The efficacy, safety and ethics of the use of testosterone-suppressing agents in the management of sex offending

Omer Khan[a] *and Asha Mashru*[b]

Purpose of review
The use of endocrine medications to reduce sexual offending recidivism is established and may involve clinicians from diverse specialities. The present review aims to outline relevant background information and note a Medical Ethics framework upon which to facilitate decision-making.

Recent findings
There have been several systematic reviews in recent years. A number of problems with research in the area of the medical treatment of sex offenders have been highlighted. There remains scope for improvement in the research to answer a number of relevant clinical issues. Nonetheless, some very useful indicators of relevance to clinical practice have emerged.

Summary
The use of medication to manage the risk of sex offending in males is appropriate under the right circumstances. These include, for example, hypersexuality with sexual deviance and psychological-treatment interfering sexual preoccupation.

Keywords
adverse effects, androgen deprivation, chemical castration, ethics, paraphilia, recidivism, sex offending

INTRODUCTION

Sex offending is heterogeneous including voyeurism, indecent exposure, child molestation, rape and may culminate in death of the victim [1,2▪]. Human sexual behaviour arises from the interaction of biology and social factors [3–6]. The biological aspect is partly mediated by testosterone in men [3,7,8]. Psychological therapy has become mainstream treatment [9–12], although beset by methodological issues and debates about effectiveness [13▪]. Dennis *et al.* [14] found no benefit from psychological intervention in the reduction of sexual recidivism but this has contrasted with other studies [15,16].

The role of testosterone in sexual offending is thought to be mediated by its effect on known risk factors for recidivism such as deviant sexual arousal and/or sexual preoccupation [2▪,7,8,17–19]. Guidelines for pharmacological treatment of sexual offending generally recommend it be restricted to those with a clinical diagnosis of paraphilia/paraphilic disorder (recurrent, intense, sexually arousing fantasies, sexual urges or behaviours associated with an abnormal stimulus or suffering to self or others) [7,8,17,20–22]. The validity of the diagnosis has been questioned [23–25].

Biological treatments are often offered alongside psychotherapy and often in a stepwise manner [7]. Androgen deprivation therapy (ADT), sometimes referred to as chemical castration, and surgical castration are offered in several countries to sex offenders, or those at risk of offending, in Europe and the USA [26,27]. It is important to have a clinical overview of the practical and ethical issues underpinning decisions for the prescription of hormonal treatments in sex offenders. This review will focus on males (ADT is not used in female sex offenders; for a review, see Cortoni and Gannon [28]).

[a]Chadwick Lodge, Milton Keynes and [b]The Wells Road Center, Nottingham, UK

Correspondence to Dr Omer Khan, Consultant Forensic Psychiatrist, Chadwick Lodge, Milton Keynes, MK6 5LF, UK. Tel: +44 1908 608 600; e-mail: omerkhan@priorygroup.com

Curr Opin Endocrinol Diabetes Obes 2016, 23:271–278
DOI:10.1097/MED.0000000000000257

KEY POINTS

- Androgen deprivation treatment – chemical castration – often requires clinicians from different specialities co-ordinating treatment so shared knowledge will reduce the risk of complications.
- The use of ADT for sex offenders has a level C of evidence for the reduction of recidivism and should be used with appropriate protocols and guidance.
- Ethical dilemmas may present to nonforensic clinicians, and if in doubt, appropriate advice from forensic practitioners should be sought.

ASPECTS OF ANDROGEN DEPRIVATION

Testosterone and metabolites influence human sexual behaviour including sexual activity, spontaneous functionality, erectile function, sexual desire, penile morphology, ejaculation and orgasm [2▪,3,7,8,29–32]. Testosterone levels have been implicated in the severity of sexual assault [33], with aggression [33,34] and with sexual recidivism [35]. The number of CAG repeats in the human androgen receptor has been associated with sexual and violent crime [36].

Although surgical castration is still used in Germany, Czech Republic and the USA for the management of sex offenders it has mostly been replaced with hormonal treatment [7,8,26]. As oestrogen use was abandoned many years ago because of its feminising effects, three main types of medication are used today [8,37]:

(1) Gonadotropin reducing hormone (GnRH) analogues: for example, triptorelin 3.75 mg monthly or 11.25 mg tri monthly (approved in Europe in 2007 for hypersexuality with sexual deviancy) is used to treat sex offenders in 53.1% of forensic psychiatric institutions in Germany, and 14.2 and 58.6% of treatment programs for sex offenders in the USA and Canada, respectively.
(2) Cyproterone acetate (CPA): for example, 50–200 mg a day orally or 200–400 mg once weekly or every 2 weeks by depot (registered in more than 20 countries) is used in 40.6% of German forensic psychiatric institutions and 38.2% of treatment programmes with sex offenders in Canada.
(3) Medroxyprogesterone acetate (MPA): for example, 50–100 mg a day orally or 300–500 mg per week depot is largely restricted to the USA and is used in 17.2% of treatment programs there.

All reduce gonadotrophin levels (and hence testosterone levels). CPA has additional androgen receptor antagonist activity. GnRH analogues are the most potent and reduce testosterone levels to castrate levels. For a detailed review and guidelines for the use of medication in sex offenders, see Grubin [8] or Thibaut *et al.* [7]. To minimise the adverse effect of ADT, less potent forms of ADT are used algorithmically, assessed by symptom control and offending risk. Serotonin has been implicated in human sexuality [38] and selective serotonin reuptake inhibitors (SSRIs) are often first-line treatment in reducing sexual offending, especially if depressive or compulsive features are present and in 'noncontact' offenses. Some medications used in prostate cancer, such as bicalutamide and Degarelix, have not been studied in sexual offending.

EFFICACY

The research into biological treatment of sex offending is challenging because of the relatively low frequency of offending, which can occur many years after release [2▪,39].

Attempts have been made to manipulate testosterone to control sexual offending, with the largest trials from surgical castration [40], although much was obtained prior to randomized control trials (RCTs) and some was unethical, for example in Nazi Germany [41,42]. Heim and Hursch [42] reviewed a large sample of more than a 1000 individuals as reported by Langeludekke [43] who found, in males followed for up to 20 years, a recidivism rate in the castrated group of 2.6% compared with 39.1% in the noncastrated group, with higher rates of recdivism in those castrated between age 20 and 30 and with more than three previous sexual convictions. Their review of a sample described by Cornu [44] found recidivism rates of 7.44 and 52% in 121 surgically castrated individuals and a control group, respectively, after 10 years.

A Cochrane review of drug intervention for sex offenders [2▪] focussed on RCTs with recidivism as a primary outcome and found a lack of evidence to support treatment despite some promising indications. Methodological concerns included small sample sizes, relatively short follow-up, the number of participants leaving studies, blinding of those who measured outcomes, ways in which investigators concealed allocation of treatment to those delivering it, and reporting of the primary outcome. No meta-analysis was possible. Overall, six studies assessed the impact of testosterone-suppressing drugs [45–50], and only two reported on the primary outcome. McConaghy *et al.* [49] compared intramuscular MPA and imaginal desensitization

with imaginal desensitization alone and found no reoffending at 2-year follow-up for the intervention group ($n = 10$ vs. one relapse within the group treated by imaginal desensitization alone). A three-armed trial [46] of oral MPA, alone or in combination with psychological treatment, reported a 20% rate of reoffending amongst those in the combined treatment arm ($n = 15$) and 50% of those in the psychological treatment only group ($n = 12$). Drop-out rates were very high in the MPA alone group. Of secondary outcomes, results suggested that the frequency of self-reported deviant sexual fantasies may be reduced by testosterone-suppressing drugs, but not the deviancy direction. Hormonal levels of testosterone tended to correlate with measures of sexual activity and anxiety. Important increases in depression and excess salivation were reported in one trial of oral MPA. No deaths and no suicide attempts were reported in any study, although no study tested the adverse effects of testosterone-suppressing drugs beyond 6–8 months. There were no trials of SSRIs or GnRH analogues and no trials published within the last 20 years.

Schmucker and Losel [13▪] argued evidence should not be restricted RCTs and conducted a systematic review of controlled outcome studies of all relevant interventions for sex offenders involving data from 22 181 participants. The main results featured a large effect size for surgical castration [odds ratio (OR) = 15.34; 95% confidence interval (CI), 7.34–32.05; eight studies], a reasonably large effect size for hormonal treatment (OR = 3.08; 95% CI, 1.40–6.79; six studies), and moderate effect size for CBT (OR = 1.45; 95% CI, 1.12–1.86; 35 studies). General offending was also reduced. An updated review with stricter inclusion criteria found a statistically significant OR = 1.41 for psychosocial treatments in reducing sexual recidivism [16].

Thibaut *et al.* [7] found an overall level C of evidence [51] for the use of ADT for sexual recidivism in paraphilias. Three to 5 years of treatment was recommended (level D evidence). In an observational study of the treatment of 611 sex offenders in Germany, Turner *et al.* [37] found that 10.6% were treated with GnRH analogues and 5.1% with CPA, suggesting common use. A reduction in the frequency of sexual thoughts was reported in 60% after CPA treatment and 75.4% after GnRH analogue treatment with corresponding reductions in the intensity of sexual thoughts in 52 and 66.7%, respectively. As per the findings in the Cochrane review above, this targets one of the risk factors for sexual recidivism in addition to providing personal relief for some patients and facilitating engagement in psychotherapy once the intrusive, distracting sexual thoughts have reduced [2▪,7]. They also found that only 78.1% of patients gave informed written consent before starting ADT and only 71.9% were informed about possible risks and side-effects.

In a review of treatment guidelines for adolescent sexual offenders with paraphilic disorders [52], only case reports were available. Of note, psychological treatment may be more effective in adolescents than in adults, whose sexually deviant tendencies may be more fixed [53]. Case reports have also assessed neurobiological changes in sex offenders after ADT, with positive indications [54].

Overall, more research evidence is needed to answer certain questions about the biological treatment of sex offenders though it is also certainly clear that it is an established aspect of treatment in this patient group. The impact on known risk factors for sexual recidivism is encouraging alongside evidence of actual reduced sexual recidivism.

ADVERSE EFFECTS OF ANDROGEN DEPRIVATION THERAPY

All medications have side-effects and ADT is no different. ADT, amongst other effects, results in decreased levels of testosterone and oestradiol (the latter from the reduced peripheral aromatization of androgens) with consequent effects on skeletal, cardiovascular, metabolic and brain functions [55–57]. GnRH analogues are the most potent of current treatments at reducing testosterone levels, as noted above. Of note, much of the research into adverse effects has come from ADT use in patients with prostate cancer, who are generally older and have greater physical comorbidity. Generalization may be confounded [55].

SEXUAL DYSFUNCTION

Overall, it is suggested that less than 20% of men with prostate cancer undergoing ADT maintain any sexual activity [31]. Wille and Beier [58] reported on a group of 99 voluntarily castrated sexual offenders and found sexual interest, libido, erection, and ejaculation diminished in 75% of the cases within 6 months; 10% remained sexually active for years on a slightly diminished level and 15% reported sexual outlets over a longer period of time but required more intensive stimulation for sexual release. This is important as the aim of some sex offender programs is to replace deviant with healthy sexual functioning [59]. The effect on sexual dysfunction was more marked with increasing age.

The observation that some retain sexual functioning is consistent with preliminary findings that other endogenous steroids may have a role in sexual

function in males [29,60,61]. Phosphodiesterase type 5 inhibitors [31,62,63▪] and supervised exercise [64,65] may also be helpful. Of note, the longer the duration of ADT the more difficult is recovery of testosterone and sexual functioning [31,66].

SKELETAL ABNORMALITIES

ADT is associated with a risk of fractures. It is thought to cause a 3–5% 12-month decrease in bone mineral density in patients with prostate cancer, slowing after the first year [53,63▪,68]. In one study on surgical castration for sex offenders, 82% developed osteoporosis whereas another found only 1 of 89 developed it [40]. A study of 30 young men with paraphilia receiving triptorelin (mean age 32 ± 8 years) [69] found seven of 18 men followed up did not show any change in bone density after 12 months. Kreuger and Kaplan [70] found three cases of bone demineralization out of 12 men followed from 6 months to 6 years receiving Leuprorelin for sexual deviancy. Gooren *et al.* [71] described bone mineral loss and hip fracture in a 52-year-old man after 10 years of CPA [7]. Stepan *et al.* [72] found, in their sample of eight out of 12 surgically castrated men with sexual delinquency (age range 20–42), greatest losses were in the first 2 years (mean 7% per year) than in the 6–11 years after orchidectomy (1.5% per year). One man was reported to have died from a hip fracture. Thibaut *et al.* [52] note a caution in the use of ADT in adolescence of the effect on bone growth.

The risk of fractures is also increased by the decrease of lean body mass by ADT of about 5%, which leads to an increased risk of falls, and increases with duration of ADT [56,63▪]. Shahinian *et al.* [73] found a fracture rate of 19.4% in men receiving ADT for prostate cancer who survived at least 5 years, compared with 12.6% of those not given ADT. A study of 25 544 men with prostate cancer by Wang *et al.* [67▪] found an overall increased risk of fracture requiring hospitalization with ADT (OR = 1.82; 95% CI, 1.44–2.30; adjusted for age and ethnicity) and those who received combined androgen blockade with GnRH analogues and antiandrogens (OR = 3.48; 95% CI, 3.07 to 3.96) and bilateral orchiectomy with pharmacological ADT (OR = 4.32; 95% CI, 3.34–5.58) had higher risks of fracture. Melton *et al.* [74] found the overall standardized mortality rate (SMR) of 1.2 (CI, 1.1–1.3) was highest soon after fracture and remained elevated for over a decade.

Consensus based and expert opinion guidelines exist for skeletal health management in men receiving ADT [7,63▪]. Suggested lifestyle modifications include vitamins D and calcium supplementation, cessation of smoking, decreased alcohol consumption and normalization of BMI [56,57]. Bone density management prior to starting ADT is recommended and *T* scores of more than 2.5 or more than 1 with other risk factors, indicate an elevated risk of subsequent nonmetastatic fractures [56,57]. Bisphosphonates [75] are usually the first-line treatment, especially zoledronic acid, with bicalutamide, tamoxifen, toremifene and Denosumab as alternatives [55,57,63▪,76–79]. There may be an advantage using less potent testosterone-suppressing agents [55].

DIABETES, METABOLIC SYNDROME AND CARDIOVASCULAR DISEASE

ADT has been associated with insulin resistance with short-term therapy and type 2 diabetes mellitus with longer term treatment [80]. Tsai *et al.* [81] conducted a retrospective cohort study of 12 191 men and found primary ADT compared with non-primary ADT was associated with a 1.61-fold increase in diabetes risk (95% CI, 1.38–1.88) over a median of 4.8 years. Interestingly, the association was stronger in men aged 70 or younger (HR = 2.25 vs. 1.40, $P = 0.008$). The number needed to harm was 29. ADT has also been shown to increase the risk of metabolic syndrome between 4 and 8% depending on the criteria used [82], although results of the effect on lipids have been mixed [63▪].

Low levels of testosterone after ADT have been associated with coronary artery disease (CAD) and cardiovascular events [83], although the evidence for stroke has been inconclusive [63▪]. A large study found a 16% increase in risk for CAD and sudden cardiac death in men receiving ADT for prostate cancer, with the effect evident after 4 months [84]. Nanda *et al.* [85] found this risk was confined, in their sample of 5077 men, to those with a previous history of myocardial infarction or heart failure. O'Farrell *et al.* [86] found the highest risk of cardiovascular disease to be in the first 6 months in those with two prior cardiovascular events. von Eyben *et al.* [87] followed 989 men after surgical castration, 835 of whom died, and found an increase in standardized mortality rate (SMR) for all-cause mortality of 1.30 (CI, 1.26–1.36) and SMR for MI mortality of 1.08 (1.04–1.16). Expected confounders were not found in regression analyses despite the population containing more unmarried men of social class IV and V than the general population.

Guidelines suggest pretreatment assessment of cardio-metabolic status followed by annual review [88]. Once again, the degree of suppression testosterone may be important and statins and toremifine may help ameliorate potential negative effects of

ADT on lipids and cardiovascular risk [55]. Metformin and lifestyle changes may also help considerably [65,89].

PSYCHOLOGICAL DYSFUNCTION

Testosterone deficiency is associated with low mood in men and sex offenders already have increased rates of comorbid mental health disorders [2▪,7,90,91]. Donovan *et al.* [92] highlight increased emotional lability and depressed mood in men who received ADT for prostate cancer and evidence for adverse cognitive effects with ADT. Langevin *et al.* [46] noted reports of 'psychological demasculation' in a sample of genital exhibitionists.

In a study of surgically castrated offenders, 30% reported feeling miserable after the operation with complaints of depression, irritability and isolation [40] with occasional reports after ADT [2▪,7]. In another study on surgical castration in a similar population, 71% accepted and were contented with the decision to be castrated [40]. Thibaut *et al.* [7] discuss two case reports of attempted suicide associated with ADT in sex offenders (one after failed therapy). This needs to be compared with significantly elevated rates of completed suicide amongst sex offenders [93] and notable rates of attempted suicide in a sample of 3030 incarcerated sex offenders [94].

Physical exercise has been shown in patients with prostate cancer receiving ADT to have significant potential to improve distress, fatigue, social functioning and mental health [65].

MISCELLANEOUS SIDE-EFFECTS

Vasomotor flushing can occur in up to 80% of men on ADT and affect quality of life; therapeutic options include cyproterone acetate, medroxy progesterone acetate, venlafaxine, gabapentin and acupuncture. ADT may lead to a normochromic and normocytic percentage anaemia (usually mild) in patients with prostate cancer [56,57]. Other side-effects include gynaecomastia, decreased facial and body hair growth, weight gain, fatigue, decreased testicular volume, thrombophlebitis (especially with MPA and CPA) and hepatotoxicity (with CPA) [7,21,56,57]. The presence of a pituitary adenoma may lead to pituitary apoplexy on commencement of ADT and should be excluded if there are any concerns [95].

ETHICS

Medical ethics provides a pragmatic approach to structure thinking about ethical issues in this area [96]. There is a potential tension in managing sex offenders between concern for the person/patient and public safety [9]. The standard four principles of Medical Ethics of Respect for Autonomy, Beneficence, Non-Maleficence and Justice [97] apply along with concerns about which take priority in forensic psychiatry [98,99] and attempts to address this [9,100].

Some sex offenders may be detained in prison or hospital as a result of their actions. Their capacity to consent to medical intervention has been questioned as to whether it can be truly informed if offered as an alternative to an otherwise longer period of detention [26,101]. Medical ethics can be usefully applied here, as the offer of ADT as an alternative to further incarceration may actually increase a patient's autonomy by simply increasing the choice available to the person (assuming the original detention length would not be increased by refusal) [26]. Another important issue regarding consent is explaining information to potential recipients of ADT in a way they are likely to understand [102]. It is also appropriate to offer treatment for persons to reduce their distress, which many with a paraphilia report [7], and also in providing treatment to those who have not yet offended yet desire treatment [103]. Douglas also argues that to be truly autonomous one must not be driven by desires (e.g. sexual deviancy) that 'do not reflectively endorse or are alien to the authentic self', although this may be difficult to prove [26].

Sex offenders seeking treatment for sexual dysfunction may create complex ethical issues for clinicians [104], in which case the advice of a forensic psychiatrist or psychologist may be sought with benefit (there is little specific evidence in this area to guide judgement).

There have also been concerns raised about the ethics of conducting an RCT in this population given the harm involved [105] alongside arguments in support of them [2▪,106,107].

Overall, at least two medications are licensed in Europe for the treatment of hypersexuality with deviant sexual interest, with the implication that the use of ADT in sex offenders is clinically warranted and ethically acceptable, provided standard tenets of practice are followed [108].

CONCLUSION

The toll of sexual offending on the public is considerable and there is a larger pool of unidentified victims than identified [1,109]. The highlighted recidivism rates of approximately 15% after 5 years [15] may, therefore, be higher than reported, and are generally higher for offenders against boys [110].

The evidence for psychological intervention leaves scope for improvement as does that for biological intervention. The latter has shown large effect sizes (including reduction of general offending), although with methodologically flawed trials, and hints at promise for the future.

A conclusion of this article is a need for more research evidence for the hormonal treatment of sex offenders; with sample size, bias and heterogeneity being common themes of concern but that treatment of sex offenders with pharmacological agents is potentially effective in reducing recidivism and the side-effects manageable if used with appropriate guidelines [7,8,111].

Further research should consider issues such as the interaction between psychosocial therapies and biological treatments; the impact of complicating comorbid conditions such as psychopathy and substance misuse; identifying the optimal timing and duration of treatments and cross cultural and age-related effectiveness.

Acknowledgements

The authors would like to thank Dr David Forshaw for his helpful comments on the draft manuscript.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

1. Tenbergen G, Wittfoth M, Frieling H, *et al.* The neurobiology and psychology of pedophilia: recent advances and challenges. Front Human Neurosci 2015; 9.
2. ■ Khan O, Ferriter M, Huband N, *et al.* Pharmacological interventions for those who have sexually offended or are at risk of offending. Cochrane Database Syst Rev)2015; (2).

Contains background information on sexual offending, detailed descriptions of RCTs available in the area and implications for practice.

3. Bancroft J. The endocrinology of sexual arousal. J Endocrinol 2005; 186:411–427.
4. Langstrom N, Babchishin K, Fazel S, *et al.* Sexual offending runs in families: a 37-year nationwide study. Intl J Epidemiol 2015; 44:713–720.
5. Georgiadis JR, Kringelbach ML. The human sexual response cycle: brain imaging evidence linking sex to other pleasures. Progress Neurobiol 2012; 98:49–81; 31.
6. Bancroft J; Human sexuality and its problems. Elsevier Health Sciences. Edinburgh 2009; 471–478.
7. Thibaut F, De La Barra F, Gordon H, *et al.*, WFSBP Task Force on Sexual Disorders. The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of paraphilias. World J Biol Psychiatry 2010; 11:604–655.
8. Grubin D. Medical models and interventions in sexual deviance. In: Laws DR, O'Donohue W, editors. Sexual deviancy: theory, assessment and treatment, 2nd ed New York: The Guildford Press; 2008. pp. 594–610.
9. Ward T. Ethical issues in the treatment of sex offenders: addressing the dual relationship problem. In: Wilcox DT, Garrett T, Harkins L, editors. Sex offender treatment: a case study approach to issues and interventions, 1st ed Chichester: Wiley-Blackwell; 2015. pp. 27–45.
10. Andrews DA, Bonta J, Wormith JS. THE RISK-NEED-RESPONSIVITY (RNR) model does adding the good lives model contribute to effective crime prevention? Crim Justice Behav 2011; 38:735–755.
11. Barnao M, Ward T, Robertson P. The good lives model: a new paradigm for forensic mental health. Psychiatry Psychol Law 2015; 1:1–4.
12. Jonson CL, Cullen FT, Lux JL. Creating ideological space. In: Craig LA, Gannon TA, Dixon L, editors. What works in offender rehabilitation: an evidence-based approach to assessment and treatment, 1st ed Chichester: John Wiley and Sons; 2013. pp. 50–68.
13. ■ Schumucker M, Losel F. The effects of sexual offender treatment on recidivism: an international meta-analysis of sound quality evaluations. J Exp Criminol 2015; 11:597–630.

Reports an evaluation of relevant trials including those that may not have been captured by RCT-only reviews.

14. Dennis JA, Khan O, Ferriter M, *et al.* Psychological interventions for adults who have sexually offended or are at risk of offending or are at risk of offending. Cochrane Database System Rev 2012; 12:.
15. Hanson RK, Bourgon G, Helmus L, Hodgson S. The principles of effective correctional treatment also apply to sexual offenders a meta-analysis. Crim Justice Behav 2009; 36:865–891.
16. Lösel F, Schmucker M. The effectiveness of treatment for sexual offenders: a comprehensive meta-analysis. J Exp Criminol 2005; 1:117–146.
17. Hanson RK, Morton-Bourgon KE. The characteristics of persistent sexual offenders: a meta-analysis of recidivism studies. J Consult Clin Psychol 2005; 73:1154–1163.
18. Marshall W, Obrien M. Modifying sexual preferences. In: Beech AR, Leam A, Browne KD, editors. Assessment and treatment of sex offenders: a handbook, 1st ed Chichester: John Wiley; 2009. pp. 311–329.
19. Jordan K, Fromberger P, Stolpmann G, Müller JL. The role of testosterone in sexuality and paraphilia – a neurobiological approach. Part I: Testosterone and sexuality. J Sexual Med 2011; 8:2993–3007.
20. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed Washington, DC: American Psychiatric Association; 1994
21. World Health Organisation. ICD-10 classifications of mental and behavioural disorder: clinical descriptions and diagnostic guidelines. Geneva: World Health Organisation; 1992.
22. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed Washington, DC: American Psychiatric Association; 2013.
23. McManus MA, Hargreaves P, Rainbow L, Alison LJ. Paraphilias: definition, diagnosis and treatment. F1000 Prime Rep 2013; 5:.
24. Beech AR, Miner MH, Thornton D. Paraphilias in the DSM-5. Ann Rev Clin Psychol 2016; doi: 10.1146/annurev-clinpsy-021815-093330. [Epub ahead of print]
25. Balon R. Controversies in the diagnosis and treatment of paraphilias. J Sex Marital Therapy 2013; 39:7–20.
26. Douglas T, Bonte P, Focquaert F, *et al.* Coercion, incarceration. and chemical castration: an argument from autonomy. J Bioethical Inquiry 2013; 10:393–405.
27. European Committee for the Prevention of Torture and Inhuman or Degrading Treatment or Punishment. 2009. Report to the Czech Government on the visit to the Czech Republic carried out by the European Committee for the Prevention of Torture and Inhuman or Degrading Treatment or Punishment (CPT). Strasbourg: The Council of Europe. http://www.cpt.coe.int/documents/cze/2009-08-inf-eng.pdf.
28. Cortoni F, Gannon TA. What works with female sexual offenders. In: Craig LA, Gannon TA, Dixon L, editors. what works in offender rehabilitation: an evidence based approach to assessment and treatment, 1st ed Chichester: Wiley-Blackwell; 2013.
29. Mazzola CR, Mulhall JP. Impact of androgen deprivation therapy on sexual function. Asian J Androl 2012; 14:198–203.
30. Elliott S, Latini DM, Walker LM, *et al.*, and the ADT Survivorship Working Group (2010). Androgen deprivation therapy for prostate cancer: recommendations to improve patient and partner quality of life. J Sexual Med 2010; 7:: ; 2010–2996–3010
31. White ID, Wilson J, Aslet P, *et al.* Development of UK guidance on the management of erectile dysfunction resulting from radical radiotherapy and androgen deprivation therapy for prostate cancer. Intl J Clin Pract 2015; 69:106–123.
32. Sartorius GA, Ly LP, Handelsman DJ. Male sexual function can be maintained without aromatization: randomized placebo-controlled trial of dihydrotestosterone (DHT) in healthy, older men for 24 months. J Sexual Med 2014; 11:2562–2570.
33. Kingston DA, Seto MC, Ahmed AG, *et al.* The role of central and peripheral hormones in sexual and violent recidivism in sex offenders. J Am Acad Psychiatry Law 2012; 40:476–485.
34. Batrinos ML. Testosterone and aggressive behavior in man. Int J Endocrinol Metab 2012; (3):563–568.
35. Studer LH, Aylwin AS, Reddon JR. Testosterone, sexual offense recidivism, and treatment effect among adult male sex offenders. Sex Abuse 2005; 17:171–181.
36. Rajender S, Pandu G, Sharma JD, *et al.* Reduced CAG repeats length in androgen receptor gene is associated with violent criminal behavior. Intl J Legal Med 2008; 122:367–372.

93. Pritchard C, King E. Differential suicide rates in typologies of child sex offenders in a 6-year consecutive cohort of male suicides. Arch Suicide Res 2005; 9:35–43.
94. Jeglic EL, Spada A, Mercado CC. An examination of suicide attempts among incarcerated sex offenders. Sexual Abuse 2013; 25:21–40.
95. Reilly DR, Delva NJ, Hudson RW. Protocols for the use of cyproterone, medroxyprogesterone, and leuprolide in the treatment of paraphilia. Can J Psychiatry 2000; 45:559–563.
96. Gillon R. Philosophical medical ethics. 1st ed Chichester: John Wiley & Sons; 1986; 2.
97. Gillon R. Philosophical medical ethics. 1st ed Chichester: John Wiley & Sons; 1986; 60–92.
98. Sen P, Gordon H, Adshead G, Irons A. Ethical dilemmas in forensic psychiatry: two illustrative cases. J Med Ethics 2007; 33:337–341.
99. Karn A, Kumar B, Ranjan MS. Ethical controversies in forensic psychiatry. Med Sci Recovered 2015; 4:2308–2317.
100. American Academy of Psychiatry and the Law: Ethics Guidelines for the Practice of Forensic Psychiatry. http://www.aapl.org/ethics.htm. [Accessed 15 February 2016.]
101. Vanderzyl KA. Castration as an alternative to incarceration: an impotent approach to the punishment of sex offenders. Illinois Univ Law Rev 1994; 15:107–747.
102. Berlin FS. Risk/benefit ratio of androgen deprivation treatment for sex offenders. J Am Acad Psychiatry Law 2009; 37:59–62.
103. Amelung T, Kuhle LF, Konrad A, *et al.* Androgen deprivation therapy of self-identifying. help-seeking pedophiles in the Dunkelfeld. Intl J Law Psychiatry 2012; 35:176–184.
104. Phillips EA, Rajender A, Douglas T, *et al.* Sex offenders seeking treatment for sexual dysfunction—ethics, medicine, and the law. J Sexual Med 2015; 12:1591–1600.
105. Marshall WL, Marshall LE. The utility of the random controlled trial for evaluating sexual offender treatment: the gold standard or an inappropriate strategy? Sexual Abuse 2007; 19:175–191.
106. Duggan C. The place of evidence in the treatment of sex offenders. Crim Behav Mental Health 2014; 24:153–162.
107. Seto MC, Marques JK, Harris GT, *et al.* Good science and progress in sex offender treatment are intertwined. Sexual Abuse 2008; 20:247–255.
108. General Medical Council, Good Medical Practice, 2013. http://www.gmc-uk.org/guidance/good_medical_practice.asp. [Accessed 1 March 2016.]
109. Browne KD. Working to prevent sexual abuse in the family. In: Beech AR, Leam A, Browne KD, editors. Assessment and treatment of sex offenders: a handbook, 1st ed Chichester: John Wiley; 2009. pp. 491–514.
110. Garcia FD, Delavenne HG, Assumpção AD, Thibaut F. Pharmacologic treatment of sex offenders with paraphilic disorder. Curr Psychiatry Rep 2013; 15:1–6.
111. Saleem R, Kaitiff D, Treasaden I, Vermeulen J. Clinical experience of the use of triptorelin as an antilibidinal medication in a high-security hospital. J Forensic Psychiatry Psychol 2011; 22:243–251.