NCCHTA

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A Rapid Review for the HTA Programme

Clinical effectiveness and cost-consequences of the use of SSRIs in the treatment of sex offenders

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A. This protocol is provisional and subject to change

B. Details of the review team

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C. Full title of research question

"Clinical effectiveness and cost-consequences of the use of selective serotonin re-uptake inhibitors (SSRIs) in the treatment of sex offenders."

D. Clarification of research question and scope

SSRIs are relatively new drug treatments introduced in the early 1990s for the treatment of depression. Prozac, the trade name of one of the SSRIs, received much media coverage. It has been popularised in some best-selling books and was described as the "happy pill" because it has the reputation of making patients with mild depression happier. More recently, a few reports and studies suggest that these drugs may be of benefit in the treatment of sex offenders. Therefore, the focus of this report is on the effectiveness and cost-consequences of SSRIs for sex offenders.

The questions to be addressed by this review are:

Is the use of SSRIs effective in the treatment of sex offenders? What are the cost and consequences of their use?

The main objectives of this report are:

1. To identify trials published, unpublished or ongoing, reporting the use of SSRIs in the treatment of sex offenders. If no trials are identified, the best available evidence will be sought.

2. Systematically review the available evidence of effectiveness, beneficial and harmful effects of SSRIs in treating sex offenders in the identified studies.

3. Review the evidence on the cost of SSRIs and conduct cost-consequences analysis.

E. Report Methods

This report will adhere to advice and guidance provided by the National Co-ordinating Centre for Health and Technology Assessment (NCCHTA), the NHS Centre for Review and Dissemination[1] (NHS CRD) and West Midlands Development and Evaluation Service (DES).

a. Search strategy

Studies will be identified using the following sources:

- Electronic databases: Cochrane Library, Medline, Embase, PsycINFO, Science Citation Index and National Research Register
- Home office data (UK)
- National Criminal Justice Reference System in the USA
- Canadian criminal data
- Internet search engines
- Citation lists of included studies
- Conference abstracts
- Enquiry of pharmaceutical companies
- Enquiry of experts in the field

b. Inclusion/exclusion Criteria

Inclusion:

- ***Population***: Men or women, with or without mental illnesses, who exhibit sexual behaviour that is illegal under current UK law. The participants will include 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, death (suicide or other causes), penile plethismography (measure of erection in response to fantasies or photograph and video)

- ***Design***: Ideally, we will include any randomised control trials (RCTs). However, we will include other studies that report the use of SSRIs in sex offenders i.e. cohort studies, case control studies, or case series

Exclusion:

- Studies which only consider short-term follow up; follow up should exceed the minimally adequate period i.e. two years as suggested by the Home Office

- Studies using compound drugs such as *cianoproamine* (a tricyclic compound which selectively inhibits the reuptake of serotonin) and other drug treatments that inhibit both the reuptake of serotonin and noradrenaline

- Loss to follow up not reported, or higher than 25%

- Individual case reports

- Duplication; when several series emerge chronologically from the same source, only the largest and most recent series will be included

- There will be no exclusion on the basis of language

c. Data extraction

Two reviewers will extract the data independently and discrepancies will be discussed and resolved by consensus.

d. Quality assessment strategy

The quality of the included studies will be assessed by two independent reviewers. A checklist based on the NHS CRD guidance[1] and also from a checklist developed by West Midlands Development and Evaluation Services[2] (DES) will be used.

e. Methods of analysis/synthesis

We do not anticipate at this stage that quantitative synthesis (meta-analysis) will be appropriate. Therefore, conclusions will be drawn on a qualitative basis, considering the pattern revealed in clear tabulations of the results of included studies. Conclusions will take into account issues of internal and external validity provided by the extracted data.

An issue of particular concern where case-series are being considered is the possibility of co-interventions. This will be described in greater details if data is available in the primary studies.

Should sufficient data be available, subgroup analysis will be attempted on the basis of the type of sex offences, sex, and associated mental disorders.

f. Methods for estimating quality of life, costs, cost effectiveness and /or cost/QALY

We will search for any economic evaluation studies of drug treatments in treating sex offenders. These will be systematically appraised and presented. Because formal assessment of cost-effectiveness is unlikely to be feasible, we will relate information on cost, if it is available, to effects and effectiveness information in a cost-consequences analysis.

F. Project Management

a. Timetable:

Event	Deadline for submission to HTA programme
Submission of draft protocol	14 September 2001
Submission of finalised protocol	5 October 2001
Submission of progress report	14 December 2001
Submission of draft report	29 March 2002

b. Competing interest
Members of the review team declare no competing interests.

c. External reviewers
This review will be subject to external peer review by at least two experts. These reviewers will be chosen according to academic seniority and content expertise and will be agreed with NCCHTA. We will also identify peer reviewers to scrutinise methodological aspects of the report. External expert reviewers will see a complete and near final draft of the rapid review and will understand that their role is part of external quality assurance. We will return peer reviewers' signed copies to NCCHTA. Comments from external reviewers and our responses to these will be made available to NCCHTA in strict confidence for editorial review and approval.

G. Appendices

- Data Extraction Form
- Background

Data Extraction Form

ID ____

Reviewer:		**Extraction date:**	
First author:		**Publication year:**	
Title:		**Publication type:**	
Source:		**Country:**	
Institution:			

A. Inclusion/exclusion criteria

(Title /abstract) ☐ **(Full-text)** ☐

1. Study design:

RCT ☐

Cohort ☐

Case-control ☐

Case series ☐

2. Population characteristics:

	SSRIs	**Control**
Nature of sex offender		
Number		
Setting		
Age		
Sex		
Associated mental condition(s)		
Drinking information		
Ethnicity		
Adherence to treatment		
Non-sexual violence history		
Marital status		
Social Class		
Previous sexual offence		
Others		

3. Intervention of SSRIs:

Type of SSRIs	
Age at start	
Dose	
Other details	

Co-intervention details:

4. Comparator details if any:

5. Outcome:

What was measured at baseline?

What was measured after the intervention?

6. Follow-up period:

	Length of follow up
Intervention	
Comparator	

7. Rate of drop-out if stated

	n/N (rate)	Reason(s) if stated
Intervention		
Control		

Drop-out not stated ☐

9. Decision:

This study is included ☐

This study is excluded ☐

9. Authors' inclusion and exclusion criteria:

10. What was the Outcome(s)?

11. Results:

	Intervention		**Control**	
Outcome	**No. events**	**Total No. of participants**	**No. events**	**Total No. in control**
1				
2				
3				

11. Analysis:

	Comments:
Statistical techniques used:	

12. Economic evaluation data reported?

Yes ☐ No ☐

Details:

Estimation of cost

Modelling

Summary cost results

13. Comments:

BACKGROUND:

Sex offences can be defined as any violation of established legal or moral codes in respect to sexual behaviours[3]. These include offences with victims like rape, child sexual abuse, paraphilias, exhibitionism, and offences which are not usually associated with victims like 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 in some societies, intercourse outside marriage is considered a sexual offence and in others homosexuality is considered a sexual offence. Because what is considered a sexual deviation, mental illness or sexual offence is so culturally determined, for the purposes of this we have simply used the current UK legal framework to define the nature of sexual offending list which includes[4]: Rape, indecent assaults on females, indecent assaults on males, indecency between Males, buggery, unlawful sexual intercourse with girl under 16 years old, incest, procuration, abduction and gross indecency with a child.

The treatment of sexual offenders is a difficult and complex task. For a treatment to be successful, participants should be motivated to comply with the treatment. In sex offenders these conditions are not often met. The drug treatments currently available for sex offenders not only deny sex offenders from what they see as pleasurable but also impose some unacceptable side effects for a long period. Therefore it is not surprising that only a small proportion of sex offenders would voluntarily take hormonal treatment[5]. SSRIs have been suggested as an alternative treatment to hormonal interventions, and as far as can be told, with fewer adverse effect.

Sex disorders have received comparatively limited attention of mental health professionals in comparison to other mental health conditions[6]. The pharmaceutical industry does not seem to devote resources to developing and promoting products for this problem. With little public support for stigmatised offenders, funding research is limited. This is despite the serious nature of the problem and the profound and long-term sequelae among the victims. The cost of incarceration and management is staggering (>$2 billion in the US in 1990)[7]. There is a need for the sex offenders to be rehabilitated and be integrated reasonably in the community, so they do not relapse again. Therefore the importance of a proactive treatment should be seen as an essential service to society at large.

The ultimate expected goals for the successful treatment would be to help offenders to be accountable and in control so that they will be able to understand and interrupt the type of thought that may lead to sexual offending and reduce deviant sexual arousal.

Epidemiology

Recent research has suggested that sex offending is becoming an important public health issue**.** The burden of the sex offending can be taken from an estimated prevalence of condition in the society. It was reported in the United State that more than half of all women and one fifth of all men are likely to be sexually assaulted at some point in their lives.[8] Any figures for estimating the offence, is very likely to be

underestimated, as the conviction and reconviction rates are substantially different from the offending and reoffending rates.

When using the definition that "any event/interaction that the young person reported as unwanted/abuse before they were 18" a prevalence figure of 59% for women and 27% for men was obtained. When the definition was narrowed to "the cases involving some form of penetration or coerced/forced masturbation where the abuser was at least 5 years old" the prevalence figure fell to 4% for women and 2% for men.[9]

Sex offenders are usually excluded from participating in trials because they are believed to suffer from some sort of mental illnesses, and even if they do participate initially they will not comply with the treatment.[10]

Reconviction rate of sexual offenders

The gross underreporting of sex crimes makes clinically useful research of recidivism difficult to estimate with confidence. Different studies reported different rates, however, the sexual offence recidivism rate was 13.4% in a meta-analysis[10;11] of n=23,393. The question of how much does a programme have to reduce reoffences to call itself successful is therefore is not easily addressed as only a small proportion are reconvicted, and self-reporting data from offenders are not thought to be reliable.

Current service provision

People found guilty of a serious sexual offences usually serve a prison sentence of four years or more. During that time, they will be offered counselling and cognitive-behavioural therapy (CBT). CBT is now the dominant approach used in the UK for treatment of sexual offenders.[10;12] Although there are some studies supporting the effectiveness of CBT[13;14] other studies have found CBT treatment to have little impact on recidivism rates[15].

The treatment whether chemical or hormonal is not compulsory in the UK but it is in France and parts of the United States. After release from prison, these people may be offered drug treatment. It is also possible for these offenders to receive such treatment while they are in prison, or in special treatment units or medical centres.

While some authors maintain that sex offenders can gain from treatment, others argue that the vast majority of sex offenders can not benefit from treatment. This report is therefore justified to determine what is the strength of evidence about the effectiveness of SSRIs for the treatment of sex offenders.

Punishment and incapacitation, although have a role to play, but are inadequate by themselves alone. In response to the obvious need to reduce the risk of sexual recidivism, the number of treatment programmes has dramatically increased during the last two decades.

There are mainly three different types of treatments for sex offenders:

1. Cognitive behaviour therapy (CBT): This is currently the main treatment given for sex offenders' inmates.

2. Surgery: Castration as a treatment is now regarded as unethical due to the mutilative and irreversible nature of the procedure. It was however proved an effective treatment although the rate of recidivism did not become 0%, the post-surgical reoffense rate after a minimum of 5 years was 7.4% v 76.8% rate for pre-surgical reoffense.[16] Stereotactic neurosurgery is now only of theoretical interest

3. Drug treatment:

(i) In 1960s long acting phenothiazine products were used to suppress the sexual drive but the side effects were very unpleasant, tremor, rigidity and tardive dyskinesia.

(ii) Various hormonal agents have been tried in order to achieve chemical castration state. Estrogens, antiandrogen, long acting lutenizing gonadotropin-releasing hormone agonist (LHRH), Gonadotropin releasing hormone inhibiting factors (Gn-RH). The side effects of these agents may lead to poor compliance.

(iii) SSRIs

Description of new intervention of interest
In the UK, There are five generic names of SSRIs; *citalopram*, *fluoxetine***,** *fluvoxamine***,** *paroxetine***,** and *sertraline* . Outside the UK, *femoxetine*, *ifoxetine* and *viqualine* are other types of SSRIs that are available on the market. They selectively inhibit the re-uptake of serotonin (5-hydroxytryptamine, 5-HT). The main use for SSRIs is for the management of depression.. There have been some reports suggesting that SSRIs may be helpful in reducing recidivism rates of sexual offences.

The rational stated for the use of SSRIs for the treatment of sex offenders may come form the apparent relationship that has been suggested between clinical presentation of paraphilias and obsessive compulsive disorder (OCD) with respect to the unwanted repetitive nature and insight of the paraphilic behaviour.

SSRIs are known to cause adverse effects such as reduced sexual drive, impotence and ejaculatory dysfunction. It is not known if the use of SSRIs for treating sex offenders merely reflects their side effects profile or the effects of SSRIs are treating the depression state, or the SSRIs can help offenders to benefit more from cognitive behaviour therapy. These issues need a different type of research.

Licensed indications, contraindications and warnings
SSRIs are licensed for depressive illness, obsessive-compulsive disorder, panic disorder; social phobia.

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