

**FINAL Comprehensive Research Plan:
Pharmacologic Treatment of Attention Deficit
Hyperactivity Disorder (ADHD) in Adults**

Systematic Review Unit

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Comparative safety and efficacy of pharmacologic treatments for Attention Deficit Hyperactivity Disorder (ADHD) in Adults: Protocol for an update of a systematic review and network meta-analysis

BACKGROUND

Attention deficit hyperactivity disorder (ADHD) is a common and complex neurobehavioural disorder that is usually associated with school-age children. Prevalence in children is estimated to be between 5% and 10% and may persist or develop in 1% to 6% of adults (1, 2). Clinically significant symptoms of ADHD include behavioral and cognitive symptoms such as hyperactivity, inattention, disorganization, and impulsivity. Diagnosis is multifaceted and symptoms will vary across individuals and symptom domains. The *Diagnostic and Statistical Manual of Mental Disorders, 4th edition*, (DSM-IV) diagnostic criteria requires persistent, clinically significant impairment and symptoms must be severe across several domains of a person's life once all alternative explanations for symptoms have been eliminated (3, 4). Certain symptoms like hyperactivity may decrease in adulthood, but inattention, disorganization, and impulsivity may continue or intensify making daily functioning at home and work difficult or burdensome for those with ADHD (5). It has been suggested that adults living with ADHD are more likely to experience academic failure, loss of employment, poorer socioeconomic outcomes, and even higher rates of motor vehicle accidents or divorce (6). Additionally, psychiatric and mood disorders are more prevalent in adults with ADHD than in the general population and higher than average substance abuse is also associated with this condition (2, 7).

Treatments for adults with ADHD can be psychosocial, pharmacologic, or a combination of the two. Not all adults with ADHD require medication. When pharmacological treatment is indicated, two broad categories of medications are considered – stimulants and non-stimulants. Guidelines currently recommend long acting stimulants, including methylphenidate, lisdexamfetamine and amphetamine compounds, as sustained first-line therapy for uncomplicated adults with ADHD (8, 9). The selective norepinephrine reuptake inhibitor atomoxetine, and other non-stimulants clonidine, guanfacine and bupropion, are available as a second-line choices if stimulants are not efficacious or well tolerated, or for those with concomitant mood or psychiatric disorders. Not all of the non-stimulants are approved for use in adults with ADHD in Canada, but this group of medications is often used off-label in ADHD populations with unmet treatment needs. Although there is generally consensus on pharmacotherapy, few randomized, controlled trials (RCTs) have studied the long term benefits and harms of these drugs. A large proportion of RCTs compare pharmacotherapies to placebo, making comparisons across the various medications difficult. Limited randomized evidence comparing one medication to another exists (10). Although the benefits and harms of stimulants and non-stimulants have been previously studied, new clinical trial evidence necessitates an update of syntheses is required (11-16).

We are carrying out this review to update a previous high-quality systematic review to determine the

comparative benefits and harms associated with the various pharmacologic treatments available for adults with ADHD (10).

OBJECTIVE

The objective of this review is to help policy and decision-makers, health professionals and patients in Ontario make informed choices about the use of medications for adults with attention deficit hyperactivity disorder (ADHD). We aim to summarize the comparative safety and efficacy of pharmacologic treatments (name) for adults with ADHD.

Study Questions

1. What is the comparative safety and efficacy of pharmacologic treatments (stimulants and non-stimulants) for adults with ADHD?
2. What is the comparative safety and efficacy of pharmacologic treatments for ADHD in subgroups of patients with ADHD specific co-morbidities (e.g., psychiatric or mood disorder, substance abuse)?

PICO STATEMENT

The population, intervention, comparator, and outcome (PICO) statement, including the study designs of interest, is as follows:

Study population

Adults (age ≥ 18 years) outpatients with attention deficit disorders.

- Attention deficit disorder
- Attention deficit hyperactivity disorder

We will report how ADHD was diagnosed across the included studies.

Intervention and Comparators:

We aim to compare the following pharmacotherapies to placebo or to each other in direct or indirect comparisons:

Active ingredient(s)	Common name ^a	Trade Name	Format
Amphetamine mixture (amphetamine aspartate; amphetamine sulfate; dextroamphetamine saccharate; dextroamphetamine sulfate)	Mixed amphetamine salts XR	Adderall XR	Extended-release oral capsule
Atomoxetine hydrochloride	Atomoxetine	Strattera	Oral capsule
Bupropion hydrochloride	Sustained-release bupropion	Wellbutrin SR	Oral tablet
	Extended-release bupropion	Wellbutrin XL	Oral tablet
Clonidine hydrochloride	Immediate-release clonidine	Catapres	Oral tablet
	Extended-release clonidine	Kapvay	Extended-release oral tablet
Dexmethylphenidate hydrochloride	Immediate-release dexmethylphenidate	Focalin	Oral tablet
	Extended-release dexmethylphenidate	Focalin XR	Extended-release oral capsule
Dextroamphetamine sulfate	Immediate-release dextroamphetamine	Dexedrine	Oral tablet
	Sustained-release dextroamphetamine	Dexedrine Spansule	Sustained-release oral capsule
Guanfacine hydrochloride	Immediate-release guanfacine	Tenex	Oral tablet
	Extended-release guanfacine	Intuniv SR	Extended-release oral tablet
Lisdexamfetamine dimesylate	Lisdexamfetamine	Vyvanse	Oral capsule
Methamphetamine hydrochloride	Methamphetamine	Desoxyn	Oral tablet
Methylphenidate hydrochloride	Methylphenidate osmotic-release oral system	Concerta	Extended-release oral tablet
	Methylphenidate CD	Metadate CD	Extended-release oral capsule
	Methylphenidate ER	Metadate ER	Extended-release oral tablet
	Methylphenidate chewable Methylphenidate solution	Methylin	Oral chewable tablet and Oral solution
	Immediate-release methylphenidate	Ritalin	Oral tablet
	Methylphenidate long-acting	Ritalin LA	Extended-release oral capsule
	Multilayer-release methylphenidate	Biphentin	Extended-release oral capsule
	Methylphenidate sustained-release	Ritalin SR	Extended-release oral tablet
Modafinil	Modafinil	Provigil	Oral tablet
		Alertec ^b	Oral tablet

Abbreviations: ER, extended release; LA, long acting; SR, sustained release; XR, extended release.

a: We will refer to the drug by this name throughout our review. b: May also be under the brand name Modavigil in Australia and New Zealand

Time and data permitting, and based on prioritization by the research team in consultation with clinical experts, we will consider the following sub-group comparisons:

- Co-morbid psychiatric or mood disorders;
- Standard/recommended and high doses;
- Medium (1-2 yr) or long-term (>2 yrs) efficacy and safety;
- Treatment experience;
- Immediate, sustained or extended and modified-release formulations;
- Generic and innovator (branded) products;

Analysis of subgroups may be limited to select efficacy and safety outcomes.

Combinations of stimulants and non-stimulants will be included only if they are identified during the literature search update (see Methods). Combinations of stimulants and non-stimulants will be included if they are compared to placebo, no treatment (or equivalent) or an active comparator of interest. No combinations of pharmacotherapy with any herbal, behavioural or non-drug comparators will be included.

The intervention must aim to treat adults with ADHD, regardless of comorbid conditions in the population. Complex interventions, where interventions and comparators are only one component of multi-faceted intervention (e.g., methylphenidate plus exercise plus telephone counselling) will be excluded.

Outcome(s) of Interest:

Efficacy

Proposed efficacy outcomes:

- Clinical response (dichotomous outcome) as the proportion of participants who respond to the intervention based on improvements in the standardized ratings scale.*
- Disease-specific quality of life (continuous outcome)†
- Functional (occupational) capacity (continuous outcome)∞
- Executive function (continuous outcome)∞
- Driving Behavior[§]

* If data does not permit a robust analysis for clinical response based on disease-specific scales (e.g., The Adult ADHD Investigator Symptom Rating Scale (AISRS), ADHD Rating Scale (ADHD-RS), The Conners' Adult ADHD Rating Scale (CAARS), or The Wender–Reimherr Adult Attention Deficit Disorder Scale (WRAADDs)), further analysis using a broader range of rating scores may be considered. Decisions on extraction and analysis of scales representing clinical response will be based on consultation with the ODPN research team and the clinical experts advising this review. Analysis may be limited to total symptom scores with sub-scales of the individual instruments only utilized where total scores are not reported.

† Focus will be on disease-specific instruments able to measure quality of life independent from symptom improvement (e.g.,

Attention Deficit Hyperactivity Disorder Impact Module-Adult Version (AIM-A), Adult attention deficit hyperactivity disorder quality of life (AAQoL). As time and data from the disease-specific instruments is inadequate, we may explore more general health-related quality of life (e.g., Quality of life Enjoyment and Satisfaction Questionnaire - Short Form (Q-LES-Q-SF), World Health Organization Quality of Life (WHOQoL), 36-Item Short Form Health Survey (SF-36)).

∞ Decisions on extraction and analysis of scales representing functional capacity and executive function will be decided on in consultation with the ODPN research team and the clinical experts advising this review.

§Narrative summary of outcomes only.

Safety

Proposed safety outcomes:

- Withdrawals due to adverse effects (dichotomous outcome)
- Treatment discontinuations(dichotomous outcome)
- Serious adverse effects (total count)(dichotomous outcome)
- Cardiovascular events, including outpatient myocardial infarction, stroke, unexpected cardiac death*(dichotomous outcome)
- Hospitalization (dichotomous outcome)
- Emergency Room Visits (dichotomous outcome)

*If data permits we will look at both a composite of cardiovascular events and the individual outcomes reported within.

Studies will not be excluded based on the outcomes that are reported. All studies that meet the requirements for population, intervention, comparator and study design will be formally included in the review, however, data will only be extracted for studies reporting outcomes of interest.

Included Study Designs

Included: Randomized Controlled Trials. No controlled clinical trials. Crossover designs will be included, however, only studies reporting data from the first period prior to time of crossover will be included in the analyses.

Other: We will limit inclusion to studies written in English. Abstracts will be excluded. Studies will be excluded if they are not conducted in humans or are conducted in less than 10 participants.

METHODS

The strategy for building and analyzing the evidence base for the efficacy and safety of pharmacotherapies for adults with ADHD consists of two fundamental steps*:

1. Update of an existing, high-quality systematic review

In order to meet the rigorous timelines of the review process, we propose to update a comprehensive, well-conducted, recent (within 5 years) evidence synthesis that meets the PICO requirements and contain intervention studies that meet our inclusion criteria (10). We will build onto the studies included in the existing review. A new literature search will capture studies published from the date of the last literature search (week 4, June 2011) to present, with retrospective overlap of 12 months.*

Studies identified from the existing SR will be subjected de novo to the standard SR methods following title and abstract screening, namely: eligibility assessment and data abstraction by two independent review authors (or extraction by one reviewer with checking by a second) and quality assessment. These methods and procedures will be identical to those followed for the articles identified in the literature search update, and the information on the articles from these two sources will be combined in generating the table of characteristics (with design elements and PICO elements), the risk of bias tables (at the article and review level) and the data tables for analysis.

2. A Bayesian network meta-analysis of randomized evidence

When data were available, sufficiently similar, and of sufficient quality, Bayesian network meta-analyses (NMA) will be considered for each of the efficacy and safety outcomes specified a priori. Choice of outcomes for NMA will be based on their importance and the sufficiency of the data available to derive robust and consistent network models. The methods and procedures to be followed are those developed by the Canadian Collaboration for Drug Safety, Effectiveness and Network Meta-Analysis (ccNMA), funded by the Drug Safety and Effectiveness Network (DSEN) of the Canadian Institute of Health Research.

* Evidence submission packages submitted to ODPRN from interested stakeholders will also be considered.

Protocol Development

The Preferred Reporting Items for Systematic reviews and Meta-analysis for Protocols (PRISMA-P) Statement will guide review reporting of our protocol (17). The draft protocol will be circulated and/or posted on a public website to receive feedback from key stakeholders including the broader OPDRN research team, clinical experts, patient groups, review methodologists and other interested stakeholders. Following stakeholder review, the protocol will be registered in PROSPERO (registration pending).

Literature Search

The literature search (or update of the literature search) will be conducted by a professional Information Scientist (IS). Databases and grey literature will be searched from 12 months prior to the date of the last literature search to present. All citations will be imported into an electronic reference management

database (EndNote[®], Thomson Reuters).

Literature search strategies will build on the previous literature search and be developed using medical subject headings (MeSH) and text words related to the population, interventions and comparators specified in the PICO statement. Searches will use validated filters for RCTs. All studies will be included regardless of publication status (i.e., unpublished studies) and year of publication. A limited grey-literature search will be carried out by searching the websites of health technology assessment and related agencies, professional associations, and other specialized databases (following CADTH “Grey Matters Light”)(available at: http://www.cadth.ca/media/is/cadth_Handout_greymatters_light_e.pdf).

Search strategies from the previous systematic review have been provided in Appendix A.

Eligibility Criteria

Studies will be selected and assessed for eligibility de novo whether they were previously included in a existing systematic review that is being updated or through a structured literature search update.

Selection eligibility criteria will be applied to each title and abstract by two independent review authors in a standardized manner using electronic tools customized for the project in DistillerSR, an online systematic review management and screening tool. Any uncertainties will be resolved by discussion and consensus with a third review author. All studies that meet the selection criteria will be obtained in full-text format. The eligibility criteria (Exhibit 1) will then be applied, and a final decision will be made for inclusion. The reviewers will not be blinded as to the study authors or centre of publication prior to study selection because this can complicate the review process and only weak evidence suggests that this would improve the results.

Data Extraction Process

All information will be extracted using standardized data extraction forms, which will be developed, piloted, and modified as necessary. Data will be extracted by a single review author, and checked for accuracy by a second independent review author. The following data will be extracted from included RCTs:

1. Study characteristics (design, duration, setting, funding);
2. Baseline patient characteristics;
3. Interventions evaluated, including dose, duration, and relevant concomitant medication;
4. Efficacy and safety results for specified outcomes (end of treatment and/or study);
5. Type of analysis (intention-to-treat [ITT], modifiedITT or per-protocol) and definitions if those employed were not standard;
6. Study-level definitions of ADHD.

Risk of Bias Assessment

We will assess internal validity of included studies using the Cochrane Collaboration's tool for assessing risk of bias (18).

Assessment of Reporting Bias

Reporting bias will be assessed by use of funnel plots, as well as bias indicators (e.g. Egger, Harbord-Egger), for each outcome.

Data Synthesis

Data will initially be summarized descriptively. The results will be assessed for both clinical and methodological diversity. Clinical diversity will be assessed by checking that the participants, interventions, and comparators are not too different from each other such that combining them is not appropriate. Methodological diversity will be assessed by checking that the studies are similar in terms of study design and risk of bias.

Once it has been established that the studies are minimally diverse and that it makes sense to pool them together in a meta-analysis, an assessment of the statistical heterogeneity will be undertaken by examining the forest plot and result of the I^2 statistic (forest plots provide a visual sense of heterogeneity, and the I^2 statistic indicates the presence of statistical heterogeneity). If the effects observed across trials are inconsistent and vary to a large extent (e.g., $I^2 > 50\%$), the results will be explored to assess whether the differences can be explained by some clinical or methodological feature. Inconsistency that cannot be reduced by pre-specified subgroup or meta-regression analyses will lead to an overall estimate with less confidence when interpreting the inference from the meta-analysis. In this case, a more conservative random-effects model approach would be used so that the uncertainty of the single effect estimate is reflected by wider confidence intervals.

A meta-analysis will be undertaken using fixed- or random-effects models when data are available, sufficiently similar, and of sufficient quality. The effect sizes for the identified dichotomous outcomes will be expressed in terms of risk ratio (RR) or odds ratio (OR). In the case of rare events, the Peto odds ratio will be used. For continuous outcomes, the effect size will be expressed in terms of the mean difference (MD) and standardized mean difference (SMD). A summary of findings table will highlight key results from direct comparisons.

Bayesian Network Meta-Analysis Methods

Bayesian NMA will be conducted using WinBUGS software (MRC Biostatistics Unit, Cambridge, UK) (19, 20). The use of a Bayesian NMA offers several advantages, including:

1. The ability to indirectly compare drugs that have not been compared directly with each other in a large number of studies. Bayesian network meta-analysis permits combination of all head-to-head and placebo-controlled evidence; and,
2. The number of individual pair-wise comparisons between the pharmacological treatments for ADHD is large, given the large number of available treatment options. As a result, summary effect estimates against a common comparator are likely to be of greater utility for clinical and policy decisions. Further, we will also construct graphical aids to assist in decision making.

Bayesian NMA will be considered for each of the efficacy and safety outcomes specified a priori. Choice of outcomes for NMA will be based on their importance and the sufficiency of the data available to derive robust and consistent network models. Both fixed- and random-effects network meta-analyses will be conducted and results will be transparently reported in the final publication. Model fit for Bayesian analyses will be based on the Deviance Information Criterion (DIC) and comparison of residual deviance to number of unconstrained data points (21-24). Selection of the model/measure will depend on the outcome of interest and the availability of data. Heterogeneity across trials in terms of patient characteristics, trial methodologies, and treatment protocols will be carefully assessed. To further investigate heterogeneity, subgroup analyses and meta-regressions (23, 24) may be conducted to explore the effect of various characteristics including but not limited to the variables considered for the subgroup analyses.

We may also perform analyses including removal of studies from the network of therapies that were not scored as being of high quality. We will formally (24) and informally assess consistency between direct and indirect evidence by comparing direct estimates obtained from meta-analysis with estimates from the Bayesian network meta-analysis (22, 23). Model diagnostics including trace plots and the Brooks-Gelman-Rubin statistic will be assessed to ensure model convergence. At least two chains will be fit in WinBUGS for each analysis, each employing at least 10,000 iterations, with a burn-in of at least 20,000 iterations (20, 22).

Timeline and Deliverables

Work will commence on acceptance of this protocol. The systematic review, meta-analysis, and Bayesian network meta-analysis will be completed in approximately 12 weeks to 16 weeks. Any requested re-analyses and a revised report will be available 4 weeks following receipt of stakeholder reviews.

We will provide a written censored report to ODPRN detailing methods adopted, results, discussion and key outcome highlights within 16 weeks of study protocol approval. Outcome data required for economic evaluation will be provided to the ODPRN pharmacoeconomics team approximately 12 weeks after protocol approval.

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APPENDIX A: Literature search strategy from the previous systematic review (10)

Note that not all search terms apply to this review as the previous review included children and adolescents and a number of research questions not of interest to this review. Searches were repeated in July 2011 to identify additional citations. Date limits applied were only used in the most recent update of this review.

Database: Ovid MEDLINE(R) without Revisions <1996 to January Week 4 2011>

Search Strategy:

-
1. exp Amphetamine/ or "amphetamine\$".mp. (10584)
 2. adderall.mp. (113)
 3. [atomoxetine](#).mp. (645)
 4. strattera.mp. (38)
 5. [dexmethylphenidate](#).mp. (43)
 6. focalin.mp. (15)
 7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (1340)
 8. dexedrine.mp. (21)
 9. dextrostat.mp. (0)
 10. [methylphenidate](#).mp. or exp Methylphenidate/ (3023)
 11. concerta.mp. (67)
 12. metadate.mp. (20)
 13. methylin.mp. (1)
 14. Ritalin.mp. (272)
 15. biphentin.mp. (1)
 16. [modafinil](#).mp. (816)
 17. provigil.mp. (29)
 18. Alertec.mp. (0)
 19. [methamphetamine](#).mp. or exp methamphetamine/ (4493)
 20. desoxyn.mp. (0)
 21. [lisdexamfetamine](#).mp. (52)
 22. vivanse.mp. (0)
 23. daytrana.mp. (4)
 24. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (16739)
 25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (11409)
 26. Attention deficit disorder.mp. (11586)
 27. attention deficit\$.mp. (14584)
 28. adhd.mp. (8178)
 29. 25 or 26 or 27 or 28 (14858)
 30. 24 and 29 (2712)
 31. (2009\$ or 2010\$ or 2011\$).ed. (1459797)

32. 30 and 31 (590)
33. limit 32 to (english language and humans) (435)
34. limit 33 to (clinical trial, all or clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or “review”) (248)
35. observational stud\$.mp. or exp Cohort Studies/ or cohort\$.mp. or exp Retrospective Studies/ or retrospective\$.mp. (823043)
36. 33 and 35 (67)
37. 34 or 36 (284)

Database: Ovid MEDLINE(R) without Revisions <1996 to January Week 4 2011>

Search Strategy:

-
1. exp Amphetamine/ or “amphetamine\$”.mp. (10584)
 2. adderall.mp. (113)
 3. [atomoxetine](#).mp. (645)
 4. strattera.mp. (38)
 5. [dexmethylphenidate](#).mp. (43)
 6. focalin.mp. (15)
 7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (1340)
 8. dexedrine.mp. (21)
 9. dextrostat.mp. (0)
 10. [methylphenidate](#).mp. or exp Methylphenidate/ (3023)
 11. concerta.mp. (67)
 12. metadate.mp. (20)
 13. methylin.mp. (1)
 14. Ritalin.mp. (272)
 15. biphentin.mp. (1)
 16. [modafinil](#).mp. (816)
 17. provigil.mp. (29)
 18. Alertec.mp. (0)
 19. [methamphetamine](#).mp. or exp methamphetamine/ (4493)
 20. desoxyn.mp. (0)
 21. [lisdexamfetamine](#).mp. (52)
 22. vivanse.mp. (0)
 23. daytrana.mp. (4)
 24. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (16739)
 25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (11409)
 26. Attention deficit disorder.mp. (11586)
 27. attention deficit\$.mp. (14584)
 28. adhd.mp. (8178)
 29. 25 or 26 or 27 or 28 (14858)
 30. Central Nervous system Stimulants.mp. or exp Central Nervous System Stimulants/ (38845)
 31. 24 or 30 (44848)

32. 29 and 31 (3446)
33. diversion.mp. (6404)
34. exp Substance-Related Disorders/ (135546)
35. ((drug\$ or substance\$ or stimula\$) adj3 (abus\$ or addict\$)).mp. (35433)
36. (misuse\$ or misusing).mp. (7077)
37. exp Behavior, Addictive/ (3156)
38. (addict\$ adj3 behav\$).mp. (4053)
39. (drug\$ adj3 seek\$).mp. (1272)
40. 33 or 34 or 35 or 36 or 37 or 38 or 39 (159162)
41. 32 and 40 (469)
42. illegal\$.mp. (3656)
43. unlawful\$.mp. (181)
44. illicit\$.mp. (5269)
45. criminal\$.mp. (8535)
46. 42 or 43 or 44 or 45 (16948)
47. 32 and 46 (40)
48. 41 or 47 (474)
49. limit 48 to (english language and humans) (397)
50. (2009\$ or 2010\$ or 2011\$).ed. (1459797)
51. 49 and 50 (83)
52. limit 51 to (clinical trial, all or clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or “review”) (41)
53. observational stud\$.mp. or exp Cohort Studies/ or cohort\$.mp. or exp Retrospective Studies/ or retrospective\$.mp. (823043)
54. 51 and 53 (12)
55. 52 or 54 (48)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <4th Quarter 2010>
 Search Strategy:

-
1. exp Amphetamine/ or “amphetamine\$”.mp. (1106)
 2. adderall.mp. (45)
 3. [atomoxetine](#).mp. (146)
 4. strattera.mp. (7)
 5. [dexmethylphenidate](#).mp. (17)
 6. focalin.mp. (8)
 7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (512)
 8. dexedrine.mp. (15)
 9. dextrostat.mp. (0)
 10. [methylphenidate](#).mp. or exp Methylphenidate/ (1203)
 11. concerta.mp. (31)
 12. metadate.mp. (6)
 13. methylin.mp. (0)
 14. Ritalin.mp. (104)
 15. biphentin.mp. (1)

16. [modafinil](#).mp. (277)
17. [provigil](#).mp. (7)
18. [Alertec](#).mp. (0)
19. [methamphetamine](#).mp. or exp methamphetamine/ (250)
20. [desoxyn](#).mp. (0)
21. [lisdexamfetamine](#).mp. (13)
22. [vivanse](#).mp. (0)
23. [daytrana](#).mp. (0)
24. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (2731)
25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (1154)
26. Attention deficit disorder.mp. (1274)
27. attention deficit\$.mp. (1548)
28. [adhd](#).mp. (1008)
29. 25 or 26 or 27 or 28 (1707)
30. 24 and 29 (960)
31. limit 30 to yr="2009 -Current" (74)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <4th Quarter 2010>
 Search Strategy:

-
1. exp Amphetamine/ or "amphetamine\$".mp. (1106)
 2. [adderall](#).mp. (45)
 3. [atomoxetine](#).mp. (146)
 4. [strattera](#).mp. (7)
 5. [dexmethylphenidate](#).mp. (17)
 6. [focalin](#).mp. (8)
 7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (512)
 8. [dexedrine](#).mp. (15)
 9. [dextrostat](#).mp. (0)
 10. [methylphenidate](#).mp. or exp Methylphenidate/ (1203)
 11. [concerta](#).mp. (31)
 12. [metadate](#).mp. (6)
 13. [methylin](#).mp. (0)
 14. [Ritalin](#).mp. (104)
 15. [biphentin](#).mp. (1)
 16. [modafinil](#).mp. (277)
 17. [provigil](#).mp. (7)
 18. [Alertec](#).mp. (0)
 19. [methamphetamine](#).mp. or exp methamphetamine/ (250)
 20. [desoxyn](#).mp. (0)
 21. [lisdexamfetamine](#).mp. (13)
 22. [vivanse](#).mp. (0)
 23. [daytrana](#).mp. (0)
 24. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or

- 20 or 21 or 22 or 23 (2731)
25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (1154)
 26. Attention deficit disorder.mp. (1274)
 27. attention deficit\$.mp. (1548)
 28. adhd.mp. (1008)
 29. 25 or 26 or 27 or 28 (1707)
 30. Central Nervous system Stimulants.mp. or exp Central Nervous System Stimulants/ (3771)
 31. 24 or 30 (4855)
 32. 29 and 31 (988)
 33. diversion.mp. (209)
 34. substance abuse.mp. or exp Substance-Related Disorders/ (7400)
 35. misuse.mp. (258)
 36. addictive behavior.mp. or exp Behavior, Addictive/ (215)
 37. 35 or 33 or 34 or 36 (7836)
 38. 32 and 37 (30)
 39. limit 38 to yr="2009 -Current" (3)

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to January 2011>

Search Strategy:

-
1. exp Amphetamine/ or "amphetamine\$".mp. (67)
 2. adderall.mp. (2)
 3. [atomoxetine](#).mp. (13)
 4. strattera.mp. (0)
 5. [dexmethylphenidate](#).mp. (4)
 6. focalin.mp. (4)
 7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (21)
 8. dexedrine.mp. (6)
 9. dextrostat.mp. (1)
 10. [methylphenidate](#).mp. or exp Methylphenidate/ (47)
 11. concerta.mp. (4)
 12. metadate.mp. (0)
 13. methylin.mp. (1)
 14. Ritalin.mp. (8)
 15. biphentin.mp. (0)
 16. [modafinil](#).mp. (21)
 17. provigil.mp. (3)
 18. Alertec.mp. (0)
 19. [methamphetamine](#).mp. or exp methamphetamine/ (17)
 20. desoxyn.mp. (0)
 21. [lisdexamfetamine](#).mp. (1)
 22. vivanse.mp. (0)
 23. daytrana.mp. (1)
 24. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (113)

25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (12)
26. Attention deficit disorder.mp. (21)
27. attention deficit\$.mp. (64)
28. adhd.mp. (35)
29. 25 or 26 or 27 or 28 (69)
30. 24 and 29 (30)

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to January 2011>
Search Strategy:

-
1. exp Amphetamine/ or "amphetamine\$.mp. (67)
 2. adderall.mp. (2)
 3. [atomoxetine](#).mp. (13)
 4. strattera.mp. (0)
 5. [dexmethylphenidate](#).mp. (4)
 6. focalin.mp. (4)
 7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (21)
 8. dexedrine.mp. (6)
 9. dextrostat.mp. (1)
 10. [methylphenidate](#).mp. or exp Methylphenidate/ (47)
 11. concerta.mp. (4)
 12. metadate.mp. (0)
 13. methylin.mp. (1)
 14. Ritalin.mp. (8)
 15. biphentin.mp. (0)
 16. [modafinil](#).mp. (21)
 17. provigil.mp. (3)
 18. Alertec.mp. (0)
 19. [methamphetamine](#).mp. or exp methamphetamine/ (17)
 20. desoxyn.mp. (0)
 21. [lisdexamfetamine](#).mp. (1)
 22. vivanse.mp. (0)
 23. daytrana.mp. (1)
 24. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (113)
 25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (12)
 26. Attention deficit disorder.mp. (21)
 27. attention deficit\$.mp. (64)
 28. adhd.mp. (35)
 29. 25 or 26 or 27 or 28 (69)
 30. Central Nervous system Stimulants.mp. or exp Central Nervous System Stimulants/ (23)
 31. 24 or 30 (123)
 32. 29 and 31 (31)
 33. diversion.mp. (43)

34. substance abuse.mp. or exp Substance-Related Disorders/ (187)
35. misuse.mp. (163)
36. addictive behavior.mp. or exp Behavior, Addictive/ (4)
37. 35 or 33 or 34 or 36 (331)
38. 32 and 37 (13)

Database: PsycINFO <1806 to February Week 1 2011>

Search Strategy:

-
1. exp Amphetamine/ or "amphetamine\$".mp. (11712)
 2. adderall.mp. (83)
 3. [atomoxetine](#).mp. (383)
 4. strattera.mp. (20)
 5. [dexmethylphenidate](#).mp. (24)
 6. focalin.mp. (9)
 7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (2339)
 8. dexedrine.mp. (79)
 9. dextrostat.mp. (0)
 10. [methylphenidate](#).mp. or exp Methylphenidate/ (3183)
 11. concerta.mp. (44)
 12. metadate.mp. (9)
 13. methylin.mp. (2)
 14. Ritalin.mp. (436)
 15. biphentin.mp. (1)
 16. [modafinil](#).mp. (467)
 17. provigil.mp. (14)
 18. Alertec.mp. (0)
 19. [methamphetamine](#).mp. or exp methamphetamine/ (2691)
 20. desoxyn.mp. (2)
 21. [lisdexamfetamine](#).mp. (26)
 22. vivanse.mp. (0)
 23. daytrana.mp. (3)
 24. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (15744)
 25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (9910)
 26. Attention deficit disorder.mp. (14839)
 27. attention deficit\$.mp. (18558)
 28. adhd.mp. (13031)
 29. 25 or 26 or 27 or 28 (19274)
 30. 24 and 29 (2355)
 31. limit 30 to yr="2009 - 2011" (397)
 32. limit 31 to (human and english language) (294)

Database: PsycINFO <1806 to February Week 1 2011>

Search Strategy:

-
1. exp Amphetamine/ or "amphetamine\$".mp. (11712)
 2. adderall.mp. (83)
 3. [atomoxetine](#).mp. (383)
 4. strattera.mp. (20)
 5. [dexmethylphenidate](#).mp. (24)
 6. focalin.mp. (9)
 7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (2339)
 8. dexedrine.mp. (79)
 9. dextrostat.mp. (0)
 10. [methylphenidate](#).mp. or exp Methylphenidate/ (3183)
 11. concerta.mp. (44)
 12. metadate.mp. (9)
 13. methylin.mp. (2)
 14. Ritalin.mp. (436)
 15. biphentin.mp. (1)
 16. [modafinil](#).mp. (467)
 17. provigil.mp. (14)
 18. Alertec.mp. (0)
 19. [methamphetamine](#).mp. or exp methamphetamine/ (2691)
 20. desoxyn.mp. (2)
 21. [lisdexamfetamine](#).mp. (26)
 22. vivanse.mp. (0)
 23. daytrana.mp. (3)
 24. 11 or 21 or 7 or 17 or 2 or 22 or 1 or 18 or 23 or 16 or 13 or 6 or 3 or 9 or 12 or 20 or 14 or 15 or 8 or 4 or 19 or 10 or 5 (15744)
 25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (9910)
 26. Attention deficit disorder.mp. (14839)
 27. attention deficit\$.mp. (18558)
 28. adhd.mp. (13031)
 29. 27 or 25 or 28 or 26 (19274)
 30. Central Nervous system Stimulants.mp. or exp Central Nervous System Stimulants/ (63)
 31. 30 or 24 (15784)
 32. 31 and 29 (2361)
 33. diversion.mp. (1461)
 34. substance abuse.mp. or exp Substance-Related Disorders/ (22039)
 35. misuse.mp. (5470)
 36. addictive behavior.mp. or exp Behavior, Addictive/ (768)
 37. 35 or 33 or 34 or 36 (29035)
 38. 32 and 37 (84)
 39. limit 38 to yr="2009 - 2011" (19)
 40. limit 39 to (human and english language) (14)

Database: EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2011>

Search Strategy:

-
1. exp Amphetamine/ or "amphetamine\$".mp. (15)
 2. adderall.mp. (3)
 3. [atomoxetine](#).mp. (11)
 4. strattera.mp. (0)
 5. [dexmethylphenidate](#).mp. (2)
 6. focalin.mp. (0)
 7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (14)
 8. dexedrine.mp. (0)
 9. dextrostat.mp. (0)
 10. [methylphenidate](#).mp. or exp Methylphenidate/ (41)
 11. concerta.mp. (0)
 12. metadate.mp. (0)
 13. methylin.mp. (0)
 14. Ritalin.mp. (2)
 15. biphentin.mp. (0)
 16. [modafinil](#).mp. (4)
 17. provigil.mp. (0)
 18. Alertec.mp. (0)
 19. [methamphetamine](#).mp. or exp methamphetamine/ (2)
 20. desoxyn.mp. (0)
 21. [lisdexamfetamine](#).mp. (0)
 22. vivanse.mp. (0)
 23. daytrana.mp. (0)
 24. 11 or 21 or 7 or 17 or 2 or 22 or 1 or 18 or 23 or 16 or 13 or 6 or 3 or 9 or 12 or 20 or 14 or 15 or 8 or 4 or 19 or 10 or 5 (49)
 25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (49)
 26. Attention deficit disorder.mp. (51)
 27. attention deficit\$.mp. (78)
 28. adhd.mp. (44)
 29. 27 or 25 or 28 or 26 (79)
 30. 24 and 29 (34)

Database: EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2011>

Search Strategy:

1. exp Amphetamine/ or "amphetamine\$".mp. (15)
2. adderall.mp. (3)
3. [atomoxetine](#).mp. (11)
4. strattera.mp. (0)
5. [dexmethylphenidate](#).mp. (2)
6. focalin.mp. (0)
7. [dextroamphetamine](#).mp. or exp Dextroamphetamine/ (14)
8. dexedrine.mp. (0)
9. dextrostat.mp. (0)

10. [methylphenidate](#).mp. or exp Methylphenidate/ (41)
11. [concerta](#).mp. (0)
12. [metadate](#).mp. (0)
13. [methylin](#).mp. (0)
14. [Ritalin](#).mp. (2)
15. [biphentin](#).mp. (0)
16. [modafinil](#).mp. (4)
17. [provigil](#).mp. (0)
18. [Alertec](#).mp. (0)
19. [methamphetamine](#).mp. or exp methamphetamine/ (2)
20. [desoxyn](#).mp. (0)
21. [lisdexamfetamine](#).mp. (0)
22. [vivanse](#).mp. (0)
23. [daytrana](#).mp. (0)
24. 11 or 21 or 7 or 17 or 2 or 22 or 1 or 18 or 23 or 16 or 13 or 6 or 3 or 9 or 12 or 20 or 14 or 15 or 8 or 4 or 19 or 10 or 5 (49)
25. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (49)
26. Attention deficit disorder.mp. (51)
27. attention deficit\$.mp. (78)
28. [adhd](#).mp. (44)
29. 27 or 25 or 28 or 26 (79)
30. Central Nervous system Stimulants.mp. or exp Central Nervous System Stimulants/ (28)
31. 30 or 24 (60)
32. 31 and 29 (38)
33. [diversion](#).mp. (22)
34. substance abuse.mp. or exp Substance-Related Disorders/ (116)
35. [misuse](#).mp. (33)
36. addictive behavior.mp. or exp Behavior, Addictive/ (0)
37. 35 or 33 or 34 or 36 (161)
38. 32 and 37 (2)

Database: Ovid MEDLINE(R) without Revisions <1996 to February Week 1 2011>

Search Strategy:

-
1. [Guanfacine](#).mp. (229)
 2. [Tenex](#).mp. (3)
 3. [Intuniv](#).mp. (4)
 4. [Clonidine](#).mp. (4849)
 5. [Catapres](#).mp. (5)
 6. [Kapvay](#).mp. (0)
 7. [Nexiclon](#).mp. (0)
 8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (4980)
 9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (11432)
 10. Attention deficit disorder.mp. (11609)

11. attention deficit\$.mp. (14613)
12. adhd.mp. (8191)
13. 9 or 10 or 11 or 12 (14889)
14. 8 and 13 (205)
15. (200405\$ or 200406\$ or 200407\$ or 200408\$ or 200409\$ or 20041\$ or 2005\$ or 2006\$ or 2007\$ or 2008\$ or 2009\$ or 2010\$ or 2011\$).ed. (4431682)
16. 14 and 15 (109)
17. limit 16 to (english language and humans) (95)
18. limit 17 to (clinical trial, all or clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or “review”) (59)
19. observational stud\$.mp. or exp Cohort Studies/ or cohort\$.mp. or exp Retrospective Studies/ or retrospective\$.mp. (825408)
20. 17 and 19 (12)
21. 18 or 20 (63)

Database: Ovid MEDLINE(R) without Revisions <1996 to March Week 1 2011>

Search Strategy:

-
1. [Guanfacine](#).mp. (229)
 2. Tenex.mp. (3)
 3. Intuniv.mp. (4)
 4. [Clonidine](#).mp. (4905)
 5. Catapres.mp. (5)
 6. Kapvay.mp. (0)
 7. Nexiclon.mp. (0)
 8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (5036)
 9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (11573)
 10. Attention deficit disorder.mp. (11753)
 11. attention deficit\$.mp. (14794)
 12. adhd.mp. (8297)
 13. 9 or 10 or 11 or 12 (15074)
 14. 8 and 13 (206)
 15. diversion.mp. (6509)
 16. exp Substance-Related Disorders/ (137658)
 17. ((drug\$ or substance\$ or stimula\$) adj3 (abus\$ or addict\$)).mp. (35977)
 18. (misuse\$ or misusing).mp. (7183)
 19. exp Behavior, Addictive/ (3206)
 20. (addict\$ adj3 behav\$).mp. (4120)
 21. (drug\$ adj3 seek\$).mp. (1300)
 22. 15 or 16 or 17 or 18 or 19 or 20 or 21 (161663)
 23. 14 and 22 (24)
 24. illegal\$.mp. (3716)
 25. unlawful\$.mp. (183)
 26. illicit\$.mp. (5340)

27. criminal\$.mp. (8663)
28. 24 or 25 or 26 or 27 (17201)
29. 14 and 28 (1)
30. 23 or 29 (24)
31. limit 30 to (english language and humans) (24)
32. (200405\$ or 200406\$ or 200407\$ or 200408\$ or 200409\$ or 20041\$ or 2005\$ or 2006\$ or 2007\$ or 2008\$ or 2009\$ or 2010\$ or 2011\$).ed. (4508311)
33. 31 and 32 (12)
34. limit 33 to (clinical trial, all or clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or “review”) (7)
35. observational stud\$.mp. or exp Cohort Studies/ or cohort\$.mp. or exp Retrospective Studies/ or retrospective\$.mp. (837641)
36. 33 and 35 (2)
37. 34 or 36 (8)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <1st Quarter 2011>
Search Strategy:

-
1. [Guanfacine](#).mp. (116)
 2. Tenex.mp. (0)
 3. Intuniv.mp. (0)
 4. [Clonidine](#).mp. (2355)
 5. Catapres.mp. (18)
 6. Kapvay.mp. (0)
 7. Nexiclon.mp. (0)
 8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (2432)
 9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (1180)
 10. Attention deficit disorder.mp. (1302)
 11. attention deficit\$.mp. (1585)
 12. adhd.mp. (1038)
 13. 9 or 10 or 11 or 12 (1750)
 14. 8 and 13 (39)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <1st Quarter 2011>
Search Strategy:

-
1. [Guanfacine](#).mp. (116)
 2. Tenex.mp. (0)
 3. Intuniv.mp. (0)
 4. [Clonidine](#).mp. (2355)
 5. Catapres.mp. (18)
 6. Kapvay.mp. (0)
 7. Nexiclon.mp. (0)
 8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (2432)

9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (1180)
10. Attention deficit disorder.mp. (1302)
11. attention deficit\$.mp. (1585)
12. adhd.mp. (1038)
13. 9 or 10 or 11 or 12 (1750)
14. Central Nervous system Stimulants.mp. or exp Central Nervous System Stimulants/ (3816)
15. 8 or 14 (6216)
16. 13 and 15 (734)
17. diversion.mp. (211)
18. exp Substance-Related Disorders/ (6996)
19. ((drug\$ or substance\$ or stimula\$) adj3 (abus\$ or addict\$)).mp. (2636)
20. (misuse\$ or misusing).mp. (284)
21. exp Behavior, Addictive/ (205)
22. (addict\$ adj3 behav\$).mp. (275)
23. (drug\$ adj3 seek\$).mp. (62)
24. 17 or 18 or 19 or 20 or 21 or 22 or 23 (8687)
25. 16 and 24 (33)
26. illegal\$.mp. (75)
27. unlawful\$.mp. (0)
28. illicit\$.mp. (329)
29. criminal\$.mp. (295)
30. 26 or 27 or 28 or 29 (671)
31. 16 and 30 (2)
32. 25 or 31 (33)
33. limit 32 to yr="2004 -Current" (21)

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to January 2011>
 Search Strategy:

-
1. [Guanfacine](#).mp. (10)
 2. Tenex.mp. (1)
 3. Intuniv.mp. (0)
 4. [Clonidine](#).mp. (81)
 5. Catapres.mp. (5)
 6. Kapvay.mp. (0)
 7. Nexiclon.mp. (0)
 8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (81)
 9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (12)
 10. Attention deficit disorder.mp. (21)
 11. attention deficit\$.mp. (64)
 12. adhd.mp. (35)
 13. 9 or 10 or 11 or 12 (69)
 14. 8 and 13 (7)
-

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to January 2011>
Search Strategy:

-
1. [Guanfacine](#).mp. (10)
 2. Tenex.mp. (1)
 3. Intuniv.mp. (0)
 4. [Clonidine](#).mp. (81)
 5. Catapres.mp. (5)
 6. Kapvay.mp. (0)
 7. Nexiclon.mp. (0)
 8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (81)
 9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (12)
 10. Attention deficit disorder.mp. (21)
 11. attention deficit\$.mp. (64)
 12. adhd.mp. (35)
 13. 9 or 10 or 11 or 12 (69)
 14. Central Nervous system Stimulants.mp. or exp Central Nervous System Stimulants/ (23)
 15. 8 or 14 (104)
 16. 13 and 15 (14)
 17. diversion.mp. (43)
 18. [exp Substance-Related Disorders/] (0)
 19. ((drug\$ or substance\$ or stimula\$) adj3 (abus\$ or addict\$)).mp. (293)
 20. (misuse\$ or misusing).mp. (173)
 21. [exp Behavior, Addictive/] (0)
 22. (addict\$ adj3 behav\$).mp. (24)
 23. (drug\$ adj3 seek\$).mp. (19)
 24. 17 or 18 or 19 or 20 or 21 or 22 or 23 (446)
 25. 16 and 24 (7)
 26. illegal\$.mp. (43)
 27. unlawful\$.mp. (3)
 28. illicit\$.mp. (74)
 29. criminal\$.mp. (92)
 30. 26 or 27 or 28 or 29 (160)
 31. 16 and 30 (2)
 32. 25 or 31 (7)

Database: PsycINFO <1806 to February Week 3 2011>
Search Strategy:

-
1. [Guanfacine](#).mp. (164)
 2. Tenex.mp. (2)
 3. Intuniv.mp. (2)
 4. [Clonidine](#).mp. (1903)
 5. Catapres.mp. (8)
 6. Kapvay.mp. (0)

7. Nexiclon.mp. (0)
8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (2007)
9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (9953)
10. Attention deficit disorder.mp. (14883)
11. attention deficit\$.mp. (18608)
12. adhd.mp. (13077)
13. 9 or 10 or 11 or 12 (19328)
14. 8 and 13 (185)
15. limit 14 to yr="2004 -Current" (81)
16. limit 15 to (human and english language) (71)

Database: PsycINFO <1806 to February Week 3 2011>

Search Strategy:

-
1. [Guanfacine](#).mp. (164)
 2. Tenex.mp. (2)
 3. Intuniv.mp. (2)
 4. [Clonidine](#).mp. (1903)
 5. Catapres.mp. (8)
 6. Kapvay.mp. (0)
 7. Nexiclon.mp. (0)
 8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (2007)
 9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (9953)
 10. Attention deficit disorder.mp. (14883)
 11. attention deficit\$.mp. (18608)
 12. adhd.mp. (13077)
 13. 9 or 10 or 11 or 12 (19328)
 14. Central Nervous system Stimulants.mp. or exp Central Nervous System Stimulants/ (64)
 15. 8 or 14 (2070)
 16. 13 and 15 (195)
 17. diversion.mp. (1466)
 18. substance abuse.mp. or exp Substance-Related Disorders/ (22095)
 19. misuse.mp. (5492)
 20. addictive behavior.mp. or exp Behavior, Addictive/ (770)
 21. 17 or 18 or 19 or 20 (29117)
 22. 16 and 21 (5)
 23. limit 22 to yr="2004 -Current" (3)
 24. limit 23 to (human and english language) (2)

Database: EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2011>

Search Strategy:

-
1. [Guanfacine](#).mp. (4)
 2. Tenex.mp. (0)

3. Intuniv.mp. (0)
4. [Clonidine](#).mp. (56)
5. Catapres.mp. (0)
6. Kapvay.mp. (0)
7. Nexiclon.mp. (0)
8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (58)
9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (49)
10. Attention deficit disorder.mp. (51)
11. attention deficit\$.mp. (78)
12. adhd.mp. (44)
13. 9 or 10 or 11 or 12 (79)
14. 8 and 13 (6)

Database: EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2011>

Search Strategy:

-
1. [Guanfacine](#).mp. (4)
 2. Tenex.mp. (0)
 3. Intuniv.mp. (0)
 4. [Clonidine](#).mp. (56)
 5. Catapres.mp. (0)
 6. Kapvay.mp. (0)
 7. Nexiclon.mp. (0)
 8. 1 or 2 or 3 or 4 or 5 or 6 or 7 (58)
 9. Attention Deficit Disorder with Hyperactivity.mp. or exp Attention Deficit Disorder with Hyperactivity/ (49)
 10. Attention deficit disorder.mp. (51)
 11. attention deficit\$.mp. (78)
 12. adhd.mp. (44)
 13. 9 or 10 or 11 or 12 (79)
 14. Central Nervous system Stimulants.mp. or exp Central Nervous System Stimulants/ (28)
 15. 8 or 14 (83)
 16. 13 and 15 (22)
 17. diversion.mp. (22)
 18. [exp Substance-Related Disorders/] (0)
 19. ((drug\$ or substance\$ or stimula\$) adj3 (abus\$ or addict\$)).mp. (165)
 20. (misuse\$ or misusing).mp. (35)
 21. [exp Behavior, Addictive/] (0)
 22. (addict\$ adj3 behav\$).mp. (12)
 23. (drug\$ adj3 seek\$).mp. (0)
 24. 17 or 18 or 19 or 20 or 21 or 22 or 23 (210)
 25. 16 and 24 (3)
 26. illegal\$.mp. (8)
 27. unlawful\$.mp. (0)
 28. illicit\$.mp. (24)

- 29. criminal\$.mp. (31)
- 30. 26 or 27 or 28 or 29 (57)
- 31. 16 and 30 (0)
- 32. 25 or 31 (3)

APPENDIX A: Draft eligibility criteria

Level 1 screening: Titles and Abstracts (from literature search update)

1. Does this study include ADULTS with ADD or ADHD?

YES _____
NO _____
UNCLEAR _____

2. Is this an randomized interventional study?

YES _____
NO _____
UNCLEAR _____

3. Does this study examine ANY of the interventions specified in the study PICO [in any combination]?

YES _____
NO _____
UNCLEAR _____

4. Does this study compare the interventions specified in the PICO with placebo, no treatment(or reasonable equivalent) or other interventions specified in the PICO [in any combination]?

YES _____
NO _____
UNCLEAR _____

5. This study likely fulfills our eligibility criteria but is:

Not written in English _____
Conducted with less than 10 participants _____
I do not have an abstract to assess (title only) _____
An abstract _____
A trial protocol _____
A relevant SR, MA, NMA/ITC _____ (need to scan references)

Level 2 screening: Full Text (all included studies from previous review and those from the updated literature search passing level 1 screening)

If you answer NO to any one of questions 1 through 4, the citation/study will be excluded.

All other citations/studies will be included. We will keep track of studies which:

- Do not report outcomes of interest;
- Are SR, MA or NMA/ITCs that have potentially relevant material. We will scan their reference lists to ensure all studies have been captured;
- Identified with a flag on question 6. Notes will be kept to either identify reason for exclusion (language, abstract) or until protocols can either be linked to a primary publication or authors contacted if no publication can be located (note if link cannot be made and no publication is located).
- Have missing full-text. These will be screened again at Level 2 once full text is located or, highlighted in the PRISMA flow diagram if the process to locate them is too lengthy for the review.

1. Does this study include ADULTS with ADD or ADHD?

YES _____

NO _____

UNCLEAR _____

2. Is this an randomized interventional study?

YES _____

NO _____

UNCLEAR _____

3. Does this study examine ANY of the interventions specified in the study PICO [in any combination]?

YES _____

NO _____

UNCLEAR _____

4. Does this study compare the interventions specified in the PICO with placebo/no treatment (or reasonable equivalent) or any other interventions specified in the PICO [in any combination]?

YES _____

NO _____

UNCLEAR _____

5. Does this study report on ANY of the following outcomes that were prioritized by the ODPRN?:

YES _____

NO _____

UNCLEAR _____

6. This study likely fulfills our eligibility criteria but:

Is not written in English _____

Is an abstract _____

Is a trial protocol (need to link to an included study and/or contact authors) _____

We cannot locate the full-text _____

Is a relevant SR, MA, NMA/ITC (need to scan references) _____

Other _____