). Anti-aging medicine: A patient/practitioner movement to redefine aging. *Social Science & Medicine (1982), 62*(3), 643–653. 10.1016/j.socscimed.2005.06.021.

Nieschlag, E., & Nirschlag, S. (2017). The history of testosterone and the testes: From antiquity to modern time. In A. Holh (Ed.), Tesosterone: From basis to clinical aspects. Switzerland: Springer.

Peeling, P., Binnie, M.J., .Goods, P.S.R., Sim, M., & Burke, L.M. (.2018). Evidence-Based Supplements for the Enhancement of Athletic Performance. 28(2), 178. doi:10.1123/ijsnem.2017-0343.

Perls, T. T. (2004). Anti-aging medicine: The legal issues: anti-aging quackery: Human growth hormone and tricks of the trade—more dangerous than ever. *The Journals of Gerontology: Series A, 59*(7), B682–B691. 10.1093/gerona/59.7.B682.

Pope, H. G., Jr., Wood, R. I., Rogol, A., Nyberg, F., Bowers, L., & Bhasin, S. (2014). Adverse health consequences of performance-enhancing drugs: An Endocrine Society scientific statement. *Endocrine Reviews, 35*(3), 341–375. 10.1210/er.2013-1058.

Rattan, S. I. S. (2018). Biogerontology: Research status, challenges and opportunities. *Acta bio-medica: Atenei Parmensis, 89*(2), 291–301. 10.23750/abm.v89i2.7403.

Razzaque, M. S. (2018). Can adverse effects of excessive vitamin D supplementation occur without developing hypervitaminosis D? *The Journal of Steroid Biochemistry and Molecular Biology, 180*, 81–86. 10.1016/j.jsbmb.2017.07.006.

Reiner, P. B. (2010). Distinguishing between restoration and enhancement in neuropharmacology. *Virtual Mentor, 12*(11), 885–888. 10.1001/virtualmentor.2010.12.11.msoc1-1011.

Ritchie, H. (2019). Age Structure. Retrieved from https://ourworldindata.org/age-structure

Sinclair, D. A. (2019). Lifespan: Why we age - and Why we don't have to. London: HarperCollins.

Subramanian, G. C., Mat Yusoff, Y., Esa, E., Zakaria, Z., & Ponnampalam, S. N. (2018). Recombinant human growth hormone: A medical miracle or cause for concern? *GSC Biological and Pharmaceutical Sciences, 5*(1), 26–33.

Tircova, B., Bosakova, Z., & Kozlik, P. (2019). Development of an ultra-high performance liquid chromatography-tandem mass spectrometry method for the determination of anabolic steroids currently available on the black market in the Czech Republic and Slovakia. *Drug Testing and Analysis, 11*(2), 355–360. 10.1002/dta.2541.

Travison, T. G., Araujo, A. B., Hall, S. A., & McKinlay, J. B. (2009). Temporal trends in testosterone levels and treatment in older men. *Current Opinion in Endocrinology, Diabetes, and Obesity, 16*(3), 211–217. 10.1097/med.0b013e32832b6348.

Travison, T. G., Araujo, A. B., O'Donnell, A. B., Kupelian, V., & McKinlay, J. B. (2007). A population-level decline in serum testosterone levels in American men. *Journal of Clinical Endocrinology and Metabolism, 92*(1), 196–202. 10.1210/jc.2006-1375.

Underwood, M., van de Ven, K., & Dunn, M. (under review). Testing the boundaries: Self-medicated testosterone replacement and why it is practiced. *International Journal of Drug Policy*.

United Nations Department of Economic and Social Affairs Population Division. (2017). World population prospects: The 2017 revision. United Nations. Retrieved from New York.

United Nations Department of Economic and Social Affairs Population Division. (2019). World population prospects 2019: Highlights. United Nations. Retrieved from New York.

van Amsterdam, J., Nutt, D., Phillips, L., & Van Den Brink, W. (2015). European rating of drug harms. *Journal of Psychopharmacology, 29*(6), 655–660. 10.1177/0269881115581980.

Van de Ven, K., Maher, L., Wand, H., Memedovic, S., Jackson, E., & Iversen, J. (2018). Health risk and health seeking behaviours among people who inject performance and image enhancing drugs who access needle syringe programs in Australia. *Drug and Alcohol Review, 37*(7), 837–846. 10.1111/dar.12831.

van de Ven, K., & Mulrooney, K. J. (2017). Social suppliers: Exploring the cultural contours of the performance and image enhancing drug (PIED) market among bodybuilders in the Netherlands and Belgium. *International Journal of Drug Policy, 40*, 6–15.

Van Hout, M. C., & McVeigh, J. (2020). The use of sunless synthetic tanning products. In K. van de Ven, K. J. D. Mulrooney, & J. McVeigh (Eds.), *Human enhancement drugs*. New York: Routledge.

von Zglinicki, T., Varela Nieto, I., Brites, D., Karagianni, N., Ortolano, S., Georgopoulos, S., et al. (2016). Frailty in mouse ageing: A conceptual approach. *Mechanisms of Ageing and Development, 160*, 34–40. 10.1016/j.mad.2016.07.004.

Wang, C., Jackson, G., Jones, T. H., Matsumoto, A. M., Nehra, A., Perelman, M. A., et al. (2011). Low testosterone associated with obesity and the metabolic syndrome contributes to sexual dysfunction and cardiovascular disease risk in men with type 2 diabetes. *Diabetes care, 34*(7), 1669–1675. 10.2337/dc10-2339.

Weintraub, A. (2010). Selling the fountain of youth: How the anti-aging industry made a disease out of getting old-and made billions. New York: Basic Books.

World Health Organisation. (2018). Noncommunicable diseases. Retrieved from https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases.

Yeap, B. B., Araujo, A. B., & Wittert, G. A. (2012). Do low testosterone levels contribute to ill-health during male ageing? *Critical reviews in Clinical Laboratory Sciences, 49*(5–6), 168–182. 10.3109/10408363.2012.725461.