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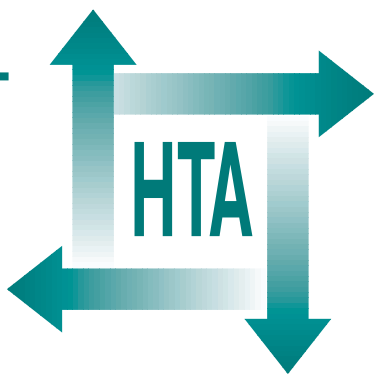
NHS R&D HTA Programme



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Contents

Glossary and list of abbreviations

Technical terms and abbreviations are used throughout this report. The meaning is usually clear from the context, but a glossary is provided for the non-specialist reader. In some cases, usage differs in the literature, but the term has a constant meaning throughout this review.

Glossary

Attrition bias Systematic differences between comparison groups in withdrawals or exclusions of participants from the results of a study. For example, patients may drop out of a study because of side-effects of the intervention. Excluding these patients from the analysis could result in an over-estimate of the effectiveness of the intervention.

Detection bias (ascertainment bias) Systematic differences between comparison groups in how outcomes are ascertained, diagnosed or verified.

Exhibitionism A disorder in which fantasies about or the act of exposing the genitals to an unsuspecting stranger produces sexual excitement with no attempt at further sexual activity with the stranger.

Fetishism (psychiatric) A condition in which inanimate objects are utilised as a preferred or exclusive method of stimulating erotic arousal.

Frotteurism Behaviour that involves touching and rubbing against a non-consenting person. This usually occurs in crowded places where the individual can more easily escape arrest.

Heterogeneity Variability or differences between studies.

Masochism Pleasure derived from being physically or psychologically abused, whether inflicted by oneself or by others. Masochism includes sexual masochism.

Paraphilias Disorders that include recurrent, intense sexually arousing fantasies, sexual urges or behaviours generally involving non-human objects, suffering of oneself or partners or children or other non-consenting partners.

Paedophilia A sexual disorder occurring in a person 16 years or older and that is recurrent with intense sexually arousing fantasies, sexual urges or behaviours involving sexual activity with a pre-pubescent child (aged ≤ 13 years).

Performance bias Systematic differences in the care provided apart from the intervention being evaluated. For example, if patients know they are in the control group they may be more likely to use other forms of care. Patients who know they are in the experimental (intervention) group may experience placebo effects, and care providers may treat patients differently according to what group they are in.

Procuration The act of a person who induces or causes a woman to have illicit sexual intercourse with another person.

Rape Unlawful sexual intercourse without consent of the victim.

Sadism A condition in which there is a derivation of pleasure from inflicting pain, discomfort or humiliation on another person or persons. The sexual significance of sadistic wishes or behaviour may be conscious or unconscious.

Selection bias In assessments of the validity of studies of healthcare interventions, selection bias refers to systematic differences between comparison groups in prognosis or responsiveness to treatment. Random allocation with adequate concealment of allocation protects against selection bias.

Selective serotonin reuptake inhibitors Compounds that specifically inhibit the reuptake of serotonin. This increases the serotonin concentration in the synaptic cleft,

continued

Glossary *contd*

which then activates serotonin receptors to a greater extent. These agents have been used in treatment of depression, panic disorder, obsessive compulsive behaviour and alcoholism as analgesics, and to treat obesity and bulimia.

Sex offences Any violation of established legal or moral codes in respect to sexual behaviour.

Sexual child abuse Sexual maltreatment of a child or minor.

Transvestism Disorder characterised by recurrent, intense sexually arousing fantasies, sexual urges or behaviours involving cross-dressing in a heterosexual male. The fantasies, urges or behaviours cause clinically significant distress or impairment in social, occupational or other areas of functioning.

Voyeurism A paraphilia characterised by repetitive looking at unsuspecting people, usually strangers, who are either naked, in the act of disrobing or engaging in sexual activity as the method for achieving sexual excitement.

List of abbreviations

ATD	average time per day spent in paraphilia or paraphilia-related sexual behaviour
CBA	cost–benefit analysis
CBT	cognitive behavioural therapy
CGI	Clinical Global Impression
CPA	cyproterone acetate
df	degrees of freedom
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders
5-HT	5-hydroxytryptamine
IDD	Inventory to Diagnose Depression
MeSH	medical subject headings of MEDLINE
OCD	obsessive compulsive disorder
RCT	randomised controlled trial
SD	standard deviation
SOI	Sexual Outlet Inventory
SOTP	Sexual Offenders Treatment Programme
SSRI	selective serotonin reuptake inhibitor
TSO	total sexual outlet
YBOCS	Yale–Brown Obsessive Compulsive Scale

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Background

A sex offence is defined as any violation of established legal or moral codes of sexual behaviour. Sex offending can be seen as a major public health problem. According to the UK Home Office, about 1% of all recorded crimes are sexual offences. Of men born in England and Wales in 1953, seven in 1000 have a conviction for a sexual offence against a child by the age of 40 years. Currently, about 7000 sexual offenders have a conviction for a sexual offence with about 4000 residing in prison. However, these figures must be seen as an under-estimate because many sexual assaults go unreported. For those cases that do come to police attention, there is no further action in 56%, only 35% of offenders are charged and < 10% are convicted. Furthermore, men convicted of sexual offences against children claim five or more undetected sexual assaults for which they have never been apprehended or caught. Current estimates from the Prison Service suggest that 15% of those sexual offenders leaving prison are re-convicted for a further sexual offence within 2 years.

The prevalence of sexual offences against children is alarming. The National Society for the Prevention of Cruelty to Children reports that 16% of girls and 7% of boys have been sexually assaulted before the age of 13. In England, the incidence of children aged < 18 years placed on child protection registers for sexual abuse is six in 10,000. Hence, there is an urgent need to assess the effectiveness of treatment strategies for sex offenders.

Current service provision

Programmes for the treatment of sexual offenders take place both in the community (probation service) and in prison within England and Wales. Cognitive behavioural therapy is the standard treatment, however, such programmes typically do not directly target deviant sexual arousal and fantasies reported by many sexual offenders during treatment. Antiandrogens to decrease an offender's general level of arousal are sometimes used as an adjunct to treatment in psychiatric settings (e.g. special hospitals, medium secure units), but are not regularly prescribed outside of these settings due to side-effects. Pharmacological treatment of sex offenders with selective serotonin reuptake inhibitors (SSRIs) has been proposed to have additional beneficial effects, such as reducing the intensity and intrusiveness of fantasies. However, to date, no systematic review of SSRIs for the treatment of sex offenders has been conducted.

Objective

Systematic review of the currently available evidence on the clinical effectiveness and cost–consequences of the use of SSRIs for the treatment of sex offenders.

Methods

For the systematic review of effectiveness, searches of bibliographic databases, including MEDLINE, EMBASE and PsycINFO were conducted up to October 2001, and supplemented by searches of the Internet, recent conference abstracts and the National Criminal Justice Reference System. Enquiries were made to pharmaceutical companies and experts in the field. The inclusion criteria were predefined and allowed a wide range of research designs, including case series. The quality was assessed according to criteria suggested by the Cochrane Collaboration. The analysis was qualitative. The economic analysis consisted of a systematic review of past economic evaluations, collation of information about costs and a cost–consequences analysis. The search for the economic evaluation focused on MEDLINE and the NHS EED.

Results

Number and quality of studies and direction of evidence

The effectiveness review included nine case series. The methodological quality of these was generally poor: only two enrolled consecutive patients, only one was prospective and only two explicitly stated that participants were sex offenders. The length of follow-up was insufficient to assess major long-term consequences on re-offence. Two-thirds of the studies reported some significant changes from baseline in the frequency of masturbation and the

intensity of deviant fantasies. However, the scales used in assessing the outcomes were subjective and the validities not stated. This, together with the openness to bias of the study designs employed, suggested that the results should be approached with caution. Data on adverse events were reported in five of the nine studies, and, although apparently minor, were affected by the same provisos concerning internal and external validity.

Costs and efficiency

The search did not identify any cost-effectiveness studies on SSRI treatment of sex offenders. Three cost–benefit analyses assessed the efficiency of treatment of sex offenders in general, and may provide valuable frameworks for future assessment of the efficiency of SSRI treatment. The main costs associated with SSRI treatment were drug costs, estimated to be a maximum of £750/annum. The optimal duration of treatment was a major source of uncertainty concerning the total cost of SSRI treatment. Considering the main identifiable costs and consequences indicated that assessing the efficiency of SSRIs is overly speculative at present, particularly in the absence of valid information on their effectiveness and the magnitude of any effect on recidivism.

Conclusions

Although SSRIs are an intervention of clear potential importance for the treatment of sex offenders, there is great uncertainty about their effectiveness suggesting that further research should be the main priority.

Need for further research

A double-blind randomised controlled trial needs to be conducted, preferably with several participating centres, comparing existing best treatment plus SSRIs with best treatment plus placebo. Practically, psychometric methods and/or measures of sexual arousal to assess the progress of sexual offenders over at least 2 years may need to be employed. The need to assess the cost-effectiveness of SSRIs should also be anticipated in future research. Decision analytic modelling may contribute directly and help further define information to which estimates of cost-effectiveness are sensitive. Due to the fact that sex offences are not a uniform entity, distinction needs to be made between different types in future research. The relationship between benefit and cost of SSRI treatment may vary considerably.

Chapter 1

Objective and background

Objective of the review

The objective is to systematically review the available evidence on effectiveness, cost and cost-effectiveness of the use of selective serotonin reuptake inhibitors (SSRIs) in the treatment of sex offenders.

Background

Sexual offending has assumed great importance in public consciousness as a result of high profile cases.[1] Public concern has been matched by political and legislative activity in recent years. Several important questions have arisen.

The first is whether sex offenders who have victims should be punished, treated or both. This issue is currently receiving considerable attention from health, welfare and correctional authorities, but is not the main focus of this report. The second important question is which of the available treatments are successful, particularly in terms of reduction in future re-offending. SSRIs are a treatment option about which there is particular debate.

In the early 1990s, there were some reports and case series of treatment of sex offenders with SSRIs. Researchers supporting this type of treatment believe that sexual offenders are somehow related to obsessive repetitive disorders, which are impulsive control disorders. If SSRIs work well on such patients, so too might SSRIs in sex offenders.

A recent systematic review in the Cochrane Library for convicted sexual offenders in which the selection criteria were relevant randomised controlled trials (RCTs), concludes.[2]

> "It is disappointing to find that this area lacks a strong evidence base, particularly in the light of the controversial nature of the treatment and the high levels of interest in the area. The relapse prevention programme did seem to have some effect on violent reoffending but large, well-conducted randomised trials of long duration are essential if the effectiveness or otherwise of these treatments are to be established".

What the Cochrane review did not consider was the use of SSRIs for treatment of sex offenders. One of the authors of this Cochrane review explained that SSRIs were not considered to be one of the recognised treatments that were supported with data from trials at the start of their review in 1997. Therefore, they were not included in their search strategy (Dr Ferriter, Rampton Hospital Authority, UK: personal communication, January 2002).

Given the debate about SSRIs and the lack of a systematic review of their effects, this report was commissioned in July 2001.

Description of the underlying health problem

Nature of sex offences

Sex offences can be defined as any violation of established legal or moral codes with respect to sexual behaviours. These include offences with victims, such as rape, child sexual abuse, paraphilias and exhibitionism, and offences that are not usually associated with victims, such as fetishism, masochism and transvestism. The problem with this definition is that what is considered to be a mental illness, to offend a moral code and to be illegal will vary from place to place and over time and is socially constructed. Thus, intercourse outside marriage is considered a sexual offence in some societies and homosexuality is considered a sexual offence in others.

Rape or indecent sexual assaults are clearly sexual offences, but it becomes more difficult to justifiably classify some other offences, such as voyeurism or indecent exposure of genitals, in the same frame. In practice, a sexual offence as defined by the police differs from the sexual offences defined for sentencing purposes.

The Home Office in the UK attempted to solve the complexity of the definition of sex offenders by a review considering the following classification system.[3]

- General classification schemes – single, comprehensive schemes applicable to all sex

offenders, for example schemes based solely on the type of offences committed.
- Psychometrically derived typologies – based on psychological tests, some of which have been designed specifically for use with sex offenders.
- Psychiatric classification – broad systems that seek to bring uniformity to the debate over classifying abnormal behaviour, including deviant sexual behaviour.
- Physiological/behavioural classification – for example, penile plethysmograph used for measuring sexual arousal.
- Specific classification schemes for child molesters and rapists.

After review of this classification system by various professionals working in the field of sex offending, it was concluded that none of the schemes were useable in the criminal justice context.

Definition used in this report

In the absence of a generally agreed working definition of sex offenders, this report has had to make a decision about what constitutes a sex offence. Without clarity of definition, rigorous search strategies and inclusion/exclusion criteria cannot be constructed. The working definition of sex offence, therefore, used is that employed by the police in England and Wales to officially record notifiable sexual offences.[4] These are set out in *Table 1*.

It should be stated that although the review deals with the effectiveness of SSRIs in sex offences broadly defined, the practical focus was on those sex offences where the consequences on the victims are of greatest public concern – such as rape, indecent assault and gross indecency with a child.

Diagnostic criteria for the main sex offences

In addition to understanding the variation in sex offences as described in law, it is important to understand the distinctions recognised clinically.

Paraphilia

Paraphilias are a sexual deviance defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[5] as recurrent, intense sexual arousing fantasies, sexual urges or behaviours generally involving:

- a non-human object
- the suffering or humiliation of oneself or one's partner

TABLE 1 *Notifiable sex offences recorded by the police in England and Wales*

Sexual offence	Details
Buggery	Intercourse by anum. Sections 12 and 16 of the Sexual Offences Act, 1956 and section 128 (1) of the Mental Health Act, 1959. There is no statutory definition of buggery and, hence, this offence is governed by the common law. In 1967, the Sexual Offences Act provided that a homosexual acting in private between two consenting males was not an offence. In 1994, the age of consent became 18
Indecent assault on a male	Section 15 of the Sexual Offences Act, 1956
Indecent assault between males	Section 13 of the Sexual Offences Act, 1956
Rape	Sections 1 and 7 of the Sexual Offences Act, 1956
Indecent assault on a female	Section 14 of the Sexual Offences Act, 1956
Unlawful sexual intercourse with a girl aged < 13	Section 5 of the Sexual Offences Act, 1956
Unlawful sexual intercourse with a girl aged < 16	Section 16 of the Sexual Offences Act, 1956
Incest	Sections 10 and 11 of the Sexual Offences Act, 1956 and section 54 of the Criminal Law Act, 1977
Procuration	Sections 2, 3 and 4 of the Sexual Offences Act, 1956
Abduction	Section 17 of the Sexual Offences Act, 1956
Bigamy	Section 57 of the Offences Against the Persons Act, 1861
Soliciting or importuning by a man	Section 32 of the Offences Against the Persons Act, 1956
Gross indecency with a child	Section 1 of the Indecency with Children Act, 1960
Indecent exposure	Common law and section 4 of the Vagrancy Act, 1824

- children or other non-consenting persons that occur over a period of at least 6 months.

Penile plethysmography has been used in a research setting to assess an individual's sexual arousal in response to visual and auditory stimuli. The reliability and validity have not been well established.

The named paraphilias in the DSM-IV include exhibitionism, fetishism, paedophilia, sexual masochism, sexual sadism, transvestism, frotteurism and voyeurism. Sadistic or masochistic behaviours may lead to injuries ranging from minor to life threatening. While some paraphilias can be associated with sex offending or strange sexual behaviour, others are not "offences" at all. These present for treatment because of associated distress to personal lives and relationships.

DSM-IV[5] states some associated features and disorders, which can be summarised as such individuals who do not have a consenting partner with whom their fantasies can be met. They employ prostitutes or may act out their fantasies with unwilling victims. When these individuals are caught, they are considered sex offenders. Therefore, those who are convicted represent the tip of the iceberg. Paraphiliacs may select an occupation or undertake volunteer work that brings them into contact with desired stimuli (e.g. selling women's shoes or lingerie or working with children). They may selectively collect photographs and films that focus on their preferred type of stimulus. Many individuals assert that the behaviour causes them no distress and can see their problem only as a reaction of others to their behaviour. Others report guilt, shame and depression at having to engage in unusual sexual activity. Personality disorders are frequent and symptoms of depression may develop and may be accompanied by an increase in the frequency and intensity of the paraphilic behaviour.

Paedophilia

The focus of paedophilia involves sexual activity with a child (aged 13 years or younger). A person with paedophilia must be 16 years or older, who is sexually attracted by children. Diagnostic criteria include:

- recurrent, intense sexually arousing fantasies, sexual urges or behaviours involving sexual activity with a prepubescent child or children over a period of 6 months
- acting on sexual urges or fantasies causing marked distress or interpersonal difficulty
- aged at least 16 years and at least 5 years older than the child or children in the first criterion.

There are similar specific criteria for the other paraphilias – exhibitionism, fetishism sexual masochism, sexual sadism, transvestism, frotteurism and voyeurism.

Consequences of sex offences

The consequences of sex offences clearly depend on the precise nature of the offence in question. For many types of sex offences, the consequences to the victim are serious and the effects apparent many years after the initial event. As each victim's experience of abuse will differ and their response to it will be determined by their own personal resources and perspective on life, a wide range of different long-term effects can be observed. This makes the prediction of trauma associated with sexual offences very difficult. Psychological response patterns[6] among victims are shown in *Box 1*.

The cost–consequences of sex offences are considerable. This is due to:

BOX 1 ***Psychological consequences reported in victims***

Emotional
- Fear
- Anxiety
- Intrusion
- Depression
- Self-esteem disturbances
- Anger
- Guilt and shame

Behavioural
- Aggressive behaviour
- Suicidal behaviour
- Substance abuse
- Impaired social functioning
- Personality disorders

Cognitive
- Perceptual disturbances (such as hallucinations, illusions, flashbacks and dissociation)

Interpersonal
- Sexuality problems
- Relationship problems
- Re-victimisation
- Victim becomes victimiser

Biological
- Psychological hyper-arousal
- Somatic disturbances

- the cost of special educational support functions for victims
- mental health and substance abuse programmes for victims
- Criminal Justice System expenditure and prosecution of offenders
- legal cost for public child care and rehabilitation of family breakdown
- the cost of the Sex Offenders Treatment Programme (SOTP)
- lost days from productive work.

The extent of the problem

Number of sex offences

There were over 5.2 million notifiable offences recorded in England and Wales in a 12-month period between October 1998 and September 1999. Violent crimes for this period accounted for 13% of all offences recorded and 6% of the violent crimes were sexual offences. There were 33,090 reported sexual offences (to the UK Home Office in 1997), and these are stated in *Table 2*.[7] This represents < 1% of all recorded crimes. The figure suggests an approximate incidence rate of reported sexual offences in England and Wales of seven per 10,000 per year.

However, these figures must be seen as an underestimate of the actual numbers of sexual offences committed because many sexual assaults go unreported. For those cases that do come to the attention of the police, there is no further action in 56%; only 35% of offenders are charged and < 10% of sex offenders are convicted.[8] Furthermore, men convicted of sexual offences against children claim five or more undetected sexual assaults for which they have never been apprehended or caught.[9] Therefore, sexual offending can be seen as a major public health problem, not least because current estimates from the Prison Service suggest that 15% of those sexual offenders leaving prison are reconvicted for a further sexual offence within 2 years.[10] *Table 2* indicates the distribution of sex offences by type, showing that rape and indecent assault on a female constituted by far the majority of sex offences notified to the Home Office in 1997.[4]

TABLE 2 *Type of sexual offences reported in 1997 by the UK Home Office*

Offence	Number (%)
Procuration	131 (0.4)
Unlawful sexual intercourse with girls aged < 13	148 (0.5)
Incest	183 (0.6)
Abduction	277 (0.8)
Rape (of men)	347 (1.0)
Indecency between males	520 (1.6)
Buggery	645 (1.9)
Unlawful sexual intercourse with girls aged < 16	1,112 (3.4)
Gross indecency with a child	1,269 (3.8)
Indecent assault on a male	3,503 (10.6)
Rape (of females)	6,281 (19.0)
Indecent assault on a female	18,674 (56.4)
Total	33,090 (100.0)

Number of sex offenders

The number of sex offenders who are in prison in England and Wales has increased steadily over recent years. *Figure 1* shows an upward trend in the UK Home Office figures for sexual offences.[4]

Of men born in England and Wales in 1953, seven in 1000 have a conviction for a sexual offence against a child by the age of 40.[11] Currently, about 7000 sexual offenders have a conviction for a sexual offence with about 4000 offenders residing in prison.[12]

In general, there appears to be a high ratio of reported offences to offenders. Part of the explanation for this is that only a relatively small number of reported offences result in conviction. In a study of 360 reported rape cases, only about 10% resulted in conviction.[13] In addition, convicted offenders may be responsible for more than one reported offence.

The average population in custody during 2000 was 64,600. Excluding offences not recorded and fine defaulters, the main groups of adult male prisoners in mid-2000 were those that had committed violence against a person (22%), drug offences (17%), burglary (16%), sexual offences (11%), robbery (11%), theft and fraud (10%) and other offences (11%). The main groups of adult female prisoners were those that had committed drug offences (39%), theft and fraud (25%), violent and sexual offences (15%), robbery (6%), burglary (6%) and other offences (9%; see *Figure 2*).[14]

Number of victims of sex offences

The prevalence of sexual offences against children alone is alarming. In a survey of students, when

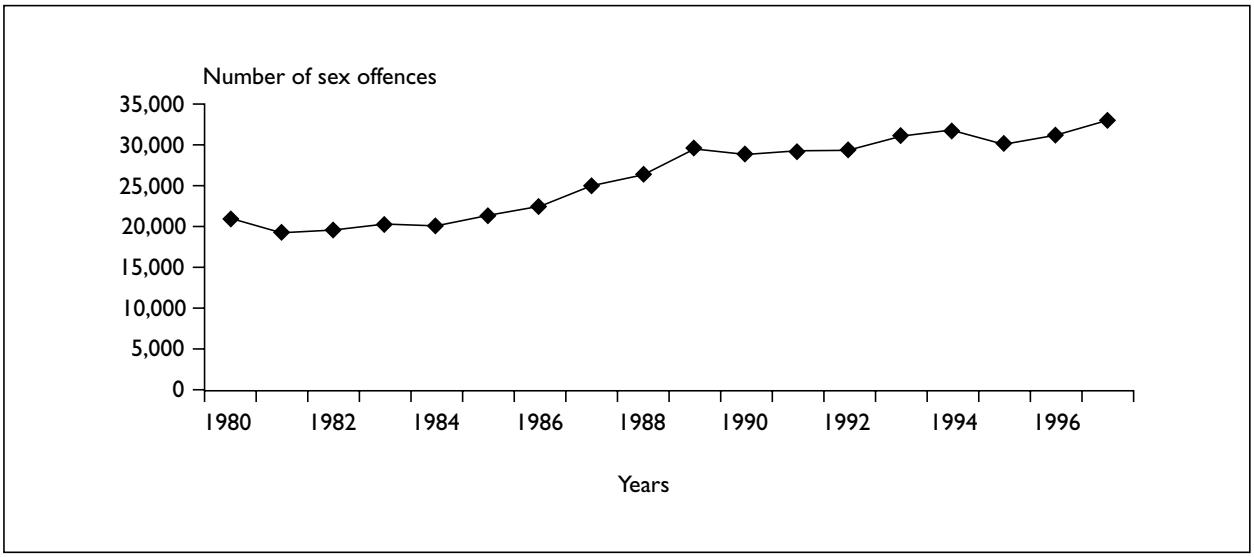

FIGURE 1 *Trend in the number of sex offences over time*

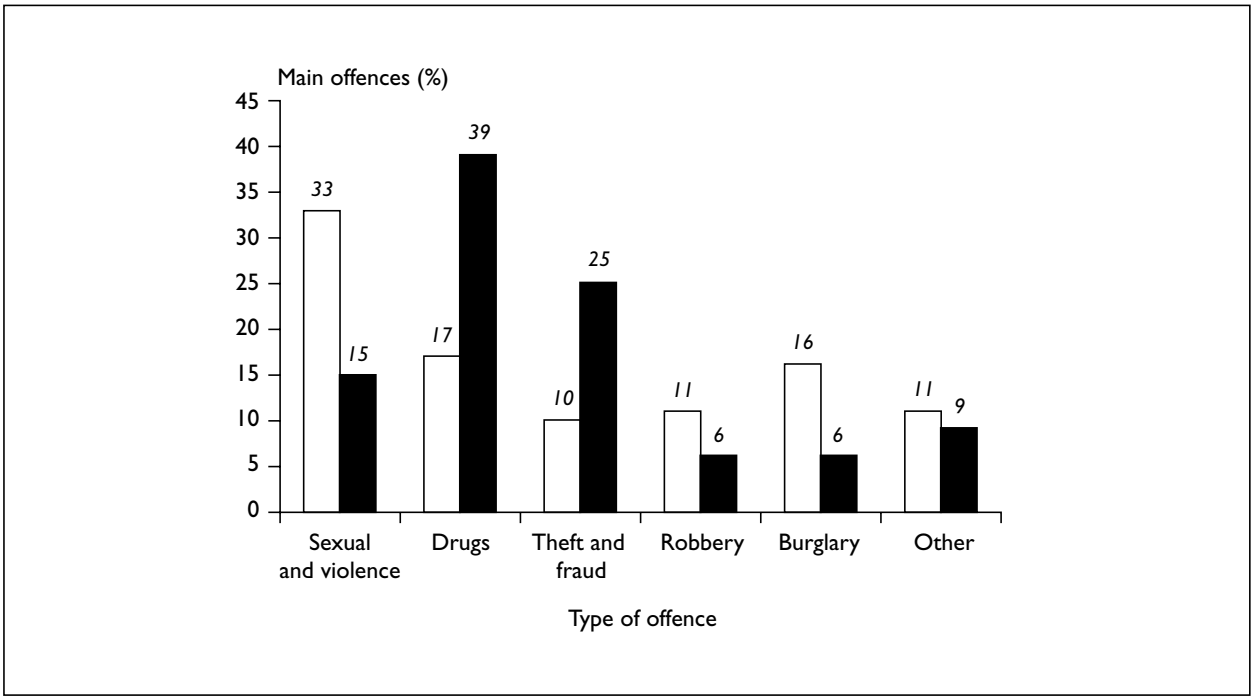

FIGURE 2 *Percentage of the main offences in the prison population reported in 2000 (□, Males; ■, females)*

using the definition of sexual abuse as "any event/interaction that the young person reported as unwanted/abusive before they were 18", a figure of 59% for women and 27% for men was obtained. When the definition was narrowed to "those cases involving some form of penetration or coerced/forced masturbation where the abuser was at least 5 years older", the figure fell to 4% for women and 2% for men.[15] The National Society for the Prevention of Cruelty to Children[16] report stated that 16% of girls and 7% of boys have been sexually assaulted before the age of 13. In England, the incidence of children under 18 years of age placed on child protection registers for sexual abuse is six in every 10,000.[17] Hence, there is an urgent need to assess the effectiveness of treatment strategies for sex offenders.

Profile of sex offenders

Age

Data from the USA[18] suggest that juveniles accounted for 16% of forcible rape arrestees in 1995 and 17% of those arrested for other sex offences. As shown in *Figure 3*, arrestees for rape concentrated

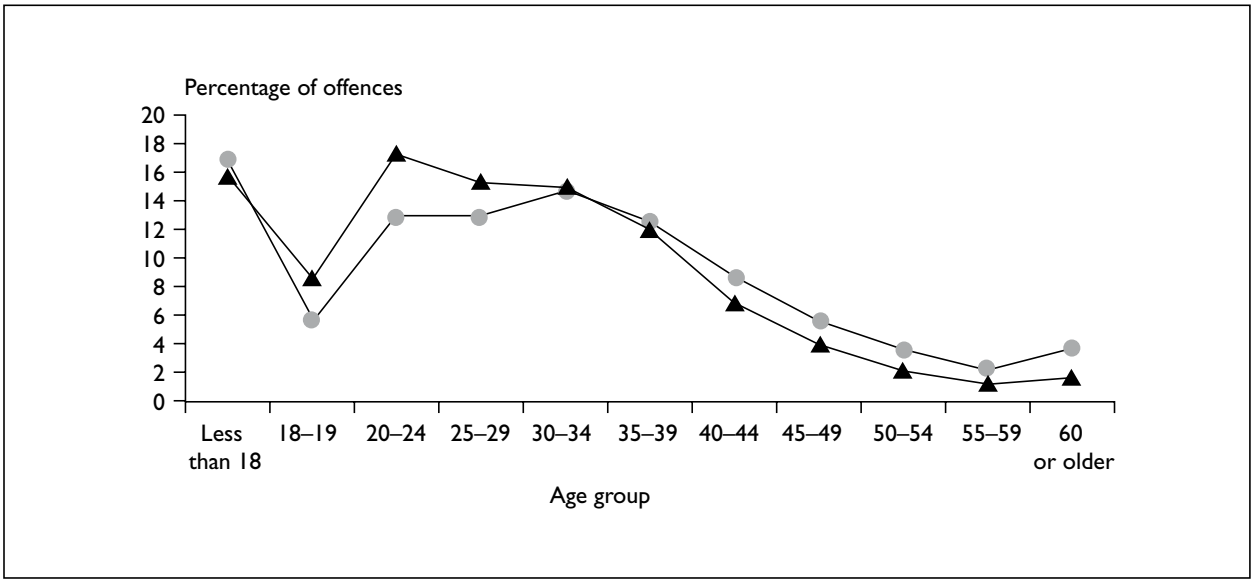

FIGURE 3 *Age of persons arrested for forcible rape and for other sex offences. (▲, Forcible rape; ●, other sex offenses)*

in younger age groups while arrestees for other sex offences were more prevalent among older arrestees.

Race
The racial distribution of arrestees for rape is similar to the racial distribution for all violent arrests.

Victim–offender relationship
For 90% of youngest victims of rape, the offender is someone known to them.

Marital status
Data suggest that 63% are single.

Living situations
Data suggest that 26% of offenders live alone and 9% live with a spouse/partner and children.

Employment status
Data suggest that 88% are unemployed.

Criminal history
Of people for whom information on criminal history was available, 75% had one or more previous convictions. Two-thirds of current and previous offences were of an acquisitive (e.g. theft) or miscellaneous nature (e.g. alcohol-/drug-related) while 23% involved an offence against another person.

Current service provision

General
Legal professionals usually deal with sexual offenders without regard for treating the deviant behaviour. When such offenders are referred to psychiatrists, they are considered as cases of sexual deviations.

The Sex Offenders Act 1997 imposed a registration requirement on newly convicted offenders, those supervised in the community from 1 September 1997, those cautioned and those offenders released from prison on or after that date. The duration of the registration requirement depends on sentence length, type of offence, age of the offender and age and gender of the victim. Offenders are required to keep the police informed of their current address.

SOTP
The SOTP[19,20] began in 1991 as part of a national strategy for the integrated assessment and treatment of sex offenders. The programme essentially serves three purposes: risk assessment, risk management and risk reduction. The length of therapy is 80 hours for short-term treatment and 160 hours for long-term treatment.

Cognitive behavioural therapy (CBT) is the treatment used in the SOTP by both the prison and probation services in the UK. This approach has developed through the combination of both cognitive and behavioural approaches to therapy. See Marshall and colleagues for an overview of the CBT approach.[21] However, to give a brief synopsis, the behavioural component addresses the overt and covert behaviour of an individual and the principles of learning theory. Originally, this was confined to the use of procedures to alter behaviour, that is, rewarding desired

behaviours and punishing unwanted behaviours, but has since broadened out to include modelling (demonstrating a desired behaviour) and skills training (teaching specific skills through behavioural rehearsal). The cognitive component of the CBT approach addresses the thoughts or cognitions that individuals experience, which are known to affect mood state and hence have an influence upon subsequent behaviour. Cognitive therapy, therefore, aims to encourage an individual to think differently about events, thus giving rise to different effects and behaviours. The use of self-instruction and self-monitoring and the development of an awareness of how one thinks affects how one feels and behaves and are vital components in cognitive therapy.

By combining these two approaches, CBT provides a comprehensive approach to treating sex offenders, which now has research evidence to support its efficacy.[22]

Group work is the usual method of delivery of CBT in the UK for sexual offenders. Beech and Fordham[23] outlined the benefits of being in a group and group work.

- Groups provide an environment that can offer both support and challenges to the individual.
- Group work provides the opportunity for discussion with peers.
- Group work provides opportunities for increasing self-esteem and empathic responding.
- Groups offer a forum for support and sharing of problems, which may be a completely new experience for many child sex abusers who are generally isolated individuals, often with interpersonal deficits and feelings of inadequacy.

Having the experience of being valued, being able to help others, practising social skills and getting to know others in detail can greatly improve an individual's self-esteem and interpersonal functioning, given that feelings of inadequacy and lack of appropriate relationships may be an important vulnerability factor for many child sex abusers.

The claimed results of the treatment in the SOTP in which 600 offenders are treated per year are shown in *Table 3*.

Identifying individuals at risk of perpetrating sex offences before the first offence is committed is clearly ideal, but is difficult with our current state of knowledge. Preventing re-offence is the main means of reducing the impact of sex offences on individuals and society at large. Indications of both the impact of sex offences and the potential impact of treatment are provided by recent estimates from the English and Welsh Prison Service.[10]

Although it was found to be important to take into account the level of problems (treatability of an offender), those who were found to have a medium to high level of problems as evidenced by previous offending behaviour were found to recidivate at a lower level if treated than those who had not been treated. *Table 4* compares the

TABLE 3 *Claimed treatment effect in SOTP in relation to deviancy/denial*

Level of deviancy/denial*	Overall treatment effect	Significant reduction in pro-offending attitude
Low deviancy/low denial	59%	84%
Low deviancy/high denial	17%	71%
High deviancy	14%	43%

* *Denial and deviancy are measures of the severity of the disorder and the likelihood of response to treatment, which are measured on specially designed scales*

TABLE 4 *Sexual and/or violent re-conviction rates for treatment and comparison groups by STATIC-99 risk group*

Risk category	Treatment group (% (*n*/*N*))	Comparison group (% (*n*/*N*))
Low	1.9 (5/263)	2.6 (25/969)
Low–medium	2.7 (7/263)	12.7 (83/655)
Medium–high	5.5 (6/109)	13.5 (31/229)
High	26.0 (13/50)	28.1 (16/57)

2-year re-conviction rates for sexual and violent offences between those who had been through the prison SOTP and those who had not. Treatability here is indicated by risk level (low, low–medium, medium–high and high) from a risk prediction instrument known as STATIC-99;[24] the assumption being made that those who are at a higher risk level are those with the most treatment needs.

Table 4 shows that CBT had an impact in the low–medium and medium–high groups. If it were assumed that those who had had treatment had been denied it, then they would have probably re-offended at the same rate as the untreated group. This would mean that, even taking the most conservative estimate of one victim per extra offence, there would have been an extra 48 victims of sexual or violent offences within this 2-year period. Therefore, even over this short period of treatment, the implications in terms of costs to prosecute and incarcerate extra offenders as well as the reductions in the tangible costs to victims of sexual and violent offences can be clearly seen.

Punishment of sex offenders

British legislation concerning sex offenders dates from 1956 and is based on common law. This stipulates that the convicted person must serve half of his sentence in prison and the other half in the community. The length of time spent in prison is important for assessing the treatment given and for the necessary close follow-up before offenders are released into the community. The effectiveness of punishment without treatment is doubted, with the likelihood of re-offence being thought high after release. *Table 5* shows the maximum sentence in the UK.

Medical approach

Chemical castration

The administration of antiandrogen medication is called chemical castration. The effect of antiandrogen is accomplished through the reduction of serum testosterone levels. In the USA, the two most commonly used hormone medications for sexual offenders are medroxyprogesterone acetate and cyproterone acetate (CPA).

A meta-analysis of the effect of treatment on recidivism of sex offenders by Hall[25] and a review by Marshall and colleagues[26] suggest that hormonal treatments were effective treatments for reducing sexual re-offending. Other effects reported were a decrease in erotic fantasy, decreased frequency of erections and orgasms, a reduction in sexual drive and activity and less irritability and aggression.[27]

Side-effects of antiandrogens

There are some potential side-effects of this medication that make it a less desirable option. When given to males, CPA inhibits spermatogenesis, reduces the volume of ejaculate and causes infertility; although these effects are slowly reversible. Gynaecomastia is common and permanent enlargement of the mammary glands may occur. There may be initial sedation and depressive mood changes. Patients may experience alterations in hair pattern, skin reactions, weight changes and anaemia. Osteoporosis may occur rarely. Altered liver function may occur with high doses. There have also been reports of hepatitis, jaundice and, sometimes fatal, hepatic failure developing during CPA therapy but its association with liver cancer is uncertain.[28] Poor compliance is a major problem in prescribing antiandrogens due to the adverse effects and antiandrogens may not be suitable for adolescent sexual offenders.

Surgical approach

Castration

Surgical castration is the removal of the testicles, where most of the male body's testosterone is produced. Due to the facts that testosterone has been implicated in aggression and castration

TABLE 5 *Sentences for sex offences*

Offence	Maximum sentence
Indecent assault	10 years
Rape of woman or man	Life imprisonment
Incest by females	7 years
Incest by males	7 years (unless the victim is aged < 13, which incurs a life sentence)
Buggery of child aged < 16 years	Life imprisonment
Buggery of child aged > 16 but < 18 years	5 years
Sexual intercourse with mentally impaired person	2 years

causes a drastic reduction in the amount of circulating testosterone, it is assumed that castration reduces aggression, thereby reducing sexual offending. Moreover, Bradford[29] reviewed a series of studies and concluded that there was sufficient evidence to support the debate that castration reduces sexual recidivism.

Although, in the past, testicle removal was the principle treatment for sexual deviates in Europe, it has now been abandoned in most Western countries due to ethical considerations.

Psychosurgery

Some research has suggested that structural brain abnormalities play a substantial role in sexual offending.[30] Most commonly, structures and functions associated with the temporal lobes of the brain are linked with sexual behaviour.[31] Psychosurgery has rarely been employed since it cannot be approved on ethical grounds because its value in the treatment of sex offenders remains questionable.

Relapse prevention

This type of treatment concerns the ability of an individual to identify risk situations and to have developed effective coping strategies to deal with such situations. Although it may be that if an individual has successfully addressed the deficits he has had in the offence-specific and social adequacy areas his risk of recidivism is very low, the reality for most offenders is that their progress is not sufficient in these areas for them not to benefit from relapse prevention work. Relapse prevention raises an individual's awareness of the variety of situations, thoughts and feelings, which are risky for them and could act as "warning signs" for future problems, and teaches them the skills to deal appropriately with these risky situations. Recent work on relapse prevention has highlighted the different pathways (approach and avoidance) to relapse for different individuals which have implications for treatment.[32] The approach pathway concerns individuals who are motivated to offend and require work on the negative consequences to themselves of offending, while the avoidant pathway concerns individuals who are motivated not to offend but do so because they lack the skills to successfully avoid and cope safely with risky situations. For this group, treatment should be about teaching appropriate skills. The approach pathway offenders are high deviancy men while avoidant pathway offenders are low deviancy men (Dr Beech, University of Birmingham, Birmingham: personal communication 2002).

Proposed intervention – SSRIs

Pharmacological effects

The sources for this section were formularies and textbooks.[28,33,34] Serotonin (5-hydroxytryptamine (5-HT)) is an important chemical that helps transmit nerve impulses from one nerve cell to the next. As SSRIs **selectively** inhibit the re-uptake of serotonin, they are termed SSRIs to contrast them with agents that inhibit the re-uptake of serotonin as part of a much more widespread effect on neurotransmitters.

In the human brain, serotonin-containing neurons are highly localised in specific clusters in the brainstem and spinal cord. From these sites, the cells send out axons that end in serotonin-containing terminals, which innervate the diverse areas throughout the brain, including spinothalamic pain fibres, the brainstem, the cerebellum, the hypothalamus, basal ganglia and the neocortex.[35]

This anatomy explains why serotonin is implicated in so many brain functions, including pain perception, sleep, thermal regulation, appetite, gut regulation, balance, reproductive function, motor function, higher cognitive function and sensory interpretation.

Given these diverse responsibilities, dysfunction of serotonin neurons have been implicated in a wide variety of diseases, including major depression. For the same reason, serotonin-active drugs can have many different clinical effects by virtue of their physiological effects on diverse brain regions. This anatomy explains why even selective drugs, such as SSRIs, can produce many diverse clinical effects (e.g. nausea, a feeling of incoordination, suppression of rapid eye movement sleep, decreased libido and akathisia) as well as being useful in such apparently disparate disorders as major depression, anxiety disorders, pain disorders and premature ejaculation. While SSRIs are selective in terms of affecting the neuronal uptake pump for serotonin, this action affects a multitude of specific postsynaptic serotonin receptors (e.g. 5-HT1A, 5-HT1D, 5-HT2A, 5-HT2C and 5-HT3), which, in turn, affects a multitude of neural systems.[36]

On the basis of the above, the main therapeutic indications for SSRIs so far are depression, obsessive compulsive disorder (OCD) and bulimia nervosa.

Rationale for using SSRIs in sex offenders

As already stated, one of the key reasons for believing SSRIs might be effective in treatment of sex offenders is the similarity between sex offences and OCD.[37] In addition, the high prevalence of sexual dysfunction has been noted in patients taking SSRIs in other settings, with highly significant results for impact on libido, arousal, time from arousal to orgasm, intensity of orgasm and duration of orgasm.[38] Observations like this raised the possibility that SSRIs might ameliorate paraphilia with fewer side-effects than chemical castration, and, in turn, improve the likelihood of long-term compliance. Enhancing central serotonin activity in the hypothalamus may inhibit sexual behaviour in some male mammalian species.[39] Mood and impulsive disorders may be mitigated by the use of SSRIs.[40,41]

Detailed information about SSRIs

There are a number of pharmaceutical products that are given the name of SSRIs, as indicated in *Box 2*. The costs of the drugs vary according to preparation, and the implications of this on annual costs are considered in detail in the Results – collation of information on costs section. Annual costs range from approximately £100–800 depending on the preparation and dose.

BOX 2 ***SSRI preparations***

Pharmacological term	Marketing names
Citalopram hydrobromide	Cipramil (UK), Seropram (Switzerland)
Fluoxetine hydrochloride	Prozac (UK, USA, Canada)
Fluvoxamine maleate	Faverin (UK), Luvox (USA, Canada)
Paroxetine hydrochloride	Seroxat (UK), Paxil (USA, Canada)
Sertraline hydrochloride	Lustral (UK), Zoloft (USA)

SSRIs should be used with caution in patients with epilepsy (avoided if poorly controlled and discontinued if convulsions develop), patients receiving concurrent electroconvulsive therapy (prolonged seizures have been reported with fluoxetine), patients with a history of mania, cardiac disease, diabetes mellitus, a history of bleeding disorders, hepatic and renal impairment and patients who are pregnant or breastfeeding. SSRIs may also impair performance of skilled tasks, such as driving.

An SSRI or related antidepressant should not be started until 2 weeks after stopping a monoamine oxidase inhibitor. Conversely, a monoamine oxidase inhibitor should not be started until at least 1 week after an SSRI or related antidepressant has been stopped (2 weeks in the case of paroxetine and sertraline and at least 5 weeks in the case of fluoxetine).

SSRIs have fewer sedative, antimuscarinic and cardiotoxic effects than tricyclic antidepressants. Side-effects of the SSRIs include gastrointestinal effects (dose-related and fairly common effects include nausea, vomiting, dyspepsia, abdominal pain, diarrhoea and constipation), anorexia with weight loss (increased appetite and weight gain are also reported with citalopram) and hypersensitivity reactions, including rash (discontinuation should be considered in such cases because it may be a sign of impending serious systemic reaction, possibly associated with vasculitis), urticaria, angioedema, anaphylaxis, arthralgia, myalgia and photosensitivity. Other side-effects include dry mouth, nervousness, anxiety, headache, insomnia, tremor, dizziness, asthenia, hallucinations, drowsiness, convulsions, galactorrhoea, sexual dysfunction, sweating, hypomania or mania movement disorders and dyskinesias, hyponatraemia (which may be due to inappropriate antidiuretic hormone secretion). SSRIs should not be used if the patient enters a manic phase and hypersensitivity to the SSRI.

The duration of treatment in sex offenders is highly uncertain in the apparent absence of a long-term study of effectiveness, and there are currently no guidelines about the length of time that SSRIs should be taken. In the intended setting in which SSRIs are likely to be administered (prison or community), no special personnel/facilities appear to be required.

Discontinuation syndromes with SSRIs

Studies designed to assess discontinuation syndromes with SSRIs reported rates of about 20% or more.[42,43] Typically, symptoms begin within 24–72 hours of stopping the treatment and last 1–2 weeks, but occasionally much longer.[44] The most commonly reported symptoms were anxiety, paraesthesia, shock-like sensation, balance problems, tremor, seating, insomnia and nightmares.[43,45]

Practical issues

Much of CBT of sex offenders takes place within the Home Office jurisdiction (i.e Probation

Services or Prison Service). Therefore, SSRI treatment in conjunction with CBT would need to be integrated with NHS provision. There are two possibilities: the court requesting the sex offender's general practitioner to prescribe SSRIs while the client attends a community CBT programme, or, alternatively, sex offenders sentenced to a prison term would be prescribed SSRIs by the prison medical service while attending the prison CBT programme.

Difficulties assessing the effectiveness of treatments for sex offences

Irrespective of the intervention in question, certain difficulties about measuring effects and effectiveness of treatments for sex offences must be considered. The key issue explored is what outcome measures should be employed.

Recidivism data

Marshall and Barbaree[46] found that treated offenders had less re-convictions than non-treated offenders both at 2-year (5.5 and 12.5%, respectively) and 4-year follow-up (25 and 64%, respectively). Their figures at 4 years were much higher than those found in other studies for sex offenders in general. Hanson and Bussiere[47] showed a re-conviction rate for sexual offences of 13%, with incest offenders lower (4%) than boy victim paedophiles (21%). Similarly in the UK, only 10–15% of sex offenders were re-convicted within 2–4 years, which is, in fact, lower than most other criminal offences.[48] Furthermore, re-conviction rates for untreated sexual offenders have been found to double (from 11 to 22%) after 5 years[49] and some sex offenders have not been re-convicted until 20 years after release from prison.[50]

Some authors argue that treatment effectiveness by reduced recidivism rate is an insensitive outcome.[51] This is because of low conviction rates relative to alleged offences. Furthermore, it has been estimated that to detect a 5% difference in re-conviction rate, a minimum sample size of each group (case and control) would be 800 participants.[52] This sample size is difficult to recruit in any trial in practice.

Psychometric scales

As an alternative to measuring recidivism directly, much research has focused on psychometric tests administered before and after treatment designed to measure changes in four key areas.[19]

Admittance/denial of sexual interests and behaviours (primary treatment target)

Scales are used to measure the offender's readiness to admit to sexual fantasising and manipulations of victims, the offender's readiness to deny their offending behaviours and harm done to victims and the level of deviant and non-deviant sexual drives and interests.

Pro-offending attitude (primary treatment target)

Scales are used to measure distorted thoughts about sexual contact with children and their sexuality (cognitive distortion), the level of denial of the impact that sexual abuse has on the offender's own victim (victim distortion) and the justification used to excuse the offender's sexual deviance.

Relapse prevention skills (primary treatment target)

These measure the offender's ability to recognise situations where there is a risk of re-offending, the offender's ability to generate effective strategies to get out of such potential risk situations and their ability to recognise that they are still a potential offender even after treatment.

Social competence (secondary treatment target)

These scales cover self-esteem, emotional loneliness, under-assertiveness and inability to deal with negative emotions.

In contrast to rates of recidivism, psychometric scales have the advantage of practicality. Further measuring effectiveness does not necessitate exposure of the community at large to offenders who may still pose a risk. Unfortunately, that recidivism is the key outcome of interest is undeniable, both in terms of the disastrous effects on victims that repeat offending represents and the high financial costs to society of continuing custody. Thus, acceptance of psychometric tests as a valid outcome implies that they act as a proxy for recidivism. Unfortunately, it is unclear just how good a proxy for repeat offending they are.

Any scale should be repeatable and sufficiently objective to give similar results for different observers.

Data on sexual arousal

Given the nature of sex offences, reduction in sexual arousal may be another important outcome measure, for example, decreased masturbation

rate, changes in fantasies and improved relations with partners. However, the validity of the outcome measures taken from self-report data is questionable and they are open to manipulation. Nevertheless, in combination with other measures they may be of some value.

Chapter 2

Effectiveness

Methods

General

The report adhered to advice and guidance provided by the National Coordinating Centre for Health Technology Assessment, the NHS Centre for Reviews and Dissemination and the Birmingham Technology Assessment Group. It was undertaken in accordance with a pre-defined protocol from which there were no major departures. Some minor modifications to inclusion/exclusion criteria were made as indicated below.

Objectives

There were two objectives for this component of the health technology assessment.

- To identify trials published, unpublished or ongoing, reporting the use of SSRIs in the treatment of sex offenders. If no trials were identified, the best available evidence would be sought.
- To systematically review the available evidence of effectiveness and beneficial and harmful effects of SSRIs in treating sex offenders in the identified studies.

Searches

The following sources were searched.

- Electronic databases: Cochrane Library, MEDLINE, EMBASE, PsycINFO and National Research Register. Science Citation Index was searched but an overwhelming number of hits were given, therefore, Science Citation Index was searched for the year 2000 in order to estimate the likely number of additional relevant references. The search identified no more relevant articles (from Science Citation Index) than were already known from MEDLINE and EMBASE.
- National Criminal Justice Reference System (USA).
- Internet search engines.
- Citation lists of included studies.
- Conference abstracts (VIII International Society of Prevention of Child Abuse and Neglect; European Conference on Child Abuse and Neglect 2001; Association for the Treatment of Sexual Abusers 2001; British Association for Study and Prevention of Child Abuse and Neglect Congress 2000).
- Enquiry to pharmaceutical companies for any information or research about the use of SSRIs for the treatment of sex offenders (Pfizer, Eli-Lilly, Lundbeck, Solvay and SmithKline Beecham).
- Enquiry to experts in the field. The following professionals were contacted and asked to provide any relevant references they were aware of regarding any published or ongoing trials or unpublished work: Dr MP Kafka, Dr JMW Bradford, Dr M Ferriter, Professor D Grubin, Dr E Coleman, Professor KD Browne and Dr AR Beech.

For databases, a high sensitivity search strategy designed by an information specialist (AF-S) was adopted. The search terms included both MeSH (medical subject headings) and keywords. All known products of SSRIs, and generic or trade names were searched. The search targeted terms in the title, abstract, registry number word or MeSH. Further details of the specific search strategies employed for MEDLINE, EMBASE, Cochrane Library, PsycINFO and Science Citation Index are provided in appendix 1. Searches were generally conducted up to October 2001. No language restrictions were operated.

Inclusion criteria

Studies identified in the search above were included in the review of effectiveness if they met the following criteria.

Population

Men or women, with or without mental illnesses, who exhibited sexual behaviour that is illegal under current UK law, including paedophilia, rape, exhibitionism and sexual assault on adults or children.

Intervention

Any SSRIs currently available.

Comparator

Any, including no treatment.

Outcomes

Rate of recidivism, level of aggressiveness, reduction in sex drive measured by any available scale, death (suicide or other causes) and penile plethysmography (measure of erection in response to fantasies or photograph and video) were considered. Studies that used any outcomes directly or indirectly related to sexual behaviour outcomes were considered.

Design

Ideally, only RCTs would have been included, however, as indicated in the protocol, because the scoping search did not identify any RCTs, other studies that reported the use of SSRIs in sex offenders were included, such as cohort studies or case series.

Exclusion criteria

- Studies that only considered short-term follow-up. Follow-up should have exceeded the minimally adequate period of 2 years as suggested by the UK Home Office.
- Studies using compound drugs, such as cianoproamine (a tricyclic compound that selectively inhibits the reuptake of serotonin), and other drug treatments that inhibit both the reuptake of serotonin and noradrenaline.
- Studies that did not report losses to follow-up, or had a rate of loss to follow-up of > 25%.
- Individual case reports.
- Duplication; when several series emerged chronologically from the same source, only the largest and most recent series was included.
- There was no exclusion on the basis of language.

The first criterion above regarding 2-year follow-up had to be abandoned because there were no follow-ups of 2 years in any of the included studies. The third criterion above about loss to follow-up had to be abandoned because of the lack of data in the included studies regarding the length of follow-up.

Initial inclusion/exclusion decisions on the basis of titles and abstracts were made by one reviewer (YA). All potentially included studies identified from this process were assessed independently by two reviewers (YA and DA) using the full version of the article. Any discrepancies were resolved by consensus.

Quality assessment strategy

If RCTs had been identified, they would have been assessed using the widely recognised Jadad checklist. In the event, all the identified studies were case series making the Jadad checklist an inappropriate tool for systematically identifying key threats to validity in the included studies.

Several checklists have been suggested to assess the quality of case series.[53,54] These were considered by an internal methods group (see 'Acknowledgements') to make an assessment of which checklist might be most appropriate to the type of included study envisaged, taking particular account of the nature of the problem being investigated. On this basis, the generic framework suggested by the Cochrane Collaboration was felt to be the most appropriate. This assesses openness to bias in four general areas: selection, performance, detection and attrition.

To these were added three further specific questions.

- Was the study prospectively conducted?
- Was the study a consecutive series?
- Were characteristics of the cases described prior to the intervention?

Using this framework, quality was assessed and recorded by one reviewer (YA).

Data abstraction and analysis

Data was abstracted independently by two reviewers (YA and DA) in relation to a predefined proforma. Analysis was primarily qualitative, that is, conclusions were based on patterns revealed in clearly tabulated characteristics and results of included studies. Quantitative analysis (meta-analysis) was not employed.

Results

Quantity of research identified

The number of potentially relevant studies identified and screened for retrieval was 130 studies. Of these, 78 studies were excluded by screening the titles and abstracts. If there was any doubt about the eligibility of the study, a hard copy was ordered.

Thus, 52 studies were carefully scrutinised by two reviewers independently. Only nine of these were included.[55–63] There was no disagreement about this between the two reviewers. The reasons for exclusions of the 43 studies are given in appendix 2. The main reasons were that the studies were reviews (but not employing systematic methods), discussed interventions other than SSRIs or restricted comments to the theoretical grounds for the likely effectiveness of SSRIs. *Figure 4* shows

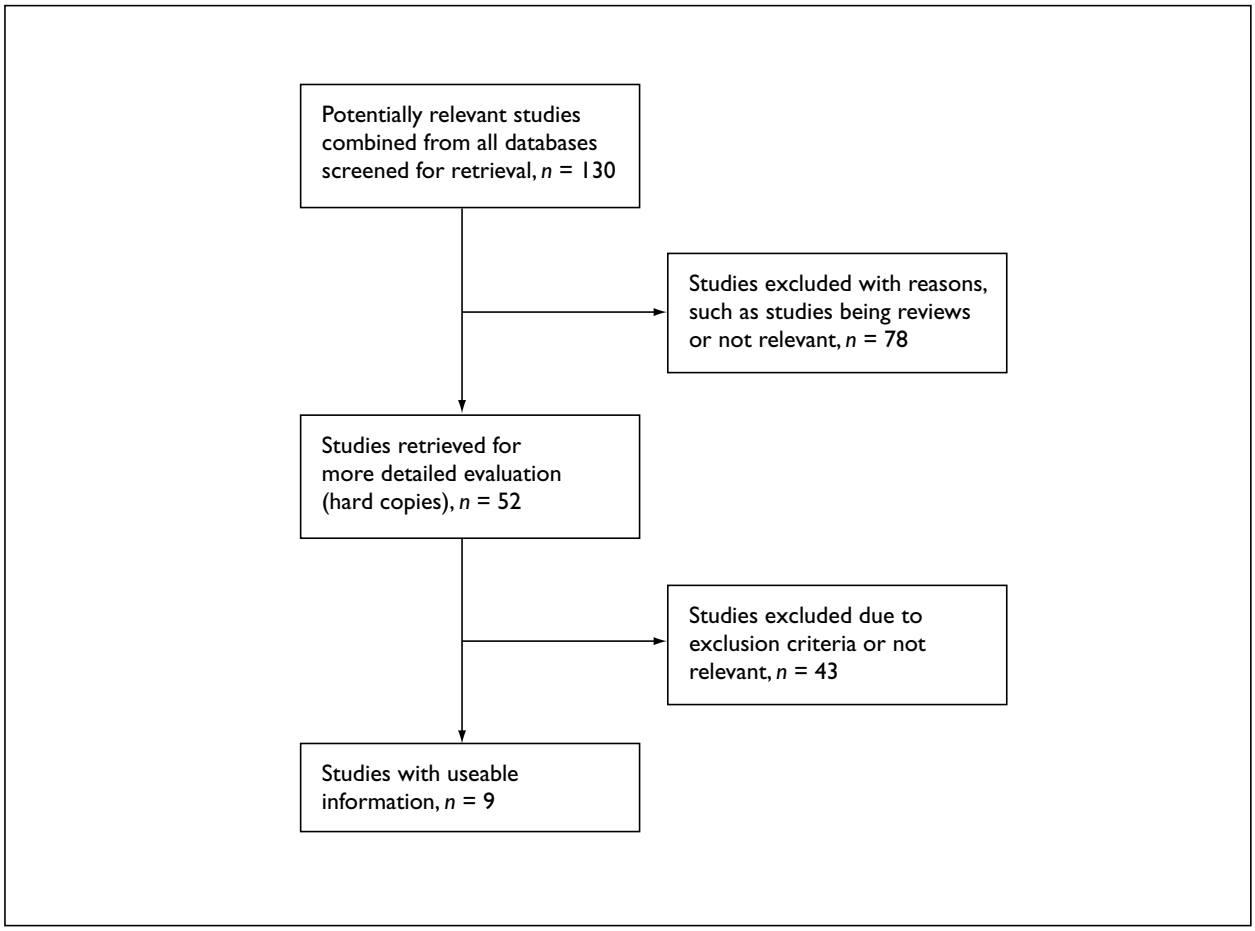

FIGURE 4 *Flow-chart of included and excluded studies*

a flow-chart of the process that led to the nine included studies.

Nature and quality of the included studies

The full data abstracted from each of the nine included studies are provided in appendices 3–6. The following text and tables focus on the data of greatest pertinence.

Table 5 shows the nature of the included studies. All were case series and relied on within-subjects pre–post comparisons. All were conducted in the USA. All were small by the standards of research in other areas, with only two studies exceeding 50 subjects. The total number of subjects included was 225, and thus represented only a tiny percentage of all those who were likely to have been convicted for sex offences since the first study in 1991. The subjects included represented a very wide range of sex offences, including offences of particular concern, such as paedophilia. However, it is also clear that a substantial proportion of subjects may not have actually been offenders, which compromises the external validity of the results in relation to the research question this report attempted to address. The studies assessed the effects of a number of the available SSRIs, particularly fluoxetine and sertraline. Outcomes were universally psychometric measures whose change was generally examined in the short term. Only one study conducted follow-up beyond 1 year for individuals recorded between 1988–1991, but the length of follow-up for each case was not clear.[55] Unfortunately, this was also the second smallest study with just 11 patients. There did not appear to have been any attempt to directly assess the impact of SSRIs on recidivism.

Table 6 summarises the results of our assessment of the quality of the nine included studies. It emphasises that all were very vulnerable to bias and that the internal validity of their results was compromised in consequence. A key source of openness to bias arose from the absence of parallel control groups. Without this, even though most of the included case series did employ pretreatment measures to provide some sort of control, any change observed could not be wholly attributed to SSRI treatment, as a component of any change may have been expected as part of the natural

TABLE 6 *Characteristics of included studies*

Study	*N*	Condition(s) (number)	Intervention	Outcomes
Perlistein *et al.*, 1991[56] (USA)	3	Paedophilia (1); exhibitionism (1); voyeurism/frotteurism (1)	Fluoxetine	Intensity of fantasy; frequency of masturbation
Stein *et al.*, 1992[57] (USA)	13	Paraphilias (5); non-paraphilic sexual addiction (5); sexual obsessions and compulsions (3)	Mostly fluoxetine	Change in fantasies in response to treatment
Kafka and Prentky, 1992[58] (USA)	20	Not offenders Paraphilias (10); non-paraphilic sexual addictions (10)	Fluoxetine	Depression; TSO; masturbation; other sexual activity; sexual desire intensity; total sexual interest ratio
Coleman *et al.*, 1992[55] (USA)	11	Sex offenders (paraphilias) Paedophilias (6); exhibitionism (2); voyeurism (3)	Fluoxetine	Depression; obsession; compulsion
Kafka, 1994[59] (USA)	24	Cases not explicitly stated as offenders Paraphilias (13); non-paraphilic-related disorders (11)	Sertraline ± fluoxetine	Depression; total sexual activity; ATD; percentage improvement from baseline measures
Bradford, 1995[60] (USA)	19	Paedophilia (19)	Sertraline	Fantasy; sexual activity; obsession; masturbation
Fedoroff, 1995[61] (Canada)	51	Paraphilic sex offenders (51) taken from a consecutive sample of 100	Fluoxetine + psychotherapy	Improvement or change in paraphilic symptoms
Greenberg *et al.*, 1996[62] (Canada)	58	Offending history not stated Paraphilias (58; 74% paedophilia)	Fluoxetine; sertraline	CGI; frequency and severity of sexual fantasies
Kafka and Hennen, 2000[63] (USA)	26	Not offenders Paraphilias (14); non-paraphilia-related disorders (12)	Fluoxetine; sertraline; paroxetine; fluvoxamine	Change of sexual behaviour

history of the condition, as an effect of coincidental treatment or as a direct consequence of the research process (repeated administration of the same psychometric measures). Further, absence of any control group made assessment of outcome independent of knowledge of treatment status impossible, again probably biasing assessments towards favourable outcomes.

Loss to follow-up was also a threat to validity, with all but one study[59] either not stating their loss to follow-up or having losses considerably in excess of 10%. Failure to account for all those originally included in a piece of research is a potential concern, as failure to complete a planned period of observation may be associated with adverse events arising from treatment or particularly poor treatment outcomes.

Finally, few studies provided sufficient information to indicate that the subjects included were typical of those seen by particular institutions. In particular, only one study appeared to have been planned prospectively;[63] only two studies stated that subjects were taken consecutively;[58,61] and few studies gave sufficient baseline characteristics to make a judgement on whether subjects were typical or atypical. *Table 7* shows the main potential biases in the included studies.

Results of the included studies

Table 8 provides a brief summary of the main results of the included studies. Most of the studies appeared to show improvements, many statistically significant, in a wide range of psychometric measures, including the Clinical Global Impression (CGI) change score for

TABLE 7 *Quality and threats to internal validity in included studies*

Study	Selection/performance	Detection	Attrition	Prospective	Consecutive	Minimum baseline characteristics
Perlistein *et al.*, 1991[56]	No parallel control group	No blinding	Not stated	Not stated	Not stated	Not sufficient
Stein *et al.*, 1992[57]	No parallel control group	No blinding	Not stated	Retrospective	Not stated	Not sufficient
Kafka and Prentky, 1992[58]	No parallel control group	No blinding	20% lost to follow-up	Not stated	Yes	Sufficient
Coleman *et al.*, 1992[55]	No parallel control group	No blinding	19% lost to follow-up	Retrospective	Not stated	Not sufficient
Kafka, 1994[59]	No parallel control group	No blinding	8% lost to follow-up	Not stated	Not stated	Sufficient
Bradford, 1995[60]	No parallel control group	No blinding	16% lost to follow-up	Not stated	Not stated	Not sufficient
Fedoroff, 1995[61]	No parallel control group	No blinding	Not stated	Retrospective	Yes	Not sufficient
Greenberg *et al.*, 1996[62]	No parallel control group	No blinding	30% lost to follow-up	Retrospective	Not stated	Not sufficient
Kafka and Hennen, 2000[63]	No parallel control group	No blinding	19% lost to follow-up	Yes	Not stated	Sufficient

TABLE 8 *Results of included studies*

Study	*N*	Intervention	Outcomes	General effect
Perlistein *et al.*, 1991[56]	3	Fluoxetine	Intensity of fantasy; frequency of masturbation	3/3 reported improvements
Stein *et al.*, 1992[57]	13	Mostly fluoxetine	Change in fantasies in response to treatment	3/13 reported improvements
Kafka and Prentky, 1992[58]	20	Fluoxetine	Depression; TSO; masturbation; other sexual activity; sexual desire intensity; total sexual interest ratio	Significant difference in depression and unconventional sexual behaviour (pre–posttreatment)
Coleman *et al.*, 1992[55]	11	Fluoxetine	Depression; obsession; compulsion	Statistical improvements in all scores for depression, anxiety, compulsion and obsession. The qualitative response statements were also positive
Kafka, 1994[59]	24	Sertraline ± fluoxetine	Depression; total sexual activity; ATD; percentage improvement from baseline measures	Overall, 17/24 treated with sertraline ± fluoxetine for ≥ 4 weeks sustained a clinically significant response in unconventional sexual behaviour for TSO
Bradford, 1995[60]	19	Sertraline	Fantasy; sexual activity; obsession; masturbation	Marked improvements detected by different outcome measures
Fedoroff, 1995[61]	51	Fluoxetine + psychotherapy	Improvement or changes in paraphilic symptoms	49 reported no current paraphilic symptoms at the time of assessment (unclear how long the treatment was). These individuals have traditionally been classified as "deniers"
Greenberg *et al.*, 1996[62]	58	Fluoxetine; sertraline	CGI; frequency and severity of sexual fantasies	Significant improvement on the CGI scale and severity in fantasy reduced
Kafka and Hennen, 2000[63]	26	Fluoxetine; sertraline; paroxetine; fluvoxamine	Change of sexual behaviour	Significant decrease in TSO and a significant decrease in ATD

sexual fantasy, the Inventory to Diagnose Depression (IDD), the Sexual Outlet Inventory (SOI) for sexual activity, the Hamilton anxiety and depression scales, the Beck Depression Inventory, the Yale–Brown Obsessive Compulsive Scale (YBOCS), total sexual outlet (TSO), the average time spent in unconventional desires (ATD), the Greenberg scores, sexual activity, penile tumescence and the Sexual Fantasy Scale. Although many of the scales used are well established, many are not and there appears to be little evidence establishing their validity, particularly whether the measures are predictive of a reduced likelihood of re-offending.

Adverse effects were stated in only five of the nine studies.[56,57,59,60,62] Other studies did not report adverse effects. It is possible that there were side-effects that were not reported, and it is also possible that it is not easy to document all events in retrospective studies. The main reported side-effects were (numbers taken from the individual studies and not combined events):

- delayed ejaculation (8/58)[62]
- less interest in sexual intercourse with a partner (1/3)[56]
- worsening of sexual symptoms reported (1/13)[57]
- impotence (1/13)[57]
- gastrointestinal distress (3/24)[59]
- sexual dysfunction (3/24)[59]
- increased depression (2/24)[59]
- headache (9/19)[60]
- insomnia (8/58)[62]
- blurred vision (2/58).[62]

There is no data to support that such adverse effects, particularly on sexual function, are the results of treatment itself or part of the pre-existing disorders, for example, depression. It is, therefore, important to establish baseline data of sexual functioning for each patient to accurately assess changes during treatment.

It was not clear from the data whether the adverse effects were serious enough to stop the treatment. It was not known from the studies the percentage of participants who withdrew due to adverse effects.

Summary and conclusions of evidence on effectiveness

All the included case series reported improvements of some sort following the intervention of SSRIs, with the exception of the study by Stein and colleagues[57] in which only three of 13 showed some improvements. Of the eight studies showing benefit, six demonstrated some differences that were statistically significant.[55,58–60,62,63]

However, against this apparently clear weight of evidence favouring use of SSRIs, the following need to be considered.

- The internal validity of the included studies was weak.
- The generalisability of the results to populations of particular interest was debatable.
- The clinical importance of the outcomes for which benefit has been demonstrated was uncertain, and, in particular, whether the effects claimed provided sufficient evidence for an effect on recidivism.
- The nature and impact of adverse events, particularly on compliance, was unknown.

Thus, on balance, although there is preliminary evidence suggesting the potential value of SSRIs in the treatment of sex offenders, the results are far from conclusive, and the emphasis should, therefore, be on further research to reduce uncertainty. In particular, further research should attempt to reduce the number of threats to validity observed in past research. Future research should employ parallel control groups ideally with random allocation of additional SSRI treatment. If such designs are employed, it is likely that psychometric measures will continue to be the most feasible outcomes, and, if so, additional research efforts should be devoted to establishing the relationship between psychometric measures commonly used to assess whether immediate treatment goals have been met and the ultimate objective of reducing recidivism.

As the current practice is psychological treatment and there is some evidence that it is effective, it may be unethical to conduct a trial of SSRIs alone (that are not proven yet) versus psychological treatment (that has some effects). If, however, the ethical issue is solved, there should, ideally, be three arms in an RCT: SSRIs plus best available treatment, best available treatment alone and a placebo and SSRIs alone. However, a considerably large sample size would be needed to enable an RCT to have three arms in order for the intervention to detect a significant effect.

Chapter 3
Economic analysis

Methods

The objective of this part of the report was to relate the costs and consequences of using SSRIs in the treatment of sex offenders. To this end:

- published economic analyses were systematically reviewed
- information on costs associated with adding SSRIs to existing treatments available for sex offenders was collated
- an attempt to relate costs to consequences, using the above two criteria in association with information obtained on effectiveness in chapter 3 was made.

The general methods were as described in the protocol. Further details are described in the following sections, subdivided into the three components above.

Systematic review of economic analyses

Search

MEDLINE (1985–October 2001) was searched for relevant cost studies and economic evaluations. The search strategy targeted studies that considered use of SSRIs, were economic evaluations (including specific assessments of impact on quality of life) and addressed sex offences. The precise health economic evaluation search strategy employed is given in appendix 7 and was designed to maximise sensitivity. As SSRIs were introduced generally in the early 1990s, the search was only extended back to 1985. There was no language restriction. An analogous search was undertaken on the DARE, focusing in particular on the NHS EED.

The database searches were amplified by searches of Internet sites of organisations producing health economic evaluations and contact with experts in the field enquiring whether articles additional to those identified in the primary search were known to them.

Inclusion/exclusion criteria

The inclusion and exclusion criteria were simply that the article dealt with the cost, impact on quality of life or cost-effectiveness of treatments for sex offenders. There was no restriction by study design. Inclusion decisions were made by one reviewer (YA).

Data abstraction and analysis

Characteristics and results of the included studies were abstracted by one reviewer (CH). These were tabulated and conclusions were drawn on the basis of patterns of results revealed. These conclusions were further scrutinised by a senior health economist (SB). The conclusions generally took into account issues of quality of conduct of the included studies.

Collation of information on costs

Information on costs provided in the included studies above was summarised. It was supplemented by direct enquiry to manufacturers with respect to costs of SSRIs and other drugs employed in the treatment of sex offenders. Costs were considered in the following categories:

- additional costs directly associated with the use of SSRIs
- other additional costs associated with the use of SSRIs
- costs potentially offset by the use of SSRIs.

A checklist proposed by the Research, Development and Statistics Directorate of the UK Home Office[52] was used to ensure that no costs had been overlooked. This checklist is reproduced in appendix 8.

Cost–consequences analysis

It was clear at the protocol stage that assessing cost-effectiveness or cost–utility was unlikely to be achievable. Relating costs to effects thus focused on a simple cost–consequences analysis. This followed the guidance provided by Mauskopf[64] in which the key costs and effects are presented in a disaggregated form. In the context of the report as a whole, this section essentially provides a summary of the key information identified in both the effectiveness and costs sections.

Results – systematic review of economic analyses

The primary searches of MEDLINE and the NHS EED identified 247 potentially relevant articles.

Most of these only mentioned costs or health economics analysis in passing and provided no substantial data or analysis. Thus, only three of the potentially relevant studies were included in the review.[65–67] No additional potentially relevant or included studies were identified from Internet searches or enquiries to experts. None of the three included studies directly addressed the efficiency of treatment of sex offenders with SSRIs, the question of greatest interest.

The details of the three included studies are summarised in *Table 9*. All the studies addressed the efficiency of treating child sex offenders. The nature of the treatment programmes was not specified in detail in any of the studies, although it is reasonably clear that in the studies by Donato and Shanahan[66] and Shanahan and Donato[67] that the programmes were administered in prison with CBT being the key component of treatment. All were cost–benefit analyses (CBAs) in which a societal perspective was taken to a greater or lesser extent. An important difference was that the studies by Prentky and Burgess[65] and Donato and Shanahan[66] performed their analyses using costings from the late 1980s, whereas Shanahan and Donato's[67] costs refer to 1998. The superficially odd situation where the recently published study by Donato and Shanahan used cost data apparently 10 years out-of-date was explained by the fact that their specific objective was to develop the previously published analysis by Prentky and Burgess.[65] Indeed, all three included studies were linked. The study by Prentky and Burgess provided the original attempt to assess cost–benefits, but was unable to deal with avoidance of the intangible victim-related costs, that is, the monetary value that should be placed on reducing the long-term psychological costs of being a victim of sex offence in childhood. The study by Donato and Shanahan thus attempted to re-visit and improve on the analysis by, amongst other things, incorporating intangible costs assessed on the basis of "revealed preference".[66] Finally, the study by Shanahan and Donato applied the same approach, attempting to incorporate intangible costs, using up-to-date (i.e. 1998) costings in Aus$.[67] The study also incorporated an assessment of the intangible costs based on "contingent valuation" (willingness to pay), although the validity of extrapolating data derived originally from New Zealand road accident research is debatable. The conclusions and key results contributing to these for each of the included studies are presented in *Table 10*.

Although the numerical data on which the conclusions were based varied, there appeared to be consistency in the view that treatment programmes for child sex offenders were likely to be cost–beneficial. Considering the analyses in detail suggests that this overall finding is probably robust, provided it is accepted that it is reasonable to consider some intangible costs to the victims of child sex offences in the CBA (it is clear that the exact level of such costs will always be highly debatable) and that treatment truly has an effect on recidivism. Of these two, the latter is probably the greatest challenge to the assessment that treatment is truly cost–beneficial, given the frequent references in the articles to the uncertainty concerning the effectiveness of the treatment programmes. A corollary of this is that both Shanahan and Donato[67] and Donato and Shanahan[66] used wide ranges of estimates of effectiveness: 2–14 or 16% improvements in rates of recidivism. Other issues of some concern are as follows.

- There was wide variation in estimates of the cost of the treatment programmes, particularly as the costs of treatment in the late 1980s appeared to be considerably greater than those a decade later.
- The analyses have not been repeated in the context of the UK, which may be important given that all costs, especially legal costs,

TABLE 9 *Characteristics of published economic evaluations*

Study	Country	Design	Currency	Cost year	Perspective	Population	Intervention
Prentky and Burgess, 1990[65]	USA	CBA	US$	1988	Societal	Child molesters	Rehabilitation
Donato and Shanahan, 2001[66]	Australia*	CBA	US$	1990	Societal	Child sex offenders	SOTPs†
Shanahan and Donato, 2001[67]	Australia	CBA	Aus$	1998	Societal	Paedophiles	Paedophile treatment programme†

* *Although conducted by an Australian group, results refer to data originally derived in the context of the USA*
† *CBT was the main specified component of the programme in each case*

TABLE 10 *Results and conclusions of published economic evaluations*

Study, cost year and currency	Treatment cost	Results* (other key parameters)		Conclusions	Comments
Prentky and Burgess, 1990[65] ***Cost year and currency*** 1988, US$	US$10,600 per man per year US$50,000 per programme	Average cost treated: US$164,000 (probability of re-offence = 0.25; average duration of imprisonment = 5.1 years)	Average cost untreated: $232,000 (probability of re-offence = 0.4; average duration of imprisonment = 7 years)	Treatment cost–beneficial Further research necessary	Intangible costs to victim not included. Analysis suggests treatment is "efficient" even when recidivism rate in treated patients is worse than in untreated patients
Donato and Shanahan, 2001[66] ***Cost year and currency*** 1990, US$	US$10,000 per programme	Cost–benefit range (low): US$6300–19,300 (reduction in recidivism rate range 2–16%; cost per offence = US$183,000; no intangible costs included) Cost–benefit range (high): US$4500–33,600 (reduction in recidivism rate range 2–16%; cost per offence = US$272,000; intangible costs = US$89,000)		Treatment cost–beneficial with even modest reductions in rates of recidivism, i.e. 4–6% Further research necessary	Costs associated with initial imprisonment were the same in treated and untreated patients, i.e. possibility of earlier discharge with treatment not considered.† Assumes that for each sex offender **not** re-offending, intangible costs for just one victim are saved
Shanahan and Donato, 2001[67] ***Cost year and currency*** 1998, Aus$	Aus$10,000 per programme	Cost–benefit range (low): Aus$6900–12,000 (reduction in recidivism rate range 2–14%; cost per offence = Aus$157,000; no intangible costs included) Cost–benefit range (high): Aus$1100–76,700 (reduction in recidivism rate range 2–14%; cost per offence = Aus$555,000; intangible costs = two at Aus$199,000 – highest estimate used in the analysis)		Treatment likely to be cost–beneficial. If intangible victim costs valued at zero, the reduction in recidivism rate must be > 6% for treatment to be cost–beneficial. With the maximum estimate of intangible victim costs, the reduction in recidivism rate must be > 2% for treatment to be cost–beneficial Further research necessary	Costs associated with initial imprisonment were the same in treated and untreated patients, i.e. possibility of earlier discharge with treatment not considered†

* *Figures in parentheses indicate negative values, i.e. treatment not cost–beneficial*

† *This aspect of the analysis was introduced to avoid the perceived anomaly in the study by Prentky and Burgess that treatment is beneficial even if the recidivism rate in the treatment group is worse than the untreated group*

expected levels of compensation and costs of imprisonment, may vary considerably from country to country.

Finally, a key issue, given the focus of this report is on SSRIs, is that none of the economic evaluations assessed the addition of SSRIs to current treatment programmes, and it seems unlikely that any of the programmes evaluated incorporated SSRI treatment. Further, the emphasis of published economic evaluations was on sex offences against children. Although this is probably less of a problem as regards generalising results, it needs to be remembered that the use of SSRIs is being considered across a wide range of sex offences.

Despite this, the economic evaluations identified are important. Firstly, they provide some general indication of the likelihood that SSRIs, if effective in reducing recidivism, might be cost–beneficial. Secondly, they indicate some key issues which would need to be addressed in a *de novo* assessment of efficiency of SSRIs in treatment of sex offences, generally or specifically against children.

Results – collation of information on costs

The focus of this component of the economic analysis was to attempt to identify plausible ranges for the additional costs that would be associated with using SSRIs as part of treatment programmes for sex offenders. In consequence, quantifying the baseline costs of existing treatment rehabilitation packages was not attempted, merely how they might change if SSRIs were used as well as other treatment modalities, such as CBT. The review of published economic analyses provides some information on this (see *Table 11*[68,69]), albeit with the proviso that there seems to be enormous (and somewhat counter-intuitive) variation and that all the figures are derived outside the UK setting. However, there were no cost-effectiveness studies examining the specific issue of the use of SSRIs in sex offenders.

Additional direct costs

It seems likely that the main additional cost would be the cost of the drugs in question. The 28-day and annual costs of the main SSRIs are detailed in *Table 11*.

The annual costs are, somewhat, greater than other drug treatments currently employed in treatment of sex offenders, such as antiandrogen plus CPA (annual cost £439.92 at a dose of 50 mg twice daily), but relatively small compared to even the most modest estimated cost of existing treatment packages (Aus$10,000 in 1998). Unfortunately, this ignores the likelihood that SSRI treatment would continue for several years. Taking this into account suggests that the drug costs of the SSRIs may represent a considerable increase in existing treatment costs.

Other additional costs

It seems unlikely that there would be other major costs associated with SSRI treatment. Additional staff/premises/running costs do not seem likely to be consequences. Need for additional patient monitoring as a consequence of adverse events of the drugs in question also seems unlikely. The need to monitor compliance over the longer term may be an issue, but it is unclear whether follow-up beyond that already offered to sex offenders would be necessary for this purpose.

TABLE 11 *SSRI costs*

SSRI	Dosage	Cost per 28 days	Annual cost
Citalopram	10 mg daily	£9.64	£125.32
	20 mg daily	£16.03	£208.39
	40 mg daily	£27.10	£352.30
	60 mg daily	£43.13	£560.69
Fluoxetine	20 mg daily*	£7.60	£98.80
	40 mg daily*	£15.19	£197.47
	60 mg daily	£44.44	£577.72
Fluvoxamine	100 mg daily*	£16.37	£212.81
	200 mg daily*	£32.74	£425.62
	300 mg daily*	£49.11	£638.43
Paroxetine	20 mg daily	£16.58	£215.54
	30 mg daily	£29.08	£378.04
	50 mg daily	£45.66	£593.58
	60 mg daily	£58.16	£756.08
Sertraline	50 mg daily	£16.20	£210.60
	100 mg daily	£26.51	£344.63
	200 mg daily	£53.02	£689.26

All prices taken from Monthly Index of Medical Specialities *February 2002,[68] except those marked *, which are taken from the Drug Tariff February 2002[69]*

Costs offset

It is thought unlikely that existing treatment packages would be substantially altered by adding SSRIs. It is possible that there would be some substitution of antiandrogen therapy with SSRIs, which would reduce the apparent cost impact of SSRI use assessed by additional drug cost alone, but the effect of this is likely to be small because the use of antiandrogens is low.

More significant issues rest on the level of cost-savings which might accrue from a reduced length in custody prior to release, that is, SSRI treatment improves confidence that a sex offender will not re-offend and they will be released more frequently when eligible for parole as a result of reduced rates of re-offence. As has been seen from published economic evaluations, assessing whether such savings will occur is critically dependent on estimates of the effectiveness of SSRIs in improving recidivism, reducing rates of re-offence and the numbers of victims affected. As this is currently unknown, attempting to quantify costs offset is too speculative at the current time. If estimates of impact on rates of recidivism were to be obtained, approaches similar to those encountered in the published economic evaluations of child SOTPs could be used to make estimates of costs offset in these domains.

Cost–consequences analysis

The key potential costs and consequences, including sources of uncertainty, of introducing SSRIs to current treatment packages for sex offences are shown in *Table 12*. This focuses particularly on sex offences against children in offenders who have already been convicted and would already be required to undertake some form of rehabilitation/treatment.

The key feature emerging from this analysis is that uncertainty precludes assessment of both costs and consequences to degrees, which makes even crude estimation of the efficiency of SSRIs for treatment of convicted child sex offenders overly speculative at this time. Although not specifically considered in *Table 12*, the same is true of SSRI use for prevention and treatment of sex offences generally. Undeniably, SSRIs have the potential to be cost–beneficial or cost-effective and deserve further investigation.

Concerning research, economic analyses require a robust evidence on the magnitude of the increase in effectiveness. Given the paucity of such data on this topic, conducting economic analysis in this area is problematic. The development of a decision-analytic model (e.g. a Markov model) to consider this policy question would be a helpful means of highlighting some of the additional key areas of uncertainty.

TABLE 12 *Cost–consequences analysis – use of SSRIs in addition to existing treatment packages in convicted child sex offenders*

Additional costs		Consequences/effects	
Nature	**Uncertainties**	**Nature**	**Uncertainties**
Direct: drug costs about £750/annum (maximum)	Average duration of treatment uncertain	Reduces psychometric measures claimed to predict likelihood of re-offence	Studies demonstrating reduction open to bias
			Predictive ability of psychological measures uncertain
Other additional: probably minimal		Rates of re-offence (detected)	Unknown
Costs off-set: potentially large cost savings if rates of re-offence reduced	Impact of SSRIs on rates of re-offence in convicted child sex offenders unknown	Rates of re-offence (detected and undetected)	Unknown
		Numbers of victims affected	Unknown

Chapter 4
Conclusion

The internal validity for all identified effectiveness studies was generally poor and the external validity was limited because cases treated with SSRIs were not particularly representative of the general population of sex offenders. Only two of nine studies stated explicitly that the participants were sex offenders.[55,61] High-quality evidence-based research on the use of SSRIs was not identified in this systematic review. The studies identified by this review did not provide sufficient data to prove that SSRIs alone or in combination with psychotherapy are more effective. Therefore, there is a need for a double-blind placebo-controlled RCT, preferably with several participating centres to establish the effect of SSRIs on sex offenders.

The need for improved assessments of cost-effectiveness and cost–benefits should also be anticipated. Uncertainty concerning evidence on effectiveness is a major factor currently limiting accurate assessment of efficiency, which should be overcome if further rigorous research on effectiveness proceeds. However, this is not the only requirement and other research on costing and modelling the treatment of sex offenders with SSRIs and other treatments should proceed in parallel.

We are aware that there is an ongoing feasibility study for an RCT of effectiveness of SSRIs to treat sex offenders funded by the UK Home Office for the National R&D Programme of the NHS Forensic Mental Health (http://www.rdinfo.org.uk/Queries/ListGrantDetails.asp?GrantID=3345). The grant holder is Professor D Grubin. This study is a double-blind comparision of placebo with fluoxetine in convicted sex offenders, either in prison or on probation programmes. This study will be evaluating the impact on a number of measures relating to obsessiveness/compulsiveness, impulsivity, sex drive, sexual deviance and mood. The total trial length is 12 weeks.

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Contributions of the authors

Yaser Adi was the lead author, and designed the protocol and data abstraction form used in assessing the quality of the studies. He searched for studies, contacted authors for further information and liaised with experts in the field to obtain background information. He extracted data from the included studies and assessed their eligibility and validity. He also organised peer-reviewers and collated and summarised the data and wrote the draft report. Darren Aschroft assessed the eligibility of the included studies, helped in designing the data abstraction form, abstracted the data from the studies and advised on the pharmaceutical aspects of the intervention. Anne Fry-Smith advised on the search strategy and undertook searches of electronic databases. Chris Hyde was the senior reviewer, and managed the project. He read and commented on the draft report and edited the final document. He advised on methodology about the quality assessment criteria and mainly wrote the economic assessment chapter of the report. He also advised on the eligibility of the studies when there was disagreement between the two reviewers (YA and DA). Professor K Browne, Professor of Forensic Psychology, and Dr T Beech, Senior Lecturer in Psychology, both read and commented on the draft report.

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Appendix 1

Search strategies for the systematic review of effectiveness

MEDLINE (Ovid; 1985–October 2001)

#1 (citalopram$ or seropram or cipramil).mp
#2 (fluoxetine$ or prozac).mp [mp = title, abstract, registry number word, MeSH] (4906)
#3 (fluvoxamine$ or faverin or luvox).mp [mp = title, abstract, registry number word, MeSH] (1252)
#4 (paroxetine$ or seroxat or paxil).mp [mp = title, abstract, registry number word, MeSH] (1914)
#5 (sertraline$ or lustral or zoloft).mp [mp = title, abstract, registry number word, MeSH] (1246)
#6 (femoxetin or ifoxetine or viqualine).mp [mp = title, abstract, registry number word, MeSH] (12)
#7 serotonin uptake inhibitors/ (4538)
#8 ssri$.mp (1487)
#9 or/#1–#8 (10779)
#10 exp sex offenses/ (8697)
#11 exp paraphilias/ (3024)
#12 (paedophilia$ or pedophilia$).mp [mp = title, abstract, registry number word, MeSH] (435)
#13 (rape$ or rapist$).mp [mp = title, abstract, registry number word, MeSH] (4702)
#14 bugger$.mp (5)
#15 (indecent$ adj assault$).mp (10)
#16 incest$.mp (1455)
#17 (scatalogia or necrophilia or zoophilia or coprophilia or urophilia or partialism or klismaphilia).mp [mp = title, abstract, registry number word, MeSH] (39)
#18 ((sex$ adj2 offend$) or (sex$ adj2 offens$)).mp [mp = title, abstract, registry number word, MeSH] (720)
#19 or/#10–#18 (13813)
#20 #9 and #19 (43)
#21 limit #20 to (human and yr = 1985–2001) (43)
#22 from #21 keep 1–43 (43)

EMBASE (Ovid; 1985–October 2001)

#1 (citalopram$ or seropram$ or cipramil$).mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (3096)
#2 (fluoxetine$ or prozac).mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (11960)
#3 (fluvoxamine$ or faverin or luvox).mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (4256)
#4 (paroxetine$ or seroxat or paxil).mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (5381)
#5 (sertraline$ or lustral or zoloft).mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (4403)
#6 (femoxetin$ or ifoxetine or viqualine).mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (218)
#7 serotonin uptake inhibitor/ (7497)
#8 ssri$.mp (1956)
#9 or/#1–#8 (20707)
#10 exp sexual abuse/ (7464)
#11 exp sexual deviation/ (2242)
#12 exhibitionism.mp (193)
#13 (paedophilia$ or pedophilia$).mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (303)
#14 (rape$ or rapist$).mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (2953)
#15 bugger$.mp (4)
#16 (indecent adj assault).mp (9)
#17 incest.mp (918)
#18 scatalogia.mp (2)
#19 (necrophilia or zoophilia or coprophilia or urophilia or partialism or klismaphilia).mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name] (29)
#20 ((sex$ adj2 offend$) or (sex$ adj2 offens$)).mp [mp = title, abstract, subject

headings, drug trade name, original title, device manufacturer, drug manufacturer name] (933)
#21 or/#10–#20 (10895)
#22 #9 and #21 (114)
#23 limit #22 to (human and yr = 1985–2002) (107)
#24 from #23 keep 1–107 (107)

Cochrane Library (2001, issue 3)

#1 ((CITALOPRAM* or SEROPRAM) or CIPRAMIL)
#2 (FLUOXETINE* or PROZAC)
#3 ((FLUVOXAMINE* or FAVERIN) or LUVOX)
#4 ((PAROXETINE* or SEROXAT) or PAXIL)
#5 ((SERTRALINE* or LUSTRAL) or ZOLOFT)
#6 ((FEMOXETIN or IFOXETINE) or VIQUALINE)
#7 (SSRI* or (SEROTONIN next (UPTAKE next INHIBITOR*)))
#8 SEROTONIN-UPTAKE-INHIBITORS*:ME
#9 (((((((#1 or #2) or #3) or #4) or #5) or #6) or #7) or #8)
#10 (SEX* and OFFEN*)
#11 SEX-OFFENSES*:ME
#12 PARAPHILIA*
#13 PARAPHILIAS*:ME
#14 (PAEDOPHIL* or PEDOPHIL*)
#15 (RAPE* or RAPIST*)
#16 BUGGER*
#17 (INDECENT next (* next ASSAULT*))
#18 INCEST*
#19 (((((((#10 or #11) or #12) or #13) or #14) or #15) or #16) or #17) or #18)
#20 (#9 and #19)

PsycINFO (1985–2001)

(serotonin uptake inhibitor? OR ssri? OR citalopram* OR fluoxetine* OR paroxetine* OR sertraline* OR femoxetin) AND (sex near offend* OR sex near offens* OR p?edophil* OR rape* OR rapist* or paraphilia* OR incest* OR indecent near assault*)

Science Citation Index (Web of Science 2000)

(citalopram* OR seropram fluoxetine* OR prozac OR fluvoxamine* OR faverin* OR paroxetine* OR seroxat* OR sertraline* OR lustral* OR femoxetin OR ifoxetine OR ssri* OR serotonin uptake inhibitor*) AND (paedophilia OR pedophilia* OR rape* OR rapist* OR paraphilia* OR indecent assault* OR incest* OR sex offend* OR sex offens*)

Appendix 2

Excluded studies and reasons for exclusion

The main reasons for exclusions were that the studies were: reviews, not trials, reported an individual case report or not relevant.

Study	Reason
Abouesh and Clayton, 1999[70]	Individual case reports of two cases
Aguirre, 1999[71]	Not a trial, but a letter with no data presented
Anonymous, 1992[72]	A review
Balon, 1998[73]	A review
Becker, 1992[74]	Not a trial, no data presented
Bianchi, 1990[75]	A case report
Bourgeois and Klein, 1996[76]	Combined pharmacological treatment
Bradford and Gratzer, 1995[77]	A case report
Bradford, 1996[78]	A review
Bradford, 1999[37]	A review
Bradford, 2000[79]	A review
Bradford, 2001[80]	A review
Butterfield *et al.*, 1999[81]	Not relevant
Coleman *et al.*, 2000[82]	Combined pharmacological treatment
Duggan, 1998[83]	Not relevant
Emmanuel *et al.*, 1991[84]	A case report
Galli *et al.*, 1998[85]	A case report
Gijs and Gooren, 1996[86]	Not relevant
Greenberg and Bradford, 1997[87]	A review
Grossman *et al.*, 1999[88]	An overview
Haywood and Cavanaugh, 1996[89]	Not relevant
Hollander and Wong, 1995[90]	A review
Hollander, 1996[91]	Not a trial, no data presented
Hollander and Rosen, 2000[92]	Not relevant
Kafka, 2001[40]	A review
Kafka, 1991[93]	Suspected duplication with 1992 study
Kafka, 1991[94]	A case report
Kafka, 1994[95]	Not relevant
Kafka, 1995[96]	Not relevant
Lane, 1997[97]	A review
Lehne *et al.*, 2000[98]	A review
Lehrman *et al.*, 1991[99]	A case report
Levitsky and Owens, 1999[100]	A review
Lorefice, 1991[101]	A case report
Meisler *et al.*, 1998[102]	Not relevant
Messiha, 1993[103]	A review

continued

continued

Study	Reason
Richer and Crison, 1993[104]	Not a trial
Rubenstein and Engel, 1996[105]	A case report
Sherak, 2000[106]	A review
Stewart and Shin, 1997[107]	Not relevant
Waldinger and Hengeveld, 2000[108]	Not relevant
Zohar *et al.*, 1994[109]	A case report
Zonana and Norko, 1999[110]	Not relevant

Appendix 3

Characteristics of the included effectiveness studies

Study	Design and data source	Condition	*N*	Age and sex	Intervention	Outcomes	Follow-up	Instrument	Comments
Perlistein *et al.*, 1991[56] (USA)	Case reports – pre–post treatment ***Data source*** Not stated	Paedophilia	1	Male, aged 26 years	Fluoxetine 40 mg/day	Intensity of fantasy; frequency of masturbation	4 months	Not stated	None of the cases were described as sex offenders, currently or in the past. The paedophilia case had a history of 18 months of compulsive masturbation. The exhibitionism case reported a 7-year history of regular exhibitionism. The voyeurism/frotteurism case had a 2-year history
		Exhibitionism	1	Male, aged 30 years	Fluoxetine 40 mg twice daily	Intensity of fantasy; frequency of masturbation	6 months	Not stated	
		Voyeurism/ frotteurism	1	Male, aged 28 years	Fluoxetine 20 mg/day	Interest in photographs; frequency of masturbation	3 months	Not stated	
Stein *et al.*, 1992[57] (USA)	Pre–post treatment retrospective case series ***Data source*** Open clinical practice	Paraphilias (*n* = 5); non-paraphilic sexual addictions (*n* = 5); sexual obsessions and compulsions (*n* = 3)	13	All males, age range 18–58 years	Fluoxetine (12 cases) Clomipramine (three cases, as adjuvant therapy to fluoxetine in two cases and as a lone therapy in one case) Fluvoxamine (one case) Fenfluramine (one case)	Change in fantasies in response to treatment	Range 6 weeks–12 months	CGI change score	There was no data about social factors. Clomipramine is conventionally classified as a tricyclic antidepressant, but the authors classed it as an SSRI. Fenfluramine, which is used in one case, is also not strictly an SSRI The stage of progression of the condition was not stated
Kafka and Prentky, 1992[58] (USA)	Pre–post treatment case series ***Data source*** Consecutive responders to advertisements – total number of responders not stated	Not offenders: paraphilias (*n* = 10); non-paraphilic sexual addictions (*n* = 10)	20	All males, mean age = 36 years	Fluoxetine 20 mg/day; titrated every 4 weeks up to 60 mg	Depression; TSO; masturbation; other sexual activity; sexual desire intensity; total sexual interest ratio	12 weeks	Structured self-reported questionnaires used: IDD and SOI	Individuals were married (*n* = 10), Catholic (*n* = 10), achieved college (*n* = 6) and postgraduates (*n* = 7). The average income was US$56,000. The average self-reported durations of sexual symptoms were 14.9 years for paraphilias and 21.8 years for non-paraphilic sexual addictions. The majority of the men reported chronic depressive symptoms of many years duration and mood disturbance. Sixteen reported chronic depressive symptoms prior to the age of 21 years

continued

Study	Design and data source	Condition	*N*	Age and sex	Intervention	Outcomes	Follow-up	Instrument	Comments
Coleman *et al.*, 1992[55] (USA)	Pre–post treatment retrospective case series ***Data source*** Referral of sex offenders to an out-patient clinic	Paraphilic sex offenders: paedophilias (*n* = 6), exhibitionism (*n* = 2), voyeurism (*n* = 3; one of the three cases was also associated with rape and obscene phone calls)	11	Age and sex not stated	Fluoxetine (dose not stated)	Depression; obsession; compulsion	Offenders recorded between 1988–1991, but unclear if fluoxetine was used for the whole period	Hamilton anxiety and depression scales; Beck Depression Inventory; YBOCS; a semi-structured interview	Participants were treated with psychotherapy and pharmacotherapy for sex offences
Kafka, 1994[59] (USA)	Pre–post treatment case series ***Data source*** Open clinical practice	Cases not explicitly stated as offenders: paraphilias (*n* = 13), non-paraphilic-related disorders (*n* = 11)	24	All male Paraphilias group mean age = 38.4 years; non-paraphilic-related dis-orders group mean age = 39.6 years	Sertraline at a mean dose of 100 mg/day Fluoxetine at a mean dose of 50 mg/day was administered to those who had an unsatisfactory response	Depression; total sexual activity; ATD; percentage improvement from baseline measures	Sertraline mean = 17.4 weeks; fluoxetine mean = 30 weeks	Structured self-reported questionnaires: IDD, TSO, ATD and CGI outcome scale	All white. 9/13 paraphilics were married in contrast to 3/11 of those with non-paraphilic-related dosorders. There was no other additional psychological therapy during the trial. It is important to note that there were eight different conditions under the term paraphilias in this study, and six different conditions under the term non-paraphilic-related disorders
Bradford, 1995[60] (USA)	Open-label case series ***Data source*** Outpatients	Paedophilia	19	All males, aged > 16 years	Sertraline, initial dose of 50 mg a day increased by 50 mg upon patient response and tolerability up to 200 mg	Fantasy; sexual activity; obsession; masturbation	12 weeks	Greenberg scores; sexual activity; penile tumescence; YBOCS	This is a conference abstract with little information. More details requested from the author and Pfizer, but no response received by 6 March 2002
Fedoroff, 1995[61] (Canada)	Retrospective case series ***Data source*** First 100 consecutive cases of an outpatient psychiatric clinic	Paraphilic sex offenders	51	All males, age not stated	Combination of fluoxetine (dose not stated) plus psychotherapy, or psychotherapy alone Buspirone prescribed if anxiety symptoms were prominent	Change in paraphilic symptoms	2 months	Patients' self-reported efficacy of the treatment, no other data provided	No details about the nature of sexual offences committed

continued

Study	Design and data source	Condition	*N*	Age and sex	Intervention	Outcomes	Follow-up	Instrument	Comments
Greenberg *et al.*, 1996[62] (Canada)	Pre–post treatment retrospective case series ***Data source*** Royal Ottawa Hospital	Paraphilias: offending history not stated (74% paedophilia) Data source was all those (*n* = 98) receiving SSRIs as part of first treatment for paraphilia in a sexual behaviour clinic between 1991–1995	58	All males, mean age = 36 years	Fluoxetine (*n* = 17) Sertraline (*n* = 25) Fluvoxamine (*n* = 16)	CGI scale; frequency and severity of sexual fantasies	Changes over time: 0–4, 4–8 and 8–12 weeks	CGI scale; Sexual Fantasy Scale (0 = no fantasy, 4 = extreme fantasies, almost constant, very disturbing and unable to stop)	There were 57% single, 26% married and 17% separated or widowed. There were 79% with concurrent psychosocial treatment. 30% had personality disorders, 27.6% had depression and 17.2% had alcohol abuse problems
Kafka and Hennen, 2000[63] (USA)	Pre–post treatment prospective case series ***Data source*** Outpatients	Not offenders: paraphilias (*n* = 14); non-paraphilic-related disorders (*n* = 12)	26	All males, mean age = 37 years	Four different types of SSRIs were used: fluoxetine, sertraline, paroxetine and fluvoxamine	Change of sexual behaviour according to TSO and ATD	Mean = 8 months on SSRIs	Structured self-reported questionnaires; TSO; ATD	14/26 were married; 73% were heterosexual; 21/26 had mood disorders and 17/26 had attention-deficit/hyperactivity disorder. White men with current primary paraphilias or non-paraphilic-related disorders were evaluated and treated during a 3-year period

Appendix 4

Results of the included effectiveness studies

Study	Intervention	Intervention group improvement rate	Results	Adverse event(s) and rate(s)	Comments
Perlistein *et al.*, 1991[56] (USA)	Case 1: fluoxetine 40 mg/day Case 2: fluoxetine 40 mg twice daily Case 3: fluoxetine 20 mg/day	3/3 cases reported improvements	Case 1: reduction in the intensity of intrusive paedophilic fantasies, frequency of masturbation decreased from six times daily to once Case 2: the sexual desire was somewhat diminished Case 3: decreased fantasies in photographs and masturbation	Case 1: retarded ejaculation, less interest in sexual intercourse with his wife Case 2: retarded ejaculation Case 3: not stated	None of the three case reported were objectively assessed. The setting was unclear and the sampling frame was not stated. 2/3 cases were previously on psychotherapy with no improvement
Stein *et al.*, 1992[57] (USA)	Fluoxetine; clomipramine; fluvoxamine; fenfluramine	4/13 cases reported improvements	0/5 paraphilia cases had improved sexual symptoms (masturbation and deviant fantasies) 2/5 non-paraphilic-related sexual addiction cases had improved compulsive masturbation 2/3 sexual obsessions and compulsions cases improved In the five cases who responded 'positively' to treatment, co-morbidities were major depression (three cases) or OCD (two cases)	One case treated by fluoxetine had worsening sexual symptoms. Impotence and retarded ejaculation were reported in one case	The cases were not consistently treated with a similar dosage and the length of treatment varied considerably between cases. None of the five cases of paraphilias treated with fluoxetine showed any positive response to treatment. 9/13 cases had OCD, 3/13 cases had major depression
Kafka and Prentky, 1992[58] (USA)	Fluoxetine 20 mg/day, titrated every 4 weeks up to 60 mg	Significant results detected by IDD score Unable to assess effect of intervention on offence/conviction rate using this study design. The sample of cases were not categorised as sex offenders, but individuals with sexual addiction	For IDD score: prior treatment mean = 25.6 (SD 11.2; n = 20); posttreatment mean = 9.4 (SD 6.8, p = 0.001; n = 16) Significant changes in all pre–post outcomes for unconventional but not conventional sexual behaviours	Not stated	Sexual behaviours were divided into two broad subcategories: conventional and unconventional. Conventional sexual behaviours reflected the culturally normative concept of reciprocal affectionate sexual activity, and did not require the presence of a stable affiliation, but merely that the intent of a sexual behaviour included a mutually consenting, relational context. Unconventional sexual behaviours corresponded to non-paraphilic sexual addictions and paraphilic activities, including the primary use of paraphilic/non-paraphilic sexual addiction fantasy during sexual activities, either alone or with a partner

continued

Study	Intervention	Intervention group improvement rate	Results	Adverse event(s) and rate(s)	Comments
Coleman *et al.*, 1992[55] (USA)	Fluoxetine (dose not stated)	Significant improvements in all scores for depression, anxiety, obsession and compulsion. Qualitative response statements were also positive	All scores showed significant improvements from baseline	Not stated	Mean scores and SDs were used to calculate the significance of scores for all scales
Kafka, 1994[59] (USA)	Sertraline; fluoxetine for cases who failed to respond to sertraline	Overall, 17/24 treated with sertraline and/or fluoxetine for ≥ 4 weeks sustained a clinically significant response in un-conventional sexual behaviour for TSO and ATD	TSO comparing baseline and final outcome: $t = 3.3$, df = 23, $p = 0.002$ ATD comparing baseline and final outcome: $t = 2.2$, df = 23, $p = 0.03$	11/24 had side-effects: gastrointestinal distress = 3/24; sexual dysfunction = 3/24; fatigue = 2/24; increased depression = 2/24 and headache = 1/24	IDD: no significant results CGI: 14/24 improvements reported, but 10/24 had no change or worsened
Bradford, 1995[60] (USA)	Sertraline at an initial dose of 50 mg/day and increased by 50 mg upon patient response and tolerability up to 200 mg	Marked improvements detected by different outcome measures	Greenberg scores for fantasies of sex with young girls ($p < 0.05$) YBOCS score ($p < 0.05$) Decrease in penile tumescence ($p < 0.05$) Decrease in the number of cases masturbating more than twice a week	Headache = 9/19; diarrhoea = 5/19; flatulence = 5/19; nausea = 5/19 and insomnia = 4/19	Insufficient details as it is a conference abstract
Fedoroff, 1995[61] (Canada)	Fluoxetine + psychotherapy. Buspirone (if there were symptoms of anxiety)	No clear data, however, it was stated that a higher proportion of men started on buspirone required a switch to fluoxetine than vice versa	49 reported no current paraphilic symptoms at the time of assessment (not clear how long treatment was for). These individuals have traditionally been classified as "deniers". It was unclear if 49 out of 51 or 49 out of the consecutive sample of 100 showed improvement	Not stated	The study authors admitted that there was no scientific evidence of the efficacy of SSRIs so far. The study implied that fluoxetine seemed to be more effective than buspirone

continued

Study	Intervention	Intervention group improvement rate	Results	Adverse event(s) and rate(s)	Comments
Greenberg *et al.*, 1996[62] (Canada)	Fluoxetine (n = 17); sertraline (n = 25); fluvoxamine (n = 16)	Significant improvement on the CGI scale and severity in fantasy reduced	Baseline–4 weeks: r = 7.96; df = 51; $p < 0.001$ 4–8 weeks: t = 4.31; df = 35; $p < 0.001$ 8–12 weeks: t = 2.76; df = 29; $p < 0.05$ At baseline: 44/58 (75.9%) At 4 weeks: 30/58 (58%; t = 6.77; df = 39; $p < 0.001$ At 8 weeks: 23/58 (57.5%; t = 2.40; df = 31; $p < 0.05$ At 12 weeks: 12/58 (30.8%; not significant)	Insomnia = 8/58; delayed ejaculation = 8/58; headaches = 7/58; drowsiness = 6/58; reduced sex drive = 4/58; diarrhoea = 3/58; nausea = 3/58; blurred vision = 2/58	Concurrent psychological treatment in 79% of cases
Kafka and Hennen, 2000[63] (USA)	Four different types of SSRIs were used: fluoxetine, sertraline, paroxetine and fluvoxamine	Significant decrease in TSO and ATD	63% decrease in mean of TSO compared with baseline, $p < 0.001$ 69% decrease in ATD compared with baseline, $p < 0.001$	Not stated	

Appendix 5

Quality assessment of the included effectiveness studies

Study	Inclusion bias	Selection bias	Performance bias	Attrition bias	Detection bias	Other points
Perlistein et *al.*, 1991[56] (USA)	No inclusion criteria were reported	No information	No information	Three reported cases. It was unclear if there were more cases treated but lost to follow-up	No information about how outcome data were collected, or who collected it	It was unclear if the data were retrospectively reported. There was no control group
Stein et *al.*, 1992[57] (USA)	No details of inclusion criteria	No information about how cases were selected	No information	Not stated	No information about how outcome data were collected, or who collected it. Validity of the CGI was not stated and the 7-point score was rather confusing due to a lack of easily defined differences between the points (1 = markedly improved, 2 = moderately improved, 3 = minimally improved, 4 = unchanged, 5 = minimally worse, 6 = moderately worse, 7 = markedly worse)	All types of biases were potentially present as well as confounding (co-morbidities). Subjectivity of the outcome measure was possible
Kafka and Prentky, 1992[58] (USA)	No clear inclusion criteria. Consecutive subjects responding to advertisement, however, the total number of responders was not stated The participants were heterogeneous in terms of the conditions they suffered: 15 different subgroups of sexual behaviour were stated. Co-morbidity was an issue, the majority (95%) of men reported chronic depressive symptoms of many years duration	Repeated measures should provide protection. However, baseline results were available for 20, but final results only available for 16	Co-intervention assumed to be operating: only 10/20 were reported as having received no concurrent therapies, 4/20 were reported as having received weekly psychotherapy, 6/20 were reported as having received pre-existing psychological treatment	Results were reported on 16/20 participants, i.e. 20% lost to follow-up	Assessment of outcomes was not stated as blind at pre- or postintervention. Validity of SOI was unclear	Stage of progression of the disease: there were no data about cases individually, average duration of sexual symptoms was 14.9 years for paraphilias and 21.8 years for non-paraphilic sexual addictions Dose–response relationship: there was no attempt to explore this, possibly due to heterogeneity in the cases and the limited sample size
Coleman et *al.*, 1992[55] (USA)	No information about selection criteria, age or years in the sexual deviance behaviours	No information on how these offenders were selected	No details	13/16 agreed to participate in the study	No blinding, and no information about the validity of the scales used	

continued

Study	Inclusion bias	Selection bias	Performance bias	Attrition bias	Detection bias	Other points
Kafka, 1994[59] (USA)	Co-morbidity (except depression) and co-treatment were excluded	People with paraphilc-related disorders were excluded if they reported any lifetime paraphilias. No logical reasons for this exclusion were stated	The cases were all treated at the same practice where the author worked	2/26	No blinding assessment at baseline or at final assessment	Stage of progression of the disease: there were no data about individual cases, and average durations of sexual deviances were not stated Dose–response relationship: there was no attempt to explore this, possibly due to heterogeneity in the cases and the limited sample size The outcome measures were very much subjective, relying on the self-report questionnaires, and their validities were not stated. However, the difference between the 7-point ordinal scale of the CGI scale to assess sexual behaviour did not seem robust enough should the same measure have been repeated (1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = unchanged, 5 = minimally worse, 6 = much worse, 7 = very much worse)
Bradford, 1995[60] (USA)	Otherwise healthy outpatient males aged > 16 years	No details	No details	3/19	No details	No control, and no blinding
Fedoroff, 1995[61] (Canada)	No inclusion criteria were stated	A consecutive sample of 100 men. 41 denied current paraphilic symptoms, 51 chose an SSRI in addition to psychotherapy, seven chose psychotherapy alone and one chose an anti-androgen	It was unclear how often the individuals were assessed, and no blinded assessment was reported	No details about loss to follow-up	No details about how the outcomes were measured and whether or not the assessor was blinded	The treatment was strictly voluntary, therefore, the individuals may have been sufficiently motivated to seek treatment (volunteers effect)

continued

Study	Inclusion bias	Selection bias	Performance bias	Attrition bias	Detection bias	Other points
Greenberg *et al.*, 1996[62] (Canada)	It is assumed that the total *n* = 96 was the number of people treated in the Royal Ottawa Hospital during 1991–1995. 15 were excluded because they were treated before (the type of treatment they had received was not stated), nine were lost to follow-up, six were taking CPA, five had psychoses and one was taking paroxetine	Repeated measures on the same subject should provide protection	Considerable proportion of individuals had co-interventions and concurrent psychiatric conditions. Any results observed following treatment with SSRIs was likely to be the combined effects of the co-interventions	17/58 (29%)	Assessment of outcomes was not stated as blinded, and the validity of the measure of frequency and severity was unclear	Stage of progression of the disease: unclear Dose–response relationship: not stated Data were retrospectively collected. There was no control group. There was possible confounding due to co-interventions and co-morbidities. The sampling frame was all people attending the sexual behaviour clinic between 1991–1995
Kafka and Hennen, 2000[63] (USA)	No clear inclusion criteria	It was unclear how the 26 participants were chosen and out of how many	SSRI was used alone in the first phase and then followed by a combined treatment	21/26 completed the trial of SSRIs and psycho-stimulant augmentation	Validation of TSO and ATD was not stated, and there was no blinding	Stage of progression of the disease: not stated Dose–response relationship: not stated Data were prospectively collected. There was no control group. There was confounding, as large proportions of participants had mental conditions and no attempts were made to control for these

Appendix 6

Concerns about internal and external validity of the included effectiveness studies

Study	Internal validity	External validity
Perlistein et *al*., 1991[56] (USA)	There was a lack of important information to address potential biases: inclusion, selection, performance, attrition and detection. The three cases reported improvement after SSRI intervention, however, the denominator was not reported. There was no control and no objective way to validate the improvement	As this study reported three cases of paraphilia treated with fluoxetine in the absence of a robust design, the study is unlikely to be generalisable to any target population
Stein et *al*., 1992[57] (USA)	Despite some details of treatment dosage and the symptoms monitored, potential biases have not been controlled for	Heterogeneity observed in the nature of the cases, co-morbidities, the SSRIs used and the dosage and length of treatment. There were no data regarding previous history of sexual offences. Therefore, the generalisability was greatly compromised, particularly in the absence of a control and unblinded outcome assessment
Kafka and Prentky, 1992[58] (USA)	There are major concerns about lack of inclusion criteria, as cases in this study were recruited following advertisement and were, therefore, likely to have volunteer bias. In addition, the number contacted was unknown and the responder rate was not stated. There are also concerns about selection, attrition and detection bias. Validity of the measure used to assess sexual behaviour (SOI) was also unclear	The cases were people in the community that claimed to have no legal charges related to current sexual misconduct. They were, however, diagnosed as individuals with paraphilia or non-paraphilic sexual addiction. Whether included individuals were representative of the groups to whom results claim to be generalisable is uncertain. The 20 participants represent 13 different sexual diagnoses: masochism (n = 6), sadism (n = 1), exhibitionism (n = 1), tranvestic fetishism (n = 1), fetishism (n = 1), frotteurism (n = 1), telephone scatalogia (n = 2), compulsive masturbation (n = 14), protracted promiscuity (n = 11), pornography (n = 9), telephone sex (n = 2), sexual incompatibility (n = 3) and sexual accessories (n = 1) Follow-up is of particular concern, as the treatment was for 12 weeks only. It is unknown what may have happened after that: would side-effects have been more prominent to cause less compliance? The relevance of outcomes was debatable; even with significant differences between pre- and posttreatment, it is unknown if an individual with a particular score on the SOI posttreatment represented safe behaviour
Coleman et *al*., 1992[55] (USA)	There was no information about selection of offenders and no random allocation. Being a retrospective study, loss of details was expected. There was no information on repeated progress at intervals between 1988 and 1991. Attrition was 3/16, but only 11 used SSRIs. Outcome assessment was not blinded	These cases were referred to this clinic due to the lack of response to psychological treatment. They had either been arrested and convicted or had been engaging in illegal sexual behaviour This study did report that participants were sex offenders. 11/16 used SSRIs for the period (1988–1991). Depression and OCD were reduced on outcome scales, but behaviour changes were taken as qualitative statements. The responses given in the semi-structured interview were all positive and no single response was negative. More details were needed about the questions asked. In addition, there were no details about the dose of fluoxetine used and the age, sex, alcohol abuse or the length of time spent in such behaviours of the subjects. The side-effects of the SSRIs were not stated. The setting in which these offenders were treated was unclear

continued

Study	Internal validity	External validity
Kafka, 1994[59] (USA)	No information was given about how this sample of 26 were selected and what the total number of all cases attending the clinic was. There was no blinding of assessments at baseline or outcomes. Attrition was relatively low at 7%	No information was given about whether or not this sample of cases represented the total number of people attending the practice, or the people with paraphilias or non-paraphilic-related disorders. It was unknown whether these people had been convicted or had a history of reported sexual offences The number of cases represent people with 14 sexual deviances and the total number was 26, thus a case may exhibit more than one sexual behaviour. The different sexual deviances were fetishistic transvestism, masochism; exhibitionism; fetishism; paraphilia not otherwise specified; telephone scattologia; paedophilia; rape; compulsive masturbation; pornography dependence; protracted promiscuity heterosexual; protracted promiscuity homosexual and sexual accessories
Bradford, 1995[60] (USA)	It was not possible to fully assess the validity due to the lack of relevant information	More information was needed
Fedoroff, 1995[61] (Canada)	Although the study was in a consecutive sample of 100, it was up to the offender to choose the treatment. The treatment was voluntary and participants may have been rather motivated. There were no details about how the outcome was assessed. Co-morbidities and co-interventions as well as the absence of a control group weakened the study despite the comparatively large number of participants. Characteristic details were seriously lacking, at both baseline and following the intervention, e.g. age, nature of offence committed and dosages of the SSRIs and their side-effects. The data were not objectively or statistically assessed. The validity could not, therefore, be assessed with this level of information	The lack of important details of the outcomes limited its generalisability
Greenberg *et al.*, 1996[62] (Canada)	Retrospective design constituted a threat to validity. There is concern about selection, attrition and detection bias. Validity of fantasies measure was unclear. The considerable proportion of co-interventions and co-morbidities would have distorted any possible significant results	It was not possible to assess the effect of the intervention on the offence and conviction using this study design. The outcomes of the intervention did not seem directly relevant to preventing sexual deviances. It was unclear, if the treatment was suggested for life, how the compliance would be affected. There is also concern about the limited follow-up time
Kafka and Hennen, 2000[63] (USA)	Lack of control, selection bias, no blinding and a lack of ability to control confounding all affected the validity of the study	Whether cases in this study had a lot in common with people who are sex offenders with charges against them was unclear. The cases were not representative of a population, therefore, external validity of this study is questionable

Appendix 7

Search strategy for the systematic review of health economic evaluations

- NHS EED and DARE
- Effectiveness strategy for Cochrane Library
- Internet sites
  - Centre of Health Economics, University of York
  - Health Economics Research Unit
  - Health Economics Research Group
- MEDLINE 1985–November 2001

Search strategy

#1 (citalopram$ or seropram or cipramil).mp [mp = title, abstract, registry number word, MeSH] (1310)
#2 (fluoxetine$ or prozac).mp [mp = title, abstract, registry number word, MeSH] (152)
#3 (fluvoxamine$ or faverin or luvox).mp (1273)
#4 (paroxetine$ or seroxat or paxil).mp (1938)
#5 (sertraline$ or lustral or zoloft).mp (1264)
#6 (femoxetin or ifoxetine or viqualine).mp (12)
#7 serotonin uptake inhibitors/ (4628)
#8 ssri$.mp (1523)
#9 or/#1–#8 (7932)
#10 economics/ (10170)
#11 exp "costs and cost analysis"/ (112828)
#12 cost of illness/ (4219)
#13 exp health care costs/ (19777)
#14 economic value of life/ (1237)
#15 exp economics medical/ (10563)
#16 exp economics hospital/ (14773)
#17 economics pharmaceutical/ (1108)
#18 exp "fees and charges"/ (23455)
#19 (cost or costs or costed or costly or costing).tw (123121)
#20 (economic$ or pharmacoeconomic$ or price$ or pricing).tw (56977)
#21 or/#10–#20 (251144)
#22 #9 and #21 (247)
#23 limit #22 to yr = 1985–2001 (247)
#24 exp sex offenses/ (9043)
#25 exp paraphilias/ (3050)
#26 (paedophilia$ or pedophilia$).mp (443)
#27 (rape$ or rapist$).mp (4891)
#28 bugger$.mp (6)
#29 (indecent$ adj assault$).mp (10)
#30 incest$.mp (1481)
#31 ((sex$ adj2 offend$) or (sex$ adj2 offens$)).mp (743)
#32 or/#24–#31 (14201)
#33 #21 and #32 (186)
#34 quality of life/ (30678)
#35 life style/ (15940)
#36 health status/ (18341)
#37 health status indicators/ (6526)
#38 or/#34–#37 (66341)
#39 #32 and #38 (122)
#40 #33 or #39 (300)
#41 limit #40 to yr = 1985–2001 (247)
#42 from #23 keep 1–199 (199)
#43 from #23 keep 200–247 (48)
#44 from #41 keep 1–199 (199)

Appendix 8

Checklist for identifying direct and indirect additional costs and background

- Staff
- Training for staff
- Premises
- Other running costs, e.g. communication, information technology, stationery and travel costs
- Equipment for implementation
- Commissioned research and data collection for project implementation
- Documentation
- Levered-in resources

These are additional resources that would not have been deployed in the absence of the project, but are external to the project.[52]

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We look forward to hearing from you.

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