Guide to Using Psychotropic Medication to Manage Behaviour Problems among Adults with Intellectual Disability

Technical Document

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Technical Document Section 3.7: Systematic Reviews: Psychostimulants

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Psychostimulants

Identification of primary trials on the use of psychostimulants in the management of behaviour problems in adults with a learning disability.

Databases used

	Search 1	Search 2	Search 3
PsycInfo	1990 to week 2 Oct 2005	1872 to 1990	1990 to week 4 June 2005
Medline	1990 to week 1 Oct 2005	1966 to 1990	1990 to week 3 June 2005
Embase	1990 to 43rd week of 2005	1980 to 1990	1990 to 26th week of 2005
Cinahl	1990 to week 2 Oct 2005	1982 to 1990	1990 to week 2 June 2005

Search terms

The databases were searched using the 84 phrases mentioned earlier, with the addition of the following search terms adapted specifically for the psychostimulant medication review:

85. cns stimulating drugs/ or exp amphetamine/ or exp caffeine/ or exp clonidine/ or exp dextroamphetamine/ or exp ephedrine/ or exp methamphetamine/ or exp methylphenidate/ or exp pemoline/
86. (atomoxetine or bupropion or zyban or dexamphetamine or dexamfetamine or Dexedrine or methylphenidate or ritalin or concerta or pemoline or clonidine or catapres or dixarit or adderal).tw.
87. exp BUPROPION/
88. exp CLONIDINE/
89. or/85-88
90. 84 and 89
91. limit 90 to (human and "300 adulthood <age 18 yrs and older>" and human and yr=1990-2005)

For search 2:
In order to perform this search, the limits of search 1 were reset so that all articles available in the databases, dated before 1990, could be retrieved. No new search terms were added to the original search.

For search 3:
In order to perform this search, the limits of search 1 were reset so that all articles related to children/ adolescents (under the age of 18 years) could be retrieved. No new search terms were added to the original search.

Results

Each of the databases retrieved the following number of citations for the different searches:

Database	Search 1	Search 2	Search 3
PsycInfo	23	11	34
Medline	28	14	45
Embase	97	9	120
Cinahl	178	3	148

Selection process

Search 1:
This search produced 326 citations altogether. In the first instance, the majority of citations were excluded based on duplication, title and abstract. This process left 5 citations to which the inclusion/ exclusion criterion was applied. 2 further citations were excluded because they did not fulfil the inclusion criteria and the full text for the remaining 3 were sought. Nevertheless, full text examination revealed that these 3 articles were not suitable for inclusion either; the reasons for excluding these 3 studies are given in table 15.

A breakdown of the selection process for this search is shown in figure 21.

Search 2:
Only 37 citations were generated by this search and each one was checked to ensure that any controlled trials would not be overlooked. All but 2 citations were excluded based on duplication, title and abstract. The full texts of 2 articles were obtained for closer inspection.

The breakdown of the selection process for this search is shown in figure 22.

Search 3:
347 citations were yielded from the databases for this search. It was possible to exclude 341 of these purely based on duplication, title and abstract. In addition to the remaining 6 citations, it was necessary to obtain the full text for a further 1 study discovered previously through hand searching.

It was identified that nearly all 7 studies investigated the use of methylphenidate in a mixed population of children with a LD, autism and ADHD. Furthermore, the outcome assessment scales consisted of those that are usually used for autism and ADHD (i.e. the Conners' rating scale). A third reviewer's opinion was therefore sought, whereby a consensus was reached between three reviewers that it would be best to exclude these studies given that methylphenidate is usually indicated for ADHD and so it is likely that symptoms of this were being targeted, as opposed to behavioural symptoms of a population with a LD. It proved difficult to tease apart the results for the two separate populations (LD and ADHD), consequently resulting in no studies being included from this search.

A breakdown of the selection process for this search is shown in figure 23.

Results: Included studies

Search 1
When updated in the 2nd week of October 2005, this search revealed one study in which ten participants were used but they were either given amphetamine or methylphenidate (Jou *et al*, 2004). As not all ten participants were taking the same psychostimulant, this study was not deemed suitable for inclusion in this review and instead referenced in the less than ten participants list, as it was possible to extract separate data for each of the participants from the full text. In addition, one further single case study was also found to be relevant and so referenced in the same list. Full texts for both of these studies were obtained and boxed.

Search 2:
Of the two full texts that were considered, one was excluded and the reason for doing so is given in table 15. The other study was on both adults and children but met all other requirements for inclusion in this review and so was included. This study explored the effectiveness of methylphenidate on various behaviour problems (Aman *et al*, 1982) and the characteristics of this study are provided in table 16.

Search 3 yielded no studies.

An overall summary of the findings for these 3 searches is provided in figure 24.

Figure 21: Search 1 – Psychostimulants

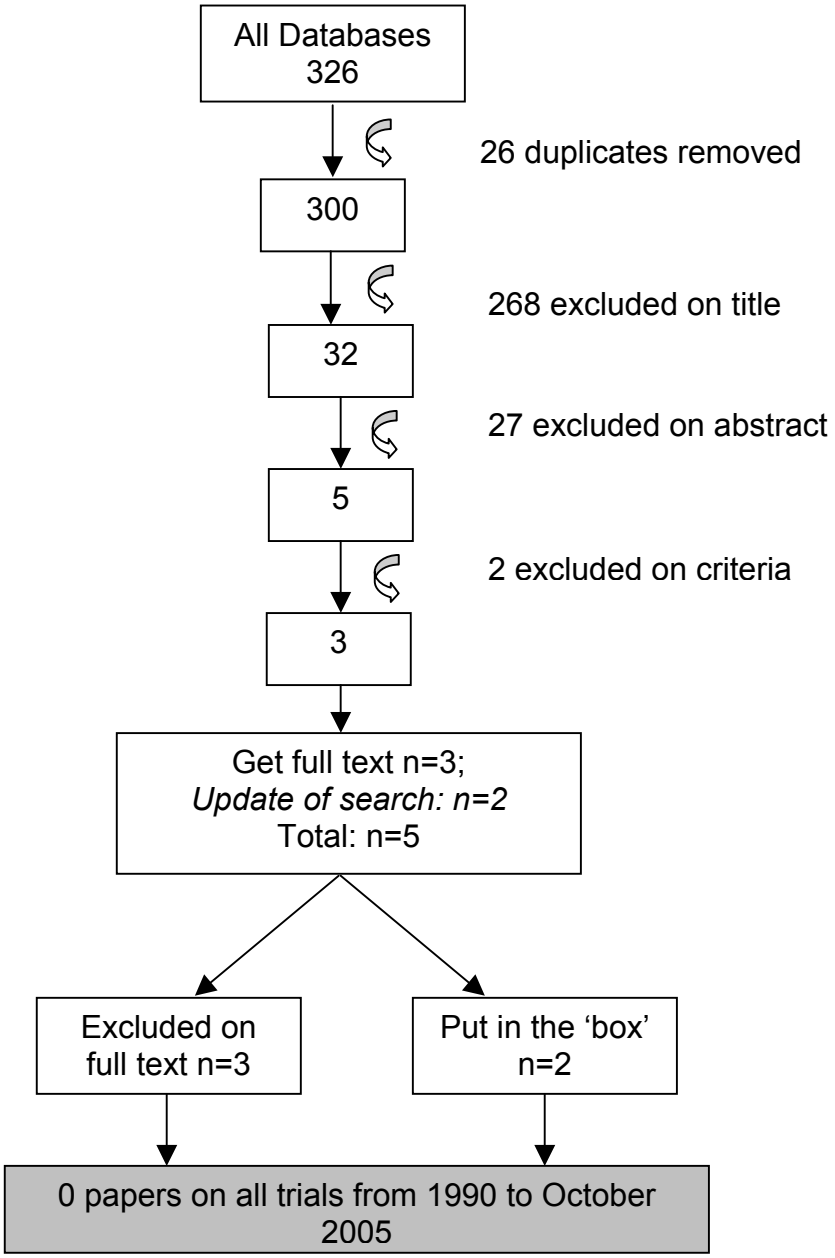


Figure 22: Search 2 - Psychostimulants

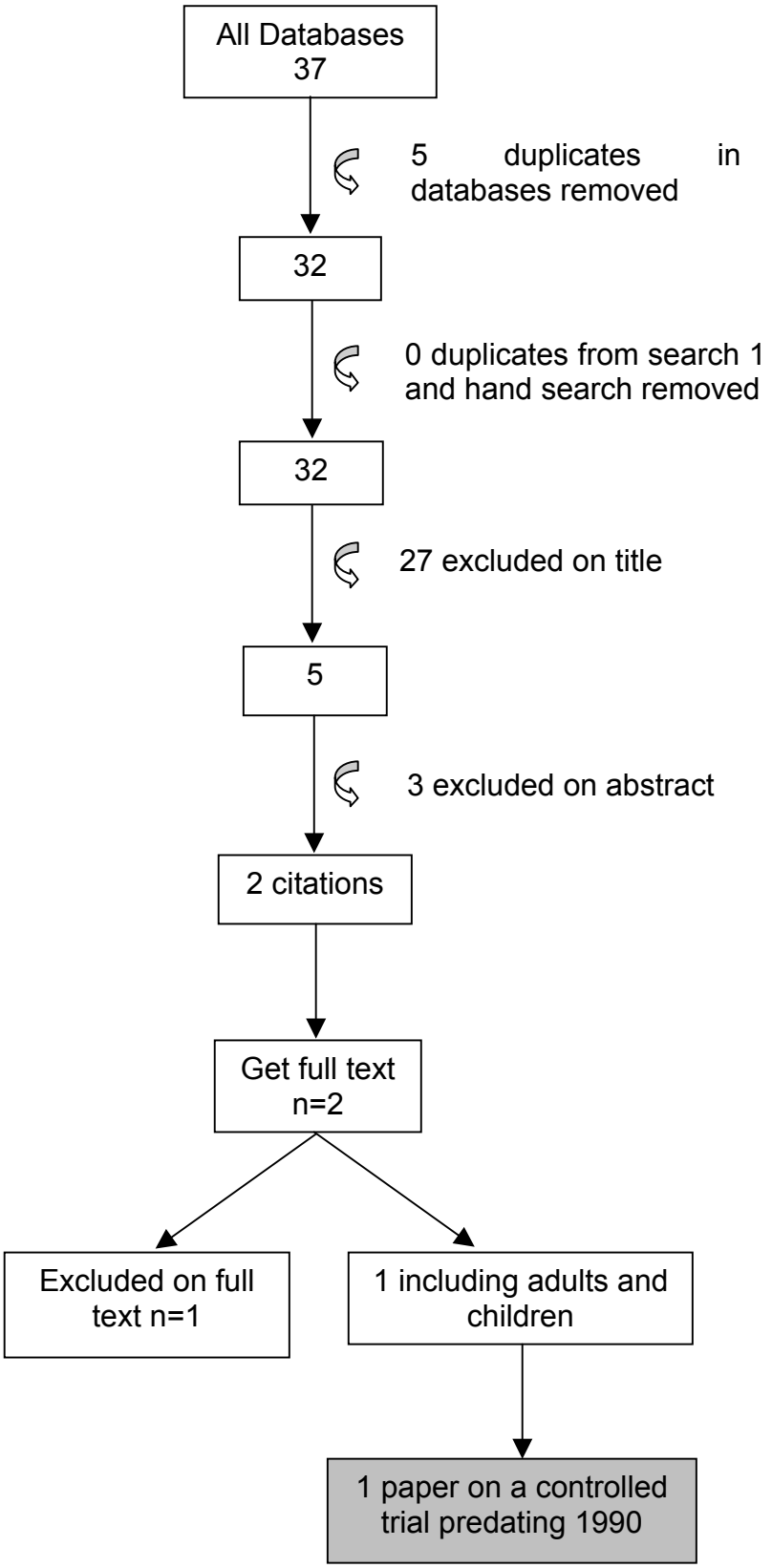


Figure 23: Search 3 - Psychostimulants

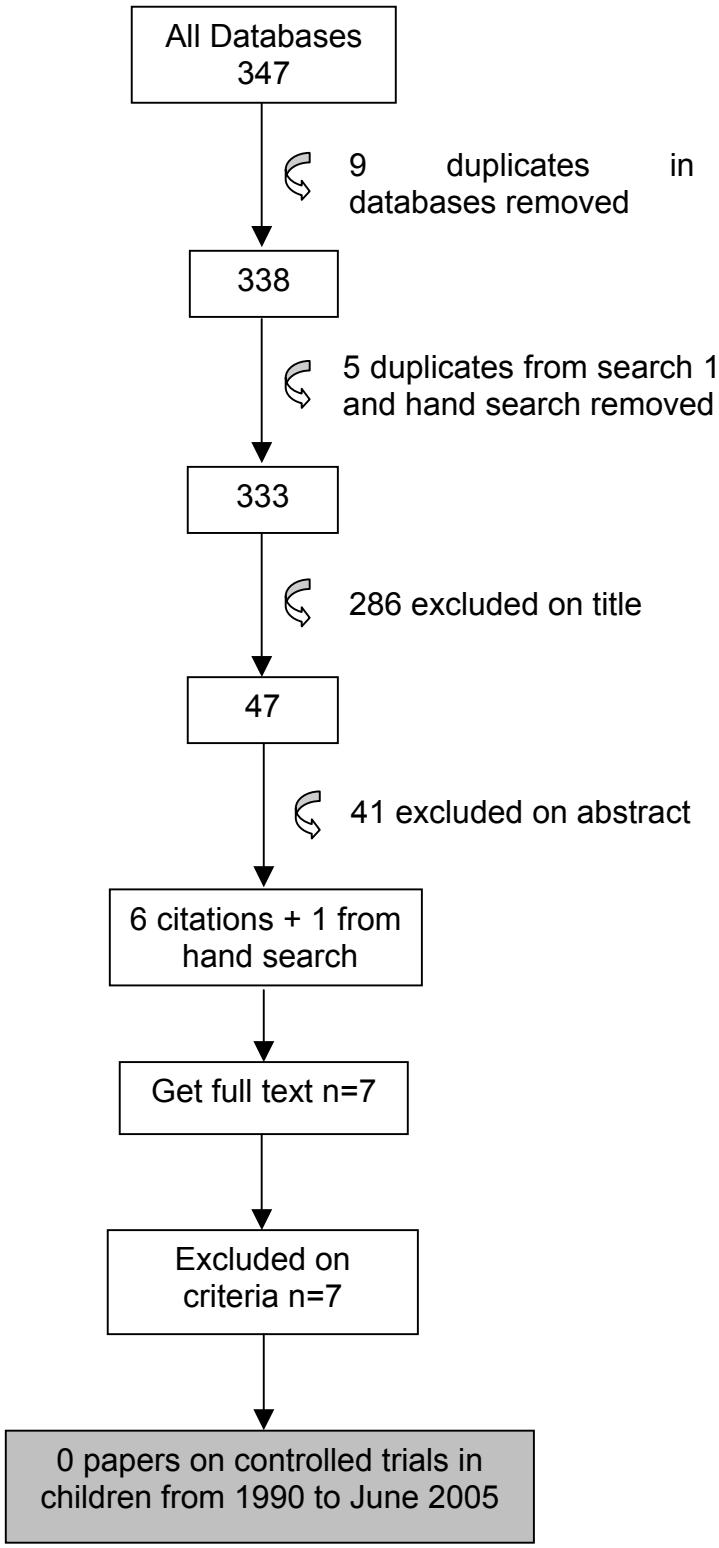
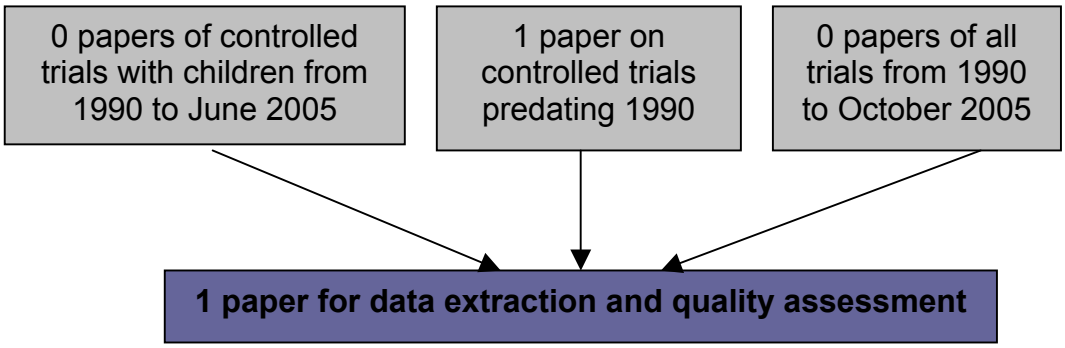


Figure 24: Summary of the psychostimulants search



Psychostimulants Review: Summaries of included studies

Controlled trials

Adults and Children

Aman et al. (1982)

Participants
28 participants, age range 13.6-26.4 years (71% male). All participants had a diagnosis of a profound or severe LD (mean IQ 11.96) with a variety of severe problem behaviours (e.g. stereotypic behaviour, severe aggressiveness, destructiveness, hyperactivity and temper tantrums).

Intervention
Methylphenidate 0.3mg/kg (low dose) and 0.6mg/kg (high dose) daily given in the morning or a matching placebo. Treatment duration was 1 week on the low dose, 1 week on the high dose and 1 week on placebo (total 3 weeks).

Method
A double blind, placebo controlled, crossover study. Following a 4-week medication free period. The participants were randomly assigned to receive the three phases of the study.

Follow-up
Participants were assessed at baseline (at the end of the 4-week washout period) and on each of the last 5 days of each week long treatment period.

Outcomes
Trained ward nurses made the outcome assessments. 1. AAMD Adaptive Behaviour Scale (using 18/44 categories that were suitable for use in the sample population). 2. Behaviour Rating Scale (developed by the authors). 3. Observational ratings of ward behaviour and mealtime behaviour.

Results
No therapeutically significant changes were observed for methylphenidate apart from on the Aggression/ Disruption factor of the Behaviour Rating Scale. Further analysis revealed that the source of this significance was comparisons between the high and low medication levels. Placebo did not differ significantly from either medication condition. There were some established effects on the categories of Aggression/ Disruption, Emotionality/ Crying and inappropriate behaviour on the ward; these findings were however, restricted to the high dose only.

Comments
Minimal medication changes were observed confined to the high dose condition. This study had rather short treatment duration of only 2 weeks on active medication. The sample size was restricted to participants with a profound or severe learning disability and it would have been beneficial to

address those who function at a higher level of intelligence but who still have a LD. This is study scored 6/14 on quality assessment (4/5 on Jadad criteria).

Table 15: Studies excluded on full text

Study	Summary	Reason for exclusion
Aman, 1985	This paper explored the effects of methylphenidate on dyskinetic symptoms in a population with a profound LD, following neuroleptic withdrawal. Methylphenidate was responsible for causing a mild worsening of symptoms.	The relevant findings from the controlled trial phase were presented in the study already included in the psychostimulants review (Aman *et al*, 1982).
Amaria, 2001	This was a survey type study exploring the various types of medication used in Fragile X Syndrome to manage hyperarousal, anxiety and mood lability. It was discovered that the adult population, both males and females, tended to make less use of stimulants and more use of SSRIs.	There was no one psychostimulant medication used to treat a behaviour problem and there was no specific data for those with an IQ level of 70 or below or for those aged 18 or over.
Thalayasingam, 1999	A single case study of an adult with a very mild LD who displayed a variety of maladaptive behaviours. In light of the failure of behavioural interventions to successfully manage his symptoms, methylphenidate treatment was initiated. This psychostimulant declined the frequency and intensity of some of the maladaptive behaviours.	The participant in this case had an IQ level of greater than 70.
Tu, 1992	A case series of three adolescents with Prader Willi Syndrome whom presented with frequent aggressive outbursts and food foraging behaviour. Carbamazepine controlled one patient and testosterone and behaviour therapy proved useful in the other two.	The participants were under 18 years of age and there was no psychostimulant medication given.

Table 16: Studies included in the psychostimulants review: Adults & Children

***Author*/ Evidence category (EC)**	**Medication/ Average daily dose**	**Target behaviour**	**Type of study**	**N**	**Outcome measures**	**Results**
Aman, 1982 EC I	Methylphenidate Low dose: 0.3mg/kg High dose: 0.6mg/kg	Various	RCT Crossover trial	28	AAMD Adaptive Behaviour Scale, Behaviour Rating Scale, direct observations	No therapeutic effect with Methylphenidate. Minimal changes were observed with the higher dose.

Evidence Categories - I: randomised controlled trial (RCT)

References for search 1

Psychostimulants Review
Relevant studies (N<10)

1. Dicesare A, McAdam DB, Toner A & Varrell J. The effects of methylphenidate on a functional analysis of disruptive behaviour: A replication and extension. *Journal of Applied Behaviour Analysis* 2005; 38 (1): 125-128.
2. Jou R, Handen B & Hardan A. Psychostimulant treatment of adults with mental retardation and attention-deficit hyperactivity disorder. *Australasian Psychiatry* 2004; 12 (4): 376-379.

Psychostimulants Review
Excluded studies

1. Amaria RN, Billeisen LL & Hagerman R. Medication use in fragile X syndrome. *Mental Health Aspects of Developmental Disabilities* 2001; 4 (4): 143-147.
2. Posey DJ, Puntney JI, Sasher TM, Kem DL & McDougle CJ. Guanfacine treatment of hyperactivity and inattention in pervasive developmental disorders: A retrospective analysis of 80 cases. *Journal of Child & Adolescent Psychopharmacology* 2004; 14 (2): 233-241.
3. Searle G F. The effect of dietary caffeine manipulation on blood caffeine, sleep and disturbed behaviour. *Journal of Intellectual Disability Research* 1994; 38(Pt 4): 383-391.
4. Thalayasingam SP. Use of methylphenidate in a young adult with intellectual disability and attention-deficit hyperactivity disorder: A single case report. *British Journal of Developmental Disabilities* 1999; 45(1): 63-68.
5. Tu JB, Hartridge C & Izawa J. Psychopharmacogenetic aspects of Prader-Willi syndrome. *Journal of the American Academy of Child & Adolescent Psychiatry* 1992; 31(6): 1137-40.

References for search 2

Psychostimulants Review
Included studies

Adults and Children:

1. Aman MG & Singh NN. Methylphenidate in severely retarded residents and the clinical significance of stereotypic behaviour. *Applied Research in Mental Retardation* 1982; 3 (4): 345-358.

Psychostimulants Review
Excluded studies

1. Aman MG & Singh NN. Dyskinetic symptoms in profoundly rertarded residents following neuroleptic withdrawal and during methylphenidate treatment. *Journal of Mental Deficiency Research* 1985; 29: 187-195.