

Complementary & Alternative therapies for children diagnosed with Attention-Deficit Hyperactivity Disorder (ADHD): a scoping review

A report prepared for Cerebra

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SUMMARY

There is considerable interest in the use of complementary therapies for the condition among parents of children with Attention-Deficit Hyperactivity Disorder (ADHD). Cerebra commissioned a team at Peninsula Medical School to carry out a scoping report describing studies which have been published evaluating the efficacy and safety of complementary and alternative medicines for children with ADHD. The aim was to guide decisions about fruitful directions for further work.

A systematic search for studies using multiple sources identified 269 studies evaluating a wide range of complementary therapies in children with ADHD.

The majority of identified studies were published in the last decade, and in English. Much of the accumulated evidence involves small samples and less than a third were randomised controlled trials. There are some systematic reviews, notably Cochrane Reviews on meditation and homeopathy with two other Cochrane Reviews on acupuncture and fatty acid supplementation in preparation. There is also a sizeable literature on biofeedback and elimination diets. Other areas with a reasonable amount of literature include relaxation and herbal medicines, which includes a reasonable number of randomised clinical trials, albeit a number of which are in Chinese.

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INTRODUCTION: BACKGROUND AND PURPOSE

Attention-deficit hyperactivity disorder

Attention-deficit hyperactivity disorder (ADHD) is a group of behavioural difficulties that encompass inattentiveness, hyperactivity and impulsiveness. The symptoms in children and teenagers are well defined and include:

- a short attention span
- restlessness
- being easily distracted
- constant fidgeting

Many children with ADHD also have additional problems, such as sleep disorders or learning difficulties. However, ADHD has no effect on intelligence.

ADHD a relatively common condition in which difficulties tend to start at an early age and may become more noticeable when a child's circumstances change, such as starting school. ADHD is normally diagnosed between the ages of three to seven, although in some cases it may not be until much later. However, even if diagnosed in adulthood, there will be a history of difficulties stretching back to early childhood, It is more commonly diagnosed in boys, but there is evidence that ADHD in boys is more likely to be diagnosed, with the gender ratio being much smaller in studies of the general population than studies of children attending clinics.

There is no cure for ADHD, but it can be managed using medication. This will usually be combined with psychological, educational and social therapies that aim to improve behaviour.*

*Information derived from: NHS **Clinical Knowledge Summaries** (formerly PRODIGY)

www.cks.nhs.uk/patient_information_leaflet/attention_deficit_hyperactivity_disorder_adhd#459891000 (website accessed 5/1/11)

Complementary and Alternative medicine (CAM)

The term **alternative medicine** refers to medical systems that do not fit with conventional medicine, having different ideas on causes of disease, methods of diagnosis and approaches to treatment and may be seen as a replacement for conventional healthcare. **Complementary medicine** refers to those methods which can be used alongside or to 'complement' conventional medicine. Today the term "CAM" is often used to include both approaches. Defining CAM is not straightforward but the general explanation is that it comprises a group of therapies, practices and approaches to healthcare which are found outside mainstream conventional medicine #. Examples may be found in the methods section of this report (page 8).

Information derived from the NHS CAM Specialist Library

www.library.nhs.uk/cam/Page.aspx?pagename=CAM (website accessed 5/1/11)

NHS therapy for ADHD

NHS therapy for ADHD is underpinned in England and Wales by NICE guidance^{1, 2} and in Scotland by SIGN guidance.³ The guidelines do not cover complementary therapies in any detail. However some guidance and discussion is given on the following:

Elimination Diets and dietary supplements

NICE guideline¹ section 1.4.2: elimination diets and fatty acid supplements are not recommended for the treatment of ADHD in children.

SIGN guideline³ Chapter 8.1 : elimination diets *may* help in some cases but inadequate evidence for iron, zinc, fatty acid supplements and antioxidants.

Antidepressants (not licensed for children with ADHD)

Section 10.12 of the full version of the NICE guideline² states that there is no evidence that tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) or serotonin and noradrenaline reuptake inhibitors (SNRIs) are of value in the treatment of ADHD. There is no specific recommendation regarding their use either in the NICE version of the guideline (section 1.5)¹ nor in the SIGN guideline section on unlicensed medications (section 7.4).³

Other approaches

There is a discussion on recreation, biofeedback and relaxation in section 7.4 of the full version of the NICE guideline.² Section 8.2 of the SIGN guideline³ briefly mentions Bach flower remedies, homeopathy, massage and biofeedback. There are no recommendations for the use of any complementary therapies and a small and poor quality trial literature is noted. Although both guidelines are relatively recent their usefulness is limited because:

- Complementary therapies are not generally provided by the NHS so are not covered in great detail
- Evidence is usually limited to Randomised Controlled Trials (RCTs) published in the English language in peer reviewed journals

In addition research is ongoing and even the most recent guidance is usually based on a literature review up to two years out of date when published.

Complementary therapies and ADHD

There is considerable interest amongst the general public in complementary therapies. Parents purchase complementary therapies for a variety of conditions in children, including ADHD, either in place of, or as an adjunct to standard treatments. Many remedies and therapeutic interventions are advertised and sold particularly on the internet. Efficacy claims may be made

for certain products that may be difficult for parents and carers to verify and there are also concerns about safety and cost.

Purpose of the review

The purpose of this literature 'scoping' exercise was to ascertain whether there is any potential evidence base (clinical studies or trials) for the use of various complementary therapies - both ingested and other - for the treatment of children diagnosed with Attention Deficit Hyperactivity Disorder.

No critical appraisal of any studies was undertaken in the scoping exercise, as this was beyond the brief. However, any evidence base that was found could, at a later stage, form the basis of a systematic review of the literature to better inform parents and carers about therapy options.

Methods: Literature Search

The following search protocol was agreed by the working group. Parameters were as follows:

Population

Children aged 0-19 with a diagnosis of ADHD i.e. NOT the general population

Interventions

Any complementary therapies, both ingested remedies and other therapies with emphasis on the following:

Ingested remedies

Herbal medicines including:

- Chinese medicines
- St John's Wort (hypericum)
- Gingko biloba
- Ginseng(panax quinquefolium)
- Valerian
- Rhodiola rosea
- Bacopa
- Kava kava
- Echinacea
- Arnica
- Flower remedies (e.g. Bach))

Homeopathy and homeopathic preparations

Therapies

- Acupuncture
- Aromatherapy
- Meditation
- Massage
- Yoga
- Hypnotherapy
- Reflexology
- Relaxation
- Vision therapy
- Ayurveda (combination of diet, yoga, massage, herbal remedies)
- Auditory/ Sensory integration therapy
- Creative therapies (including art/ drama/ dance, music)

Dietary Modifications

Supplements

- Fatty acids (Essential Fatty Acids (EFAs), Polyunsaturated fatty Acids (PUFAs), Omega 3, 6, 9, fish oils including Equazen eye Q liquid (citrus, vanilla etc)
- Vitamins

- Magnesium
- Iron
- Zinc

Elimination Diets

- Feingold diet
- Artificial food additives especially colours and preservatives
- Sugar
- Aspartame
- Cow's milk

Other Ingested

- Antidepressants of the types: Serotonin precursors, SSRIs, SNRIs, Sam-e (s-adenosylmethionine)#
- Melatonin#

Other therapies

- Biofeedback/neurofeedback*
- Commercial programmes including Brain Gym, Brainwave, BIBIC, Life Coaches, Lightning Process, DDAT, Dore, Sunrise, Da Vinci Method, Discovery Centre)*

#drugs licensed for other conditions but not for children with ADHD

* We looked for evidence for these only as stand-alone therapies not in the context of a recognised cognitive behavioural therapy (CBT) programme

Comparison

Usual care

Outcomes

These were not included in the database search but outcomes noted in any abstract from a selected study were extracted and tabulated in the results below.

Study types and exclusions

Systematic reviews, meta-analyses and all experimental, observational or qualitative research were included.

Animal studies, narrative reviews, opinions, letters and editorials were excluded

Limits

No language or date limits were used and the databases were searched from their inception

Databases

Search strategies were devised from the above protocol to interrogate the following medical and databases as agreed by the panel: (for detailed search strategies see appendix 1)

- Medline
- Embase
- Psycinfo
- Cinahl
- AMED
- Cochrane Library

The following clinical trials databases were also searched for unpublished or ongoing trials

- Current Controlled trials www.controlled-trials.com/mrct
- Clinical trials.gov www.ClinicalTrials.gov

Further searches

- SIGLE – only available to 2005 (grey literature) <http://opensigle.inist.fr>
- HSTAT database (technology appraisals - global coverage) <http://www.ncbi.nlm.nih.gov/books/>
- The following websites and databases relevant to the area of complementary therapies were also searched for any additional references:
 - ❖ Complementary and Alternative Medicine Specialist Library in the National Library for Health www.nlh.nhs.uk
 - ❖ Complementary and Alternative Therapies databases of Bandolier
 - ❖ National Center for Complementary and Alternative Medicine (NCCAM) –USA <http://nccam.nih.gov>
 - ❖ Research Council for Complementary Medicine www.rccm.org.uk
 - ❖ HerbMed (herbal medicine) www.herbmed.org
 - ❖ Hom-Inform (homeopathy) <http://hominform.soutron.com>
 - ❖ CAIRSS (music therapy literature) <http://ucairss.utsa.edu>
 - ❖ Office of Dietary Supplements-USA http://ods.od.nih.gov/Research/CARDS_Database.aspx

The reference lists of included studies from the two relevant Cochrane systematic reviews were also cross checked.^{4 5}

Clinical trials were added to the published studies found via the electronic database search but no further studies were found during the further searches.

The cut off date for all searches was **10 December 2010**.

Once all the databases were searched, results combined and duplicates removed an abstract list of the results was produced. This was scanned by hand for potentially relevant studies using the criteria in the protocol. As studies were extracted they were coded for intervention(s), outcome measure(s) and study type and size. Language other than English was also noted. Each paper was given a single study type but in many cases there

were multiple interventions (e.g. *Panax ginseng* and *Gingko biloba*) and outcome measures (e.g. Conner's parent scale and CGI- Clinical Global Impression).

Results

Search Process

Search all databases (Medline etc), and combine results = **1706** hits



Remove the duplicate references = **1087** hits



Scan abstracts for potentially relevant studies = **251** hits



Add results of search for Clinical trials (18)

Add results of other searches (0) = **269** hits

Study design

The type of study was judged from often inadequate information in the title or abstract. Even where information was given this might sometimes be misleading and it would be necessary to obtain full text to make a more accurate assessment. It is probable that the number of systematic reviews and randomised clinical trials is actually overstated and the number of studies with an inferior design understated.

Table 1: Number of studies by methodology

Study type	Number of studies
Systematic Reviews/ meta-analyses	45
Randomised trials	79
Comparative studies	55
Other study designs including qualitative	90
TOTAL	269

Language of publication

We have assumed the study language to be English unless otherwise stated. This information therefore probably slightly understates the number of studies where the full text is in a language other than English since many of the databases do not state the language of the studies. The most frequently occurring language after English is Chinese. We identified 14 studies published in Chinese - Chinese medicines (5), acupuncture (3), Chinese medicines and acupuncture (1), neurofeedback (3), sensory integration therapy (1) and SSRIs (1).

Table 2: Number of studies by language of publication

Language	Number of studies
English	247
Chinese	14
German	4
Polish	2
Portuguese	1
Russian	1
TOTAL	269

Publication dates

More of the selected studies were published in the 2000s than in the previous four decades combined. This partly reflects both a general increase in publication and growth of indexing in electronic databases but it is also an indicator of an increasing acceptance of the concept of ADHD and increasing research focus on interventions including complementary therapies. In recent years the focus has been on biofeedback and fatty acid supplements, the latter having the most studies of any topic amongst the selected studies appearing in 2009. There is also an increase in studies on herbal medicines, including Chinese remedies.

Table 3: Number of studies by date of publication

Decade	Number of studies
2010s (2010-pre-publication)	29
2000s	147
1990s	43
1980s	38
1970s	11
1960s	1
TOTAL	269

Study size

Most of the studies were small. Nearly two thirds of the studies where this information was given in the abstract (170 studies) had fewer than 50 participants. The topics of the four largest studies were; antidepressants including SSRIs (although this was a meta-analysis where the results from studies involving 4800+ participants were pooled); food colourings (a double blind challenge study with 1873 participants) and fatty acid, zinc and magnesium supplementation (an 810 participant cohort study and a 674 RCT-zinc only).

Table 4: Number of studies by number of participants

Number of Participants	Number of Studies
Less than 10	23
10-19	31
20-29	24
30-39	19
40-49	15
50-100	34
100-500	20
Over 500	4
TOTAL	170

Interventions by Study Type

Some of the topics searched for but not mentioned in the table may have been included in papers dealing with a range of substances e.g. herbal remedies in general. We have extracted individual names where these were specified in the abstract. Papers on chiropractic, transcranial magnetic stimulation (TMS), outdoor recreation and carnitine supplementation were also found though not included in the original list. The totals exceed the number of included studies as some studies dealt with more than one intervention eg fatty acids and vitamins or ginseng and ginkgo biloba.

The largest number of studies is on biofeedback, followed by fatty acid supplements and dietary modification. There are currently Cochrane protocols for systematic reviews on acupuncture and fatty acid supplements in ADHD. Contact details for these are in appendix 2. The studies on antidepressants need to be noted in the light of NICE/ SIGN guidance (see page 4).

Table 5: Number of studies of interventions by methodology

Interventions	SR	RCT	Comp	Other	Total
Herbal (general including flowers)	2	7	1	5	15
Chinese medicines	2	2	1	4	9
Gingko biloba	1	3		2	6
Ginseng	1	1		2	4
Valerian		2		1	3
St John's Wort		2		1	3
Homeopathy	4	3	2	3	12
Acupuncture		2	1	4	7
Aromatherapy				1	1
Meditation	2	2		3	7
Massage		1		1	2
Yoga		2	1	1	4
Hypnotherapy				1	1
Relaxation	1	3	1	10	15
Auditory/ Sensory Integration therapy	1	2	1	1	5
Art Therapy				1	1
Dance				1	1
Music Therapy		1	2	2	5
Outdoor recreation				1	1
Vision Therapy			1		1
Transcranial magnetic Stimulation		1			1
Chiropractic	2			3	5
Supplements (general dietary)	1	4	6	2	13
Fatty Acids	13	19	4	3	39
Vitamins	1	3	5	1	10
Magnesium		1	2	4	7
Iron	1	1		1	3
Zinc	3	4	2	1	10
Carnitine		3	2		5
Elimination Diet (general and Feingold)	3	3	14	5	25
Food colourings	3	1	8	2	14
Food Flavourings			1		1
Food preservatives			2		2
Sugar	2		2	1	5
Aspartame		1	2		3
SSRI/SNRIs	3	4	3	10	20
Melatonin	1	3		3	7
Biofeedback	6	10	24	11	51
Brainwave program	1				1
TOTALS	54	91	88	92	325

Outcomes by Intervention

Table 6: Number of studies by outcomes assessed for each intervention

*see notes on Table 6 on following page.

Intervention	Physiological tests	Psychological tasks			Rating Scales generic		Rating Scales condition Specific		N/S	TOTAL
		various	TOVA	CPT	various	CGI	ADHD	Conners		
Herbal	2		2		3	1	5	5	2	20
Chinese medicines	2				1		4		3	10
Gingko biloba			1		3	2	3	3	1	13
Ginseng			1		1	1	1	3	1	8
Valerian							1		2	3
St John's Wort						1	2		2	5
Homeopathy		1		1			1	9		12
Acupuncture					2				1	3
Aromatherapy										
Meditation		1			4		1	1		7
Massage					2				2	4
Yoga			1		3			2	1	7
Hypnotherapy									1	1
Relaxation	1	5		1	15				1	23
Auditory/ Sensory Integration therapy		4	1		1					6
Art Therapy		1			2			2	2	7
Dance										
Music Therapy		1			2			2	2	7
Outdoor recreation										
Vision Therapy									1	1
Transcranial magnetic Stimulation									1	1
Chiropractic	1	1			3				1	6
Supplements (general dietary)	2	1		2	10		2	3	2	22
Fatty Acids	3	4	3	2	17	4	3	9	6	51
Vitamins	3	1		1	4			4	4	17
Magnesium	3				3			4	4	14
Iron	1					1		4		6
Zinc	1				3		3	5	3	15
Carnitine							1	4	1	6
Elimination Diet (general and Feingold)	2	6		1	2		14	3	8	36
Food colourings		3			12			1	3	19
Food Flavourings									1	1
Food preservatives									2	2
Sugar		1		1	1				2	5
Aspartame	2	2		1	2			1	1	9
SSRI/SNRIs	3	1		1	8	4	2	1	7	27
Melatonin									7	7
Biofeedback	7	13	8	7	21		9	6	7	78
Brainwave program										
TOTAL	33	46	17	18	125	14	52	72	82	459

Details of outcomes specified in Table 6

Physiological tests

These included blood tests, EEG etc

Psychological tasks

A number of different tasks/tests are often used in the same study.

Some measure specific skills such as reading and counting. The two task measures most commonly occurring in the literature have been itemised separately. These are:

- TOVA = Test of Variable Attention ⁶ specific test used in ADHD
- CPT = Continuous Performance Test- specific test used in ADHD

Rating Scales

A large number of different rating scales are used in the studies most frequently assessed by parent or teacher and often by both.

A few studies use investigator rating scales and very few use self rating. The three most commonly occurring rating scales have been listed separately; one is used to assess symptom severity in mental conditions (CGI) and the other two are ADHD specific (ADHD and Conners).

The details of these are:

- CGI= clinical global impression ¹⁰
- ADHD Rating Scales - parent and teacher versions⁷
- Conners Rating Scales ^{8,9} the most commonly cited scales in the literature - teacher and parent versions.

In the abstracts of the selected literature, rating scales, whether generic or specifically designed for an ADHD population, typically measure hyperactivity, impulsivity, self-control, delinquent or aggressive behaviour, socialisation and anxiety/ depression.

Other

N/S= not specified; i.e. outcomes are indicated but not the measures used; commonly symptoms, cognition or behaviour improvement. Other outcomes cited include adverse events and quality of life.

As in the previous table the totals exceed the number of included studies since most of the studies which indicated outcome measures indicated several different ones.

Country of studies

It was not possible to make any meaningful overall assessment of the countries where the studies were conducted from the abstracts since most did not supply this information. Some trials may have been multicenter studies across several countries and/ or continents (but see table on language). It might be possible to obtain this information from the full text of the studies.

Conclusions

There is a large and increasing body of literature covering the area of complementary therapies in children with ADHD.

However much of the evidence originates from non-randomised clinical trials with small sample sizes which may be subject to bias.

There are some systematic reviews, notably Cochrane Reviews on meditation and homeopathy with two others on acupuncture and fatty acid supplementation in preparation. The latter in particular has generated a large body of literature including several randomised clinical trials.

There is also a sizeable literature on biofeedback. Research into the merits of elimination diets continues. Other areas with a reasonable amount of literature include relaxation and herbal medicines.

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Appendix 1: Search strategies

Population- Medline Ebsco example

S1	(MH "Attention Deficit Disorder with Hyperactivity") or ADDH or AD/DH or ADHS or ADHD or TI attention deficit* or minimal brain dysfunction or TI hyperactiv* or hyperkinetic N2 syndrome or hyperactiv* N2 disorder* or hyperactiv* N2 impuls* or hyperkinetic N2 disorder* or attention deficit N2 disorder*
S2	(MH "Adult+") or TI adult*
S3	((MH "Adolescent") OR (MH "Child+")) or TI (child* or boy* or girl* or schoolchild* or adolescen* or teen* or young person* or young people or pediatric or paediatric or youth*)
S4	S2 NOT S3
S5	S1 NOT S4

Interventions

S1	(MH "Complementary Therapies+") OR (MH "Acupuncture") OR (MH "Herbal Medicine") OR (MH "Plant Extracts+") OR (MH "Arnica") OR (MH "Echinacea") OR (MH "Kava") OR (MH "Hypericum") OR (MH "Ginkgo biloba") OR (MH "Panax+") OR (MH "Valerian") OR (MH "Bacopa")
S2	(MH "Chiropractic") OR (MH "Manipulation, Chiropractic") OR (MH "Melatonin") OR (MH "Serotonin Uptake Inhibitors") OR (MH "Diet+") OR (MH "Diet Therapy+") OR (MH "Food Habits") OR (MH "Dietary Supplements+") OR (MH "Food Additives+") OR (MH "Vitamins+") OR (MH "Fatty Acids, Unsaturated+") OR (MH "Dietary Fats, Unsaturated+") OR (MH "Fish Oils+") OR (MH "Magnesium") OR (MH "Magnesium Chloride") OR (MH "Magnesium Deficiency") OR (MH "Zinc") OR (MH "Iron") OR (MH "Ferrous Compounds+") OR (MH "Iron, Dietary") OR (MH "Flavoring Agents+")
S3	acupunctur* or chiropractic* or homeopath* or massag* or yoga or aromatherap* or meditat* or hypnotherap* or reflexolog* or ayurveda or brain gym or BIBIC or DDAT or da vinci method or dyscovery centre* or dyscovery center* or dore or melatonin or serotonin pre-cursor* or serotonin

	precursor* or serotonin reuptake inhibitor* or SSRI* or SNRI* or serotonin re-uptake inhibitor* or s-adenosylmethionine or sam-e or St John's wort or St Johns wort or hypericum or ginko or ginkgo or ginseng or panax quinquefolium or valerian* or rodeola or rhodiola or bacopa or kava or kawa or arnica or echinacea or lightning N2 therap* or lightning process or relaxation N2 therap* or relaxation N2 train* or auditory N2 integration or sensory N2 integration or life N2 coach* or brainwave N2 program* or sunrise N2 program* or alternative N2 medic* or complementary N2 medic*
S4	alternative N2 therap* or alternative N2 medic* or art therap* or dance therap* or drama therap* or music therap* or creative therap* or chinese medic* or chinese remed* or herbal remed* or herbal preparation* or herbal medic* or flower remed* or elimination diet* or restricted diet* or fengold diet* or feingold diet* or fish oil* or primrose oil* or liquid N3 citrus or fatty N4 acid* or vitamin N2 supplement* or zinc N2 supplement* or iron N2 supplement* or magnesium N2 supplement* or nutraceutical* or probiotic* or diet N2 therap* or modified diet or artificial N2 sweetener* or herb or herbs or Vitamin B
S5	exclu* N2 sugar or exclu* N2 aspartam* or exclu* N2 yeast or exclu* N2 milk or exclu* N2 orange or exclu* N2 additiv* or exclu* N2 color* or exclu* N2 colour* or exclu* N2 preservativ* or food color* or food colour* or food N2 preservativ* or food additiv* or artificial color* or artificial colour* or artificial sweeten* or artificial flavoring* or artificial flavouring* or colour* N2 agent* or color* N2 agent*
S6	elimin* N2 sugar or elimin* N2 aspartam* or elimin* N2 yeast or elimin* N2 milk or elimin* N2 orange or elimin* N2 additiv* or elimin* N2 color* or elimin* N2 colour* or elimin* N2 preservativ* or EFA* or PUFA* or omega 3 or omega 6 or omega 9 or tartrazine
S7	reduc* N2 sugar or reduc* N2 aspartam* or reduc* N2 yeast or reduc* N2 milk or reduc* N2 orange or reduc* N2 additiv* or reduc* N2 color* or reduc* N2 colour* or reduc* N2 preservativ*
S8	avoid* N2 sugar or avoid* N2 aspartam* or avoid* N2 yeast or avoid* N2 milk or avoid* N2 orange or avoid* N2 additiv* or avoid* N2 color* or avoid* N2 colour* or avoid* N2 preservativ*

S9	restrict* N2 sugar or restrict* N2 aspartam* or restrict* N2 yeast or restrict* N2 milk or restrict* N2 orange or restrict* N2 additiv* or restrict* N2 color* or restrict* N2 colour* or restrict* N2 preservativ*
S10	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9

Exclusions

S1	(MH "Letter") OR (MH "Correspondence as Topic+") OR (MH "Case Reports") OR (MH "Animals, Laboratory") OR (MH "Models, Animal") OR (MH "Animal Experimentation") OR (MH "Rodentia+")
S2	(MH "Animals+") NOT (MH "Humans")
S3	PT historical article or PT letter or PT editorial or PT comment or PT case reports
S4	S1 or S2 or S3

Study types

S1	systematic or evidence* or methodol* or quantitativ*
S2	(MH "Review") or (MH "Review Literature as Topic") or overview* or survey* or review* or PT review
S3	S1 and S2
S4	(MH "Meta-Analysis") OR (MH "Meta-Analysis as Topic") or PT meta-analysis or meta-analys* or meta analys* or metanalys* or metaanalys* or pool* N2 data or pool* N2 trials or pool* N2 studies or pool* N2 results or combined N2 data or combined N2 trials or combined N2 studies or combined N2 results or combining N2 data
S5	combining N2 trials or combining N2 studies or combining N2 results
S6	S3 or S4 or S5
S7	clinical N2 trial* or control* N2 trial* or clinical N2 study or control* N2 study or clinical N2 studies or control* N2 studies or single-blind* or double-blind* or triple-blind* or

	cross-over N2 stud* or crossover N2 stud* or cross-over N2 design or crossover N2 design or crossover N2 procedure
S8	(MH "Double-Blind Method") OR (MH "Control Group") or (MH "Single-Blind Method") OR (MH "Random Allocation") or random* or volunteer* or control arm or control arms or controls or randomiz* or randomis* or controlled trial or control group or control groups
S9	(MH "Clinical Trial+") OR (MH "Clinical Trials as Topic+") OR (MH "Placebos") OR (MH "Cross-Over Studies") or PT clinical trial or PT clinical trial, Phase I or PT clinical trial, phase II or PT clinical trial, phase III or PT clinical trial, phase IV or PT controlled clinical trial or PT randomized controlled trial or PT multicenter study
S10	cross-over procedure or cross-over trial* or crossover trial*
S11	S7 or S8 or S9 or S10
S12	follow-up N2 research or longitudinal N2 research or prospective N2 research or retrospective N2 research or cohort N2 analys* or follow-up N2 analys* or longitudinal N2 analys* or prospective N2 analys* or retrospective N2 analys* or observ* N2 analys* or comparative N2 analys* or qualitative research or qualitative stud*
S13	(MH "Research Design") OR (MH "Cohort Studies+") OR (MH "Case-Control Studies+") OR (MH "Cross-Sectional Studies") OR (MH "Comparative Study") OR (MH "Evaluation Studies") OR (MH "Evaluation Studies as Topic") or case-control or case control or observ* N2 stud* or comparative N2 stud* or cohort N2 stud* or follow-up N2 stud* or longitudinal N2 stud* or prospective N2 stud* or retrospective N2 stud* or observ* N2 research or comparative N2 research and cohort N2 research
S14	(MH "Research Design") OR (MH "Cohort Studies+") OR (MH "Case-Control Studies+") OR (MH "Cross-Sectional Studies") OR (MH "Comparative Study") OR (MH "Evaluation Studies") OR (MH "Evaluation Studies as Topic") or (MH "Qualitative Research")
S15	S12 or S13 or S14
S16	S6 or S11 or S15

Appendix 2:

Contact details for Cochrane Systematic reviews and some ongoing studies and trials in ADHD

- Cochrane Systematic review - Meditation

Contact address: Thawatchai Krisanaprakornkit, Department of Psychiatry, Faculty of Medicine, KhonKaen University, KhonKaen, 40002, Thailand.
drthawatchai@yahoo.com.

- Cochrane Systematic review - Homeopathy

Contact address: Morag Heirs, Centre for Reviews and Dissemination, University of York, York, YO10 5DD, UK. mkc500@york.ac.uk.

- Cochrane Protocol for Systematic review - Fatty acid supplements

Contact address: John KH Sinn, Neonatal Unit, Royal North Shore Hospital, Level 5, Douglas Building, Pacific Hwy, St Leonards, New South Wales, 2065, Australia. jsinn@med.usyd.edu.au.

- Cochrane Protocol for Systematic review - Acupuncture

Contact address: Bo Yu, Department of paediatrics, The Second Affiliated Hospital of Wenzhou Medical College, No 109, Xue-Yuan-Xi-Lu Street, Wenzhou, Zhejiang, 325027, China. dog4317169@hotmail.com.

- Ongoing research on St John's Wort

Wendy Weber, N.D., Ph.D., M.P.H. conducted the trial on St John's Wort in ADHD- she now a program officer at:

National Center for Complementary and Alternative Medicine

E-mail: weberwj@mail.nih.gov

- Recent research into fatty acid supplementation (MAAFA trial)

Eric Taylor, Dept of Psychiatry, de Crespigny Park, London SE5 8AF

Appendix 3: Identified studies

1. Antidepressant drugs increase suicide risk in children. *Journal of Family Practice* 2006;55 (6):488.
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