

Effekt av behandling for angst og depresjon hos barn

Notat fra Kunnskapssenteret
Systematisk litteratursøk
med sortering
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Tittel	Effekt av behandling for angst og depresjon hos barn – systematisk litteratursøk med sortert referanseliste
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Nasjonalt kunnskapssenter for helsetjenesten fremskaffer og formidler kunnskap om effekt av metoder, virkemidler og tiltak og om kvalitet innen alle deler av helsetjenesten. Målet er å bidra til gode beslutninger slik at brukerne får best mulig helsetjenester. Kunnskapssenteret er formelt et forvaltningsorgan under Helsedirektoratet, men har ingen myndighetsfunksjoner og kan ikke instrueres i faglige spørsmål.

Nasjonalt kunnskapssenter for helsetjenesten
Oslo, august 2013

Hovedfunn

Nasjonalt kunnskapssenter for helsetjenesten fikk i oppdrag å finne dokumentasjon om effekt av behandling for angst og depresjon hos barn. Kunnskapssenteret har søkt etter eksisterende retningslinjer, systematiske oversikter og oversikter over forskningsoppsummeringer (overviews of systematic reviews). Vi publiserer funnene i form av et systematisk litteratursøk med sortering. Vi har ikke kvalitetsvurdert oversiktene.

Resultater

Vi identifiserte totalt 2444 referanser. Av disse ble 74 vurdert som mulig relevante. Referansene ble gruppert i tre kategorier. Det var 16 mulige relevante retningslinjer, 12 oversikter over oversikter og 46 systematiske oversikter.

Retningslinjer	16
Oversikter over oversikter	12
Systematiske oversikter	46

Tittel:

Effekt av behandling for angst og depresjon hos barn – systematisk litteratursøk med sortert referanseliste

Publikasjonstype:

Systematisk litteratursøk med sortering

Systematisk litteratursøk med sortering er resultatet av å

- søke etter relevant litteratur ifølge en søkestrategi og
- sortere denne litteraturen i grupper presentert med referanser og vanligvis sammendrag.

Svarer ikke på alt:

- Ingen kritisk vurdering av studienes kvalitet
- Ingen analyse eller sammenfatning av studiene
- Ingen anbefalinger.

Hvem står bak denne publikasjonen?

Kunnskapssenteret har gjennomført oppdraget etter forespørsel fra Helsedirektoratet

Når ble litteratursøket utført?

Søk etter studier ble avsluttet juni 2013.

Key messages

The Norwegian Knowledge Centre for the Health Services was commissioned to find documentation about the effectiveness of treatment for anxiety and/or depression in children. We searched for existing clinical guidelines, overviews of systematic reviews, and systematic reviews. Our findings are presented in this systematic reference list. We did not assess methodological quality of the publications.

Results

We identified a total of 2444 references in the database search. 74 were potentially relevant references. The included references were grouped according to the three publication forms.

Guidelines	16
Overviews of systematic reviews	12
Systematic reviews	46

Title:

Effect of treatment for anxiety and/or depression in children – systematic literature search.

Type of publication:

Systematic reference list

A systematic reference list is the result of a search for relevant literature according to a specific search strategy. The references resulting from the search are then grouped and presented with their abstracts.

Doesn't answer everything:

- No critical evaluation of study quality
- No analysis or synthesis of the studies
- No recommendations.

Publisher:

Norwegian Knowledge Centre for the Health Services.

Commissioner:

Norwegian Directorate of Health.

Updated:

Last search for studies: June, 2013.

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Forord

Nasjonalt kunnskapssenter for helsetjenesten fikk i oppdrag fra Helsedirektoratet v/ avdelingsdirektør for avdeling psykisk helse og rus, Gitte Huus, å finne dokumentasjon for effekt av behandling for angst og depresjon hos barn og unge, i primær- og spesialisthelsetjenesten. For å finne relevant dokumentasjon som besvarte spørsmålet utførte vi et systematisk litteratursøk. Deretter sortere vi de mulig relevante referansene ut fra publikasjonsform.

Prosjektgruppen har bestått av:

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Prosjektleder

Innledning

Nasjonalt kunnskapssenter for helsetjenesten fikk i oppdrag å finne dokumentasjon for effekt av behandling for angst og depresjon hos barn. Bakgrunn for bestillingen er at det i St.prp. 1 (2012-2013) fremgår at en av hovedutfordringene og et prioritert område er å styrke tilbudet til mennesker som lider av angst og depresjoner. Dette gjelder både barn og unge og voksne. Helsedirektoratet utarbeidet i 2009 Nasjonale retningslinjer for diagnostisering og behandling av voksne med depresjoner i primær- og spesialisthelsetjenesten. Retningslinjer for behandling av angstlidelser hos voksne ble utgitt i 1999. Helsedirektoratet har ikke utarbeidet noen retningslinjer på behandling av angst og depresjoner hos barn og unge. Angst og depresjon kan medføre sosial isolasjon og lidelsen kan utvikle seg til å bli mer omfattende og alvorlig dersom den ikke behandles. For at fremtidige valg av behandlingsmetode skal hvile på kunnskap fra forskning i forhold til nytten/virkningen, er det behov for en kunnskapsoppsummering på dette området.

For å finne relevant dokumentasjon som besvarte spørsmålet utførte vi et systematisk litteratursøk for å identifisere litteratur i allerede eksisterende retningslinjer, oversikter over oversikter og systematiske oversikter. Deretter sorterte vi de mulig relevante referansene ut fra publikasjonsform.

Vi har ikke søkt spesifikt etter norsk dokumentasjon. Det finnes allerede en oppdatert "Faglig veileder for barne- og ungdomspsykiatri" som kom i 2011. Denne, og andre mulige relevante faglige veiledere, retningslinjer og behandlingslinjer er tilgjengelig gjennom Helsebiblioteket på nettsiden

<http://www.helsebiblioteket.no/retningslinjer/barn-og-unge>

Styrker og svakheter ved litteratursøk med sortering

Ved litteratursøk med sortering gjennomfører vi systematiske søk i databaser for en gitt problemstilling. Vi gjennomgår treffene fra søket og sorterer ut ikke-relevante referanser. Resultatene blir i sin helhet overlevert oppdragsgiver. Dette gjøres basert på tittel og eventuelt sammendrag. Artikkene innhentes ikke i fulltekst. Det gjør at vi kan ha inkludert titler som ville vist seg ikke å være relevante ved gjennomlesning av fulltekst.

Vi benytter kun databaser for identifisering av litteratur og kan derfor ha gått glipp av potensielt relevante studier. Andre måter å identifisere studier på, som søk i referanselister, kontakt med eksperter på fagfeltet og upublisert litteratur, er ikke utført i dette oppdraget. Vi gjennomfører ingen kvalitetsvurdering av artiklene.

Ved en full forskningsoppsummering ville vi ha innhentet artiklene i fulltekst for endelig vurdering opp mot inklusjonskriteriene. Inkluderte studier ville så blitt kvalitetsvurdert i henhold til våre sjekklister og resultater sammenstilt, gradert og diskutert.

Problemstilling

Helsedirektoratet ønsker å vite hva som er de(n) mest effektive behandlingen for ulike typer angst og depresjoner hos barn og unge. Aktuelle spørsmål kan være:

- Hvilke psykoterapiformer er mest effektive for ungdom som har symptomer på angst og depresjoner?
- Hvilke former for medikamenter er mest effektive for barn som har symptomer på angst og depresjoner?
- Hvilke former for medikamenter er mest effektive for ungdom som har symptomer på angst og depresjoner?
- Hvilke psykoterapiformer og medikamenter fungerer best sammen for barn og ungdom?
- Er det noen behandlingsmetoder som er mer effektive når det gjelder ulike aldersgrupper?
- Er det noen behandlingsmetoder som er mer effektive når det gjelder ulike typer angst og depresjoner?
- Er det noen behandlingsmetoder som er mest effektive i spesialisthelsetjenesten, og andre metoder innen primærhelsetjenesten?

I prosjektet har vi søkt etter forskning om effekt av behandling for angst og/eller depresjon hos barn.

Det betyr at vi ikke spesifikt har søkt etter dokumentasjon om spørsmål knyttet til screening, forebygging, omfang, årsaker, opplevelsen for pasienter/pårørende og andre forskningsspørsmål om angst og depresjon hos barn.

Metode

Litteratursøking

Vi søkte systematisk etter litteratur i følgende databaser:

- Medline
- Embase
- PsycINFO
- Cinahl
- PubMed
- BMJ Clinical Evidence
- NHS
- Up-To-Date
- Evidence-Based Child Health
- Cochrane Database of Systematic Reviews
- Data-base of Abstracts of Reviews of Effect
- Cochrane Methodology Register
- Health Technology Assessment Database
- NHS Economic Evaluation Data-base
- G-I-N
- National Guidelines Clearinghouse
- TRIP

Forskningsbibliotekar Malene Gundersen planla og utførte samtlige søk. Den fullstendige søkestrategien er gjengitt bakerst i notatet. Søket bestod av emneord og tekstord for ”behandling” og diagnose ”angst” og ”depresjon” og ”barn”. Vi avgrenset søket til retningslinjer, oversikter over oversikter og systematiske oversikter publisert etter 2008. Søket ble avsluttet i juni 2013.

Inklusjonskriterier

Populasjon:	Barn med angst og/eller depresjon.
Tiltak:	<ul style="list-style-type: none">• Psykoterapi• Medikamentell behandling• Psykososial behandling• Kombinasjonsbehandling

	<ul style="list-style-type: none"> • Alternativ behandling • Fysisk aktivitet, trening, treningsterapi
Sammenlikning:	<ul style="list-style-type: none"> • Ingen behandling • Placebo • Annen behandling • Vanlig behandling • Venteliste
Utfall:	Symptomer på angst og/eller depresjon, livskvalitet og bivirkninger / uheldige hendelser.
Studiedesign:	Retningslinjer Oversikter over oversikter (overviews of systematic reviews) Systematiske oversikter om effektstudier
Språk:	Ingen begrensinger
Årstall:	Nyere enn 2008

Artikkelutvelging

Prosjektleder gikk gjennom alle titler for å vurdere relevans i henhold til inklusjonskriteriene. Utvelging av litteratur ble kun gjort basert på tittel og sammendrag. Vi innhentet ikke fulltekstversjonen av artiklene.

Artikkelsortering

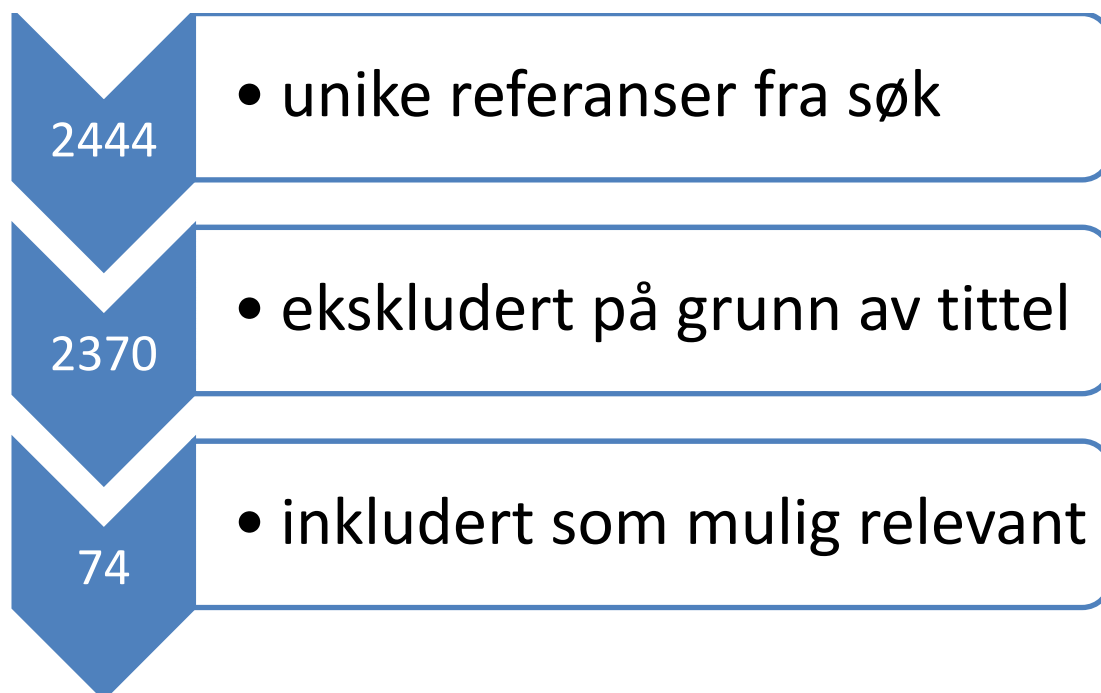
En person gikk gjennom alle de inkluderte referansene og sorterte dem i henhold til de forhåndsdefinerte kategoriene/publikasjonsform. Vurderingene ble gjennomgått av en annen person i etterkant. Sorteringen av litteratur ble kun gjort basert på tittel og sammendrag. Vi leste ikke fulltekstversjonen av artiklene.

Resultat

Resultat av søk

Søket resulterte i 2444 referanser. Vi vurderte 74 av de identifiserte referansene til å være mulig relevante i henhold til inklusjonskriteriene.

Hovedårsaken til eksklusjon av litteratur var at publikasjonen ikke så ut til å være relevant for vår problemstilling eller den hadde ikke relevant metodologisk design slik vi hadde forhåndsdefinert det i inklusjonskriteriene. Vi ekskluderte ikke på basis av utfallsmål siden det ofte er mangelfullt rapportert i tittel/sammendrag.



Figur 1. Flytskjema over identifiserte publikasjoner

Resultat av sorteringen

De 74 mulig relevante referansene ble sortert i tre kategorier ut fra publikasjonsform (se tabell 1).

Tabell 1: inkluderte referanser sortert etter publikasjonsform

Tiltak	Antall referanser
Retningslinjer	16
Oversikter over oversikter (oversikter over systematiske oversikter)	12
Systematiske oversikter publisert i Cochrane-biblioteket	46

Vi presenterer de 74 inkluderte referansene fordelt alfabetisk etter førsteforfatter. De 16 retningslinjene som er inkludert har som oftest ikke et sammendrag tilgjengelig (1-16). Det var 12 inkluderte oversikter over oversikter og de har i stor grad basert seg på eksisterende Cochrane-oversikter (17-28). Vi presenterer de 46 inkluderte systematiske oversiktene med sammendrag (der de er tilgjengelig) (29-74).

Mulige relevante retningslinjer

1. **Guideline Summary: Screening and treatment for major depressive disorder in children and adolescents: U.S. Preventive Services Task Force recommendation statement.** [U.S. Preventive Services Task Force]. info@guidelinegov (NGC) 2009.
2. **Clinical Practice Guideline on Major Depression in Childhood and Adolescence.** GuiaSalud 2009.
3. **Guideline Summary: Clinical practice guideline on major depression in childhood and adolescence.** [Galician Health Technology Assessment Agency]. info@guidelinegov (NGC) 2009.
4. **Guideline Summary: Best evidence statement (BEST). Treatment of children and adolescents with major depressive disorder (MDD) during the acute phase.** [Cincinnati Children's Hospital Medical Center]. info@guidelinegov (NGC) 2010.
5. **Best evidence statement (BEST). Treatment of children and adolescents with major depressive disorder (MDD) during the acute phase.** [Cincinnati Children's Hospital Medical Center]. info@guidelinesgov (NGC) 2010.
6. **Anxiety and Depression in Children and Youth - Diagnosis and Treatment.** Clinical Practice Guidelines and Protocols in British Columbia 2010.

7. **Guideline Summary: Anxiety and depression in children and youth** diagnosis and treatment. [Medical Services Commission, British Columbia]. info@guidelinegov (NGC) 2013.

8. Cheung AH, Zuckerbrot RA, Jensen PS, Ghalib K, Laraque D, Stein REK. **Guidelines for adolescent depression in primary care (GLAD-PC): II treatment and ongoing management (Pediatrics (2007) 120, (e1313-e1326))**. Pediatrics 2008;121(1):227.

9. McDermott B, Baigent M, Pope S. **The beyondblue/NHMRC Clinical Practice Guidelines: Depression in adolescents and young adults-process considerations, key findings and implications for policy and practice**. Australian and New Zealand Journal of Psychiatry 2011;Conference: Royal Australian and New Zealand College of Psychiatrists, RANZCP Annual Congress 2011 Darwin, NT Australia. Conference Start: 20110529 Conference End: 20110602. Conference Publication:(var.pagings):A10-A11.

Abstract: Depression, anxiety and related disorders affect approximately one in five adolescent girls and one in nine adolescent boys, and can seriously affect quality of life for these young people and their families. There are many factors which influence the risk of depression and rate of recovery following depression. In order to address these factors and provide comprehensive and appropriate care for adolescents and young adults it is vital that prevention, diagnosis and treatment strategies are underpinned by high quality research evidence. In 2008 beyondblue was charged with the task of updating the revoked NHMRC Clinical Practice Guidelines: Depression in Young People (1997), to assist health professionals to accurately identify and effectively treat depression amongst adolescents and young adults. The development of the updated guidelines involved adherence to NHMRC guideline development methodology, and through this process has highlighted a number of recommendations for health professionals as well as areas where the evidence is not sufficient. Attendees at the symposium will learn about the key processes which were undertaken by an expert panel of academic, clinical and consumer representatives to ensure that the updated guidelines were of high scientific and ethical quality; the key findings from the comprehensive literature search, and final guideline recommendations will be reported and discussed, including a discussion about how these evidence-based recommendations can be incorporated into practice and policy; and areas for further research will be highlighted

10. Raphael S. **New recommendations on screening and treatment for major depressive disorder in children and adolescents**. Journal of Child and Adolescent Psychiatric Nursing Vol22(3), Aug 2009, pp170-171 2009 (3):Aug-171.

Abstract: The purpose of this brief article is to describe the contents of the recommendation statement, including the clinical considerations of the statement and its implications for advanced practice nurses in both mental health and primary care settings. Efforts to provide evidence-based preventive services for children at risk of depression have been stymied by a lack of research support that routine screening is effective. The recommendation statement is based on an extensive review that is well described in the April 1, 2009, issue of Pediatrics. This recommendation statement comes in the context of significant shortages of mental health specialists, especially child and adolescent psychiatric nurses. Screening all adolescents for depression offers providers the opportunity for preventive

services before the illness leads to lifelong negative outcomes. Finally, implementation of these recommendations will require collaborative effort between providers in both primary care and mental health settings. These recommendations also require all providers to participate in ensuring that any adolescent who screens positively for depression has the necessary follow-up care, especially when that care comes from a different provider. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

11. Research AAFH, Quality. **Best evidence statement (BEST). Screening of children and adolescents for major depressive disorder (MDD). Cincinnati Children's Hospital Medical Center. NGC:007859.** 2010.
12. Services USP. **Screening and treatment for major depressive disorder in children and adolescents: US Preventive Services Task Force Recommendation Statement.** Pediatrics 2009;123(4):1223-1228.
Abstract: DESCRIPTION: This is an update of the 2002 US Preventive Services Task Force recommendation on screening for child and adolescent major depressive disorder METHODS: The US Preventive Services Task Force weighed the benefits and harms of screening and treatment for major depressive disorder in children and adolescents, incorporating new evidence addressing gaps in the 2002 recommendation statement. Evidence examined included the benefits and harms of screening, the accuracy of primary care-feasible screening tests, and the benefits and risks of treating depression by using psychotherapy and/or medications in patients aged 7 to 18 years RECOMMENDATIONS: Screen adolescents (12-18 years of age) for major depressive disorder when systems are in place to ensure accurate diagnosis, psychotherapy (cognitive-behavioral or interpersonal), and follow-up (B recommendation). Evidence is insufficient to warrant a recommendation to screen children (7-11 years of age) for major depressive disorder (I statement)
13. Societies AAoSM. **Behandlung von depressiven Störungen bei Kindern und Jugendlichen. S2e-LL (DGKJP).** 2012.
14. Societies AAoSM. **Behandlung von Angststörungen bei Kindern und Jugendlichen. S2e-LL (DGKJP, BKJPP, BAG).** 2013.
15. Moreland CB, L. **Psychopharmacological treatment for adolescent depression.** http://www.uptodate.com/contents/psychopharmacological-treatment-for-adolescent-depression?detectedLanguage=en&source=search_result&search=depression&selectedTitle=7~150&provider=noProvider: Up top date; 2013.

There have been few well-designed controlled trials of treatments for adolescent depression. Current practice guidelines for treating adolescent depression are based upon existing data from studies in depressed adolescents, adult depression research, and clinical expertise. (See "Overview of treatment for adolescent depression".)

The combination of medication and psychosocial intervention appears to be most effective for the treatment of major depressive disorder in adolescents. (See "Overview of treatment for adolescent depression", section on 'Efficacy' and "Psychosocial treatment for adolescent depression".)

Decisions regarding the use of medication in adolescents with MDD must be individualized. Factors to be considered include the severity of the depression, presence of suicidality, comorbid diagnoses, difficulty with other treatments or prior response to treatments, the motivation of the patient and

family, and their assessment of the balance of risks and benefits of therapy. (See 'Initiation of pharmacotherapy' above and "Effect of antidepressants on suicide risk in children and adolescents".)

The patient and family should be educated about depression and the various treatment modalities. Regarding medication, the risks, benefits, side effects, criteria for discontinuation, and the United States Food and Drug Administration black box warning should be fully explained (table 5 and table 6). (See 'Education' above and 'Adverse reactions' above and "Effect of antidepressants on suicide risk in children and adolescents".)

We suggest combination therapy with fluoxetine and cognitive behavioral therapy as the initial treatment for adolescents with major depressive disorder (Grade 2B). An agent other than fluoxetine can be used if there is sound clinical reasoning to do so. Cognitive behavioral therapy is discussed separately. (See 'Resistant depression' above and "Overview of treatment for adolescent depression", section on 'Efficacy' and "Psychosocial treatment for adolescent depression".)

Antidepressant therapy should be started only when careful monitoring of the patient can be assured. If symptoms are not improved after four to six weeks at the target dose (ie, six to eight weeks after treatment initiation), the dose should be increased, an alternative agent should be tried, or the patient referred to a specialist for further assessment. (See 'Dose titration' above.)

We recommend that adolescents who are treated with antidepressants be closely monitored by the clinician and family for worsening depression and suicidality (Grade 1C). (See 'Monitoring' above and "Effect of antidepressants on suicide risk in children and adolescents".)

We suggest that patients who develop abrupt or severe suicidal ideation during treatment with a selective serotonin reuptake inhibitor (SSRI) undergo a change in their pharmacologic regimen (Grade 2C). This may include adjusting the SSRI dose, changing to an alternative SSRI, or discontinuing the SSRI. These changes should occur under the care of the prescribing clinician. (See 'Monitoring' above.)

For adolescents who do not respond to initial monotherapy with SSRI, we suggest switching to a different SSRI and the addition of CBT (Grade 2B). (See 'Resistant depression' above.)

We suggest that antidepressant therapy be continued for 9 to 12 months after the patient has returned to baseline mood (Grade 2B). (See 'Duration' above.)

We recommend that antidepressant medication be tapered before discontinuation (Grade 1B). A taper of 10 to 25 percent per week provides a gradual decrease and allows the body time to adjust to the lower dose.

16. Bonin LM, CS. **Psychosocial treatment for adolescent depression.** http://www.uptodate.com/contents/psychosocial-treatment-for-adolescent-depression?detectedLanguage=en&source=search_result&search=depression&selectedTitle=15~150&provider=noProvider: Up to date; 2013.

Abstract: SUMMARY

Psychosocial treatments are an important component of the treatment of depression in adolescents. Among the psychosocial treatments, only cognitive-behavioral therapy (CBT) and interpersonal therapy for adolescents (IPT-A) have been shown to be effective in controlled trials. (See 'Introduction' above.)

CBT is based upon the assumption that targeting changes in thoughts and/or behaviors can effect therapeutic change. Effective forms of CBT focus on:

Increasing involvement in pleasurable, mood-enhancing activities
Increasing quantity and improving quality of social interactions
Improving conflict resolution and social problem-solving skills
Reducing physiologic tension

Modifying or restructuring depressogenic thoughts
(See 'Description' above.)

In the acute phase of therapy for moderate or severe depression, CBT is most effective when combined with antidepressant medication. Its role in the durability of response during the maintenance phase of therapy remains to be determined, but it appears to be beneficial [12,25]. (See 'Studies of CBT' above.)

IPT-A is based upon the assumption that, independent of the cause of depression, depression is associated with disrupted relationships. It focuses on relationship problems associated with the adolescent's depression. (See 'Interpersonal psychotherapy for adolescents (IPT-A)' above.)

When choosing a therapist, it is important to consider the therapist's training and experience implementing evidence-based approaches with adolescents, as well as whether or not family members will be incorporated in the adolescent's treatment. (See 'Choosing a therapist' above.)

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Mulige relevante oversikter over oversikter

17. **Depression in children.** NICE Clinical Knowledge Summaries 2009.
18. Bachmann M, Bachmann C, Rief W, Matthejat F. **Efficacy of psychiatric and psychotherapeutic interventions in children and adolescents with psychiatric disorders-A systematic evaluation of meta-analyses and reviews. Part I: Anxiety disorders and depressive disorders.** Zeitschrift für Kinder- und Jugendpsychiatrie und Psychotherapie Vol36(5), Sep 2008, pp309-320 2008 (5):Sep-320.
Abstract: Objective: In recent years, a large and growing body of research on the effectiveness of treatments for psychiatric disorders in childhood and adolescence has been published; however, the large number makes it difficult to get an overview on the current status of research. The aim of this article is to systematically review the existing meta-analyses and reviews on the four most frequent childhood and adolescent psychiatric disorders (anxiety disorder, depression, ADHD, conduct disorder) and to present an up-to-date summary on the effects of treatment for those disorders. Methods: This article is based on a systematic literature search, which produced 112 meta-analyses and reviews on efficacy of psychological and psychiatric interventions in childhood and adolescence published between 2000 and 2007. The articles resulting from the literature search were evaluated according to clearly defined criteria. Presentation of the results follows a dichotomous classification (internalizing vs. externalizing disorders), with Part I of this article reporting the results on anxiety disorders and depressive disorders. Results: The majority of reviews published between 2000 and 2007 focuses on the treatment of depressive disorders and ADHD. Only for ADHD is the use of medication (stimulants) considered to be the most efficacious treatment option available. For the remaining three disorders, psychotherapy is recommended as the most effective treatment of choice. A combination of psychological and pharmacological treatments is an important option in ADHD and depressive disorders. Considering the efficacy, treatments for ADHD and anxiety disorders produce higher effect-sizes than do interventions for depressive and conduct disorders. For all disorders, there are several desiderata (content and methodological aspects) to be incorporated into future research. Discussion: Empirically supported

treatment recommendations can be derived for anxiety disorders, depressive disorders, ADHD and conduct disorders. Finally, important implications for research and practice are discussed. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

19. Elmquist JM, Melton TK, Croarkin P, McClintock SM. **A systematic overview of measurement-based care in the treatment of childhood and adolescent depression.** *Journal of Psychiatric Practice* 2010;16(4):217-234.

Abstract: Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders affecting children and adolescents. The significant psychiatric, social, and functional impairments associated with this disorder coupled with the high incidence of relapse indicate a need for continued efforts to enhance treatment. Current empirically supported treatments for childhood and adolescent MDD include psychotropic medications, psychotherapy, and a combination of both treatments, with selection of the most appropriate strategy depending on symptom severity. One strategy to enhance treatment outcome is the use of measurement-based care. This article provides a systematic review of measurement-based care in the treatment of childhood and adolescent MDD. It also presents a comprehensive analysis of widely used depression rating scales and discusses their utility in clinical practice. This review found evidence supporting the utility and benefit of depression rating scales to document depression severity in children and adolescents. We also found evidence suggesting that many of these scales are time efficient, and that both clinician-rated and self-rated scales provide accurate assessment of depressive symptomatology. Future research is warranted to examine the utility of measurement-based care in clinical practice with child and adolescent populations

20. Kaminski A, Gartlehner G. **Children and adolescents with major depressive disorders: Are some second generation antidepressants better than others?** *European Psychiatry* 2011;Conference: 19th European Congress of Psychiatry, EPA 2011 Vienna Austria. Conference Start: 20110312 Conference End: 20110315. Conference Publication:(var.pagings).

Abstract: Introduction: Since the black box warning of the FDA (Food and Drug Administration) regarding an increased risk of suicidality in children and adolescents treated with antidepressants, cautious prescription of antidepressant drugs in young patients became even more important. In the light of potentially severe side effects the comparative effectiveness and harms of antidepressants should be known to clinicians to provide optimal treatment. Objectives: To compare the benefits and harms of second-generation antidepressants for the treatment of Major Depressive Disorder (MDD) in children and adolescents. Aims: To provide an evidence base for clinicians and policymakers when making informed decisions regarding the prescription of Selective Serotonin Reuptake Inhibitors and other newer antidepressants. Methods: We updated a comparative effectiveness report of the Oregon Drug Effectiveness Review Project searching MEDLINE, Embase, The Cochrane Library, and the International Pharmaceutical Abstracts up to August 2010. Two persons independently reviewed the literature, abstracted data, and rated the risk of bias. Results: We could not identify any head-to-head trials. There is insufficient evidence to compare one second-generation antidepressant to another in pediatric outpatients with MDD. Evidence from a systematic review of published and unpublished data indicates, that in children and adolescents only fluoxetine shows a good risk-benefit ratio. Conclusions: To date, the evidence is insufficient to make any clear

inferences about the comparative benefits and harms of second-generation antidepressants for the treatment of MDD in children. Clinicians must be aware of the small benefits and the high potential risks when prescribing antidepressant medications to children and adolescents

21. Manassis K, Russell K, Newton AS. **The Cochrane Library and the treatment of childhood and adolescent anxiety disorders: an overview of reviews.** Evidence-Based Child Health: A Cochrane Review Journal 2010;5(2):541-554.

Abstract: Background Anxiety disorders are among the most common psychiatric disorders diagnosed during childhood and adolescence. Reported lifetime prevalence of children or adolescents meeting criteria for at least one anxiety disorder in industrialized countries ranges from 8%–27%. Current treatment includes psychotherapy (cognitive and behavioural therapies) as well as medication which is almost always used together with psychotherapy, rather than as a stand-alone treatment. Objective To synthesize the evidence currently in the Cochrane Database of Systematic Reviews (CDSR) related to the question: “In the treatment of childhood and adolescent anxiety disorders, which pharmacologic or nonpharmacologic treatments are known to improve symptom response, response rates, functional capacity, adherence, persistence, and acceptability as well as increase diagnostic remission and decrease adverse events?”TM. Methods The CDSR was searched using the term “anxiety disorders”TM in the title for all systematic reviews examining pharmacologic and nonpharmacologic interventions for the treatment of anxiety disorders in children and adolescents, including pharmacotherapy and psychotherapy. Data were extracted and entered into tables; data were synthesized using qualitative and quantitative methods. Main Results Of the studies included in the CDSR, treatment of childhood and adolescent anxiety disorders with cognitive behavioural therapy (CBT) led to significant reductions in anxiety symptoms and increased recovery. Treatment with CBT or behavioural therapy (BT) led to notable reductions in Obsessive–Compulsive Disorder (OCD) severity and a reduced risk of treatment failure. Use of selective serotonin reuptake inhibitors (SSRIs) and the selective norepinephrine reuptake inhibitor (SNRI) venlafaxine were superior to placebo in treating OCD and other anxiety disorders. There was no clear evidence that any particular SSRI or venlafaxine was most efficacious or best tolerated. While few studies were available, CBT combined with a SSRI or SNRI led to significant reductions in both anxiety and OCD symptoms. Psychotherapy (CBT/BT), used alone or in combination with medication, had a mixed impact on reducing risk of treatment failure for OCD. Author’s Conclusions For childhood and adolescent anxiety disorders, including OCD, the CDSR reviews suggest that psychotherapy treatments are efficacious in reducing symptom severity. Although the CDSR does not include a number of recent research publications on CBT, these newer studies further reinforce CBT efficacy. Pharmacotherapy evidence from the CDSR supports using medication in treating anxiety disorders, and while few studies examined combined pharmacological and psychological treatment, results to date are also favourable for this combination. Clinicians should rely on expert consensus guidelines vis-à-vis this evidence as treatment decision-making should be moderated by the patient’s illness severity. Psychotherapy remains the first line treatment for mild to moderate symptoms, whereas pharmacotherapy is used for severe or treatment-resistant disorders. In conclusion, there is a body of literature in the CDSR to support evidence-based treatment decisions for pediatric anxiety disorders; however, as this is a field that is rapidly expanding its knowledge base, efforts must be made to ensure the

22. Zinck S, Bagnell A, Bond K, Newton AS. **The Cochrane library and the treatment of major depression in children and youth: an overview of reviews.** Evidence-Based Child Health: A Cochrane Review Journal 2009;4(4):1336-1350.

Abstract: Background Major depression (MDD) in children and adolescents is a mood disorder that has up to 25% lifetime prevalence by the end of adolescence. Pharmacological and nonpharmacological treatments are recommended to reduce symptoms, increase psychosocial functioning, and prevent relapse. Traditionally, decisions for these treatments were made based on reported effects for adults, but a body of pediatric-based evidence is now emerging to inform treatment decisions. Objectives To synthesize the evidence currently in the Cochrane Library Database of Systematic Reviews (CDSR) related to the question: "In children and youth with diagnosed major depression, do pharmacologic or nonpharmacologic treatments improve symptom response, response rates, functional capacity, adherence and persistence, and decrease cost and adverse events?"TM. Methods CDSR was searched using the term "depression"TM in the title for all systematic reviews examining pharmacologic and nonpharmacologic interventions for the treatment of depression in children & 18 years. Data were extracted and entered into tables; data were synthesized using qualitative and quantitative methods. Main Results Of the studies included in the CDSR, there was no significant improvement in treatment outcomes in depressed children and adolescents treated with pharmacological (tricyclic antidepressant [TCA] or selective serotonin reuptake inhibitor [SSRI]) or nonpharmacological (exercise) interventions. Author's Conclusions Although this overview indicates no clear evidence for pharmacological and nonpharmacological interventions for treatment of depression in this age group, the CDSR does not include several recent research publications in this area that demonstrate beneficial effects of treatment. In context of existing research there may be a moderate effect of SSRI in moderate to severe depression in children and youth. Best practice recommendations are consideration of treatment with SSRI (fluoxetine first line) in moderate to severe depression with close monitoring and weighing risk/benefit profile based on individual assessment. Psychotherapeutic interventions not in this overview, including Cognitive Behavioral Therapy (CBT) and Interpersonal Therapy (IPT), have some evidence of effectiveness in mild to moderate depression. Although exercise remains an important part of healthy living, there is no evidence to support its use in treatment of depression in children and adolescents. This overview in the context of recent research indicates the need for ongoing study in this important area of child and youth mental health. Copyright -© 2009 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd. The Cochrane Collaboration

23. Hazell P. **Electroconvulsive therapy in children and adolescents.**

Clinical Evidence. <http://clinicalevidence.bmj.com/x/systematic-review/1008/intervention/sr-1008-i3.html>; BMJ; 2011.

Abstract: We found no direct information from RCTs about electroconvulsive therapy in the treatment of depression in children and adolescents.

24. Hazell P. **MAOIs in children and adolescents.**

<http://clinicalevidence.bmj.com/x/systematic-review/1008/intervention/sr-1008-i5.html>; BMJ; 2011.

Abstract: We don't know whether moclobemide is effective in children and adolescents with depression.

25. Gale CM, J. **CBT in children and adolescents.**
<http://clinicalevidence.bmj.com/x/systematic-review/1002/intervention/sr-1002-i1175161344758.html>: BMJ; 2011.
Abstract: CBT improves symptoms compared with waiting list control or active control. Most RCTs of CBT in children and adolescents have included other anxiety disorders. We found no trials in participants with GAD alone.
26. Hazell P. **CBT (individual) in children and adolescents.**
<http://clinicalevidence.bmj.com/x/systematic-review/1008/intervention/sr-1008-i21.html>: BMJ; 2011.
Abstract: We don't know whether individual CBT improves symptoms of depression in children and adolescents.
27. Hazell P. **Omega-3 polyunsaturated fatty acids (fish oil).**
<http://clinicalevidence.bmj.com/x/systematic-review/1008/intervention/sr-1008-i1178642179259.html>: BMJ; 2011.
Abstract: We found no direct information about omega-3 polyunsaturated fatty acids in the treatment of depression in children or adolescents.
28. Hazell P. **Fluoxetine plus CBT in adolescents.**
<http://clinicalevidence.bmj.com/x/systematic-review/1008/intervention/sr-1008-i11.html>: BMJ; 2011.

Mulige relevante systematiske oversikter

29. Larun L. **Exercise in prevention and treatment of anxiety and depression among children and young people.** Cochrane Database of Systematic Reviews 2009.
30. **Day therapy programs for adolescents with mental health problems: a systematic review.** 2011.
Abstract: Bibliographic details Deenadayalan Y, Perraton L, Machotka Z, Kumar S. - Day therapy programs for adolescents with mental health problems: a systematic review.- Internet Journal of Allied Health Sciences and Practice- 2010;- 8(1):- 1-14 Status This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn. CRD summary This review concluded that day therapy programmes with a multimodal and multidisciplinary approach may be effective interventions for adolescents with mental health issues. These conclusions reflect the evidence of the review, but concerns over selection bias and poor reporting mean that they should be interpreted with caution
31. Brendel KE. **A systematic review and meta-analysis of the effectiveness of child-parent interventions for children and adolescents with anxiety disorders.** Dissertation Abstracts International Section A: Humanities and Social Sciences Vol72(8-A), 2012, pp2965 2012 (8-A):2012, pp.
Abstract: Anxiety disorders are the most prevalent psychiatric disorders in childhood (Hirshfeld-Becker & Biederman, 2002; Walkup & Ginsburg, 2002), occurring in approximately twenty percent of the population (APA,

2000; Langley Lindsey, Bergman & Piacentini, 2002). Children and adolescents with anxiety disorders often experience many detrimental effects such as low-self esteem, issues with social and family relationships, and a decrease in overall functioning, including academic performance. In addition, if left untreated or unrecognized, anxiety disorders in childhood often lead to more severe symptoms in adulthood including depression, substance abuse, suicidal ideation, and other comorbid anxiety disorders. Evidence suggests that anxiety disorders are transmitted intergenerationally, with 60 to 80 percent of parents with anxiety disorders having children with anxiety disorders (Last, Hersen, Kazdin, Orvaschel & Perrin, 1991; Merikangas, Dieker & Szatmari, 1998), which can further exacerbate anxious symptoms. With children and parents cohabitating with anxious symptoms and passing down anxious symptoms to the next generation, the need exists to explore effective family based interventions. The present study is a systematic review and meta-analysis that explores the effectiveness of child-parent interventions for childhood anxiety disorders. The research located during the literature search was coded for inclusionary criteria and resulted in eight qualifying individual randomized controlled trials (RCT) with a total of 710 participating children and adolescents (440 completer data). Statistical information from the studies were meta-analyzed using Hedges' g via CMA software [Version 2]. Results of the meta-analysis yielded a small, positive effect size of 0.263 (SE=0.103, 95% CI= 0.062 to 0.465) favoring child-parent cognitive behavioral interventions over individual and group cognitive behavioral therapy. Results were homogeneous indicating that any variance in effect size can be confidently attributed to sampling error (Q=7.728, df=7, p=0.357). (PsycINFO Database Record (c) 2012 APA, all rights reserved)

32. Brown HE, Pearson N, Braithwaite RE, Brown WJ, Biddle SJ. **Physical activity interventions and depression in children and adolescents : a systematic review and meta-analysis.** Sports Medicine 2013;43(3):195-206.

Abstract: CONTEXT: Evidence suggests chronic physical activity (PA) participation may be both protective against the onset of and beneficial for reducing depressive symptoms OBJECTIVE: The aim of this article is to assess the impact of PA interventions on depression in children and adolescents using meta-analysis DATA SOURCES: Published English language studies were located from manual and computerized searches of the following databases: PsycInfo, The Cochrane Database of Systematic Reviews and The Cochrane Central Register of Controlled Trials, Trials Register of Promoting Health Interventions (TRoPHI; EPPI Centre), Web of Science and MEDLINE STUDY SELECTION: Studies meeting inclusion criteria (1) reported on interventions to promote or increase PA; (2) included children aged 5-11years and/or adolescents aged 12-19years; (3) reported on results using a quantitative measure of depression; (4) included a non-physical control or comparison group; and (5) were published in peer-reviewed journals written in English, up to and including May 2011 (when the search was conducted) DATA EXTRACTION: Studies were coded for methodological, participant and study characteristics. Comprehensive Meta-Analysis version-2 software was used to compute effect sizes, with subgroup analyses to identify moderating characteristics. Study quality was assessed using the Delphi technique RESULTS: Nine studies were included (n=581); most were school-based randomized controlled trials, randomized by individual. Studies used a variety of measurement tools to assess depressive symptoms. The summary treatment effect was small but significant (Hedges' g=-0.26, standard error=0.09, 95% confidence intervals=-0.43, -0.08,

p=0.004). Subgroup analyses showed that methodological (e.g. studies with both education and PA intervention; those with a higher quality score; and less than 3 months in duration) and participant characteristics (e.g. single-gender studies; those targeting overweight or obese groups) contributed most to the reduction in depression. **CONCLUSIONS:** There was a small significant overall effect for PA on depression. More outcome-focused, high-quality trials are required to effectively inform the implementation of programmes to reduce depressive symptoms in children and adolescents

33. Calati R, Pedrini L, Alighieri S, Alvarez MI, Desideri L, Durante D, et al. **Is cognitive behavioural therapy an effective complement to antidepressants in adolescents? A meta-analysis.** *Acta Neuropsychiatrica* 2011;23(6):263-271.
Abstract: Calati R, Pedrini L, Alighieri S, Alvarez MI, Desideri L, Durante D, Favero F, Iero L, Magnani G, Pericoli V, Polmonari A, Raggini R, Raimondi E, Riboni V, Scaduto MC, Serretti A, De Girolamo G. Is cognitive behavioural therapy an effective complement to antidepressants in adolescents? A meta-analysis. Objective: Evidence on effectiveness of combined treatments versus antidepressants alone in adolescents consists on a few studies in both major depressive and anxiety disorders. A meta-analysis of randomised 12-week follow-up studies in which antidepressant treatment was compared to combined treatment consisting of the same antidepressant with cognitive behavioural therapy has been performed. Methods: Data were entered into the Cochrane Collaboration Review Manager software and were analysed within a random effect framework. A quality assessment has been performed through Jadad Scale. Results: Higher global functioning at the Children's Global Assessment Scale was found in the combined treatment group ($p < 0.0001$) as well as higher improvement at the Clinical Global Impressions Improvement Scale ($p = 0.04$). No benefit of combined treatment was found on depressive symptomatology at the Children's Depression Rating Scale - Revised. Conclusion: Combined treatment seems to be more effective than antidepressant alone on global functioning and general improvement in adolescents with major depressive and anxiety disorders. 2011 John Wiley & Sons A/S
34. Calcar AL, Christensen H. **Systematic review of school-based prevention and early intervention programs for depression.** *Journal of Adolescence* 2010;33(3):429-438.
Abstract: A systematic review was conducted to identify and describe school-based prevention and early intervention programs for depression and to evaluate their effectiveness in reducing depressive symptoms. Forty-two randomised controlled trials, relating to 28 individual school-based programs, were identified through the Cochrane Library, PsycInfo and PubMed databases. A large proportion of the programs identified were based on cognitive behavioural therapy (CBT), and delivered by a mental health professional or graduate student over 8-12 sessions. Indicated programs, which targeted students exhibiting elevated levels of depression, were found to be the most effective, with effect sizes for all programs ranging from 0.21 to 1.40. Teacher program leaders and the employment of attention control conditions were associated with fewer significant effects. Further school-based research is required that involves the use of attention controls, long-term follow-ups and which focuses on the training and evaluation of sustainable program leaders, such as teachers. [References: 80]
35. Carandang C, Jabbar R, MacBride A, Elbe D. **A review of escitalopram and citalopram in child and adolescent depression.** *Journal of the*

Canadian Academy of Child and Adolescent Psychiatry / Journal de l'Académie canadienne de psychiatrie de l'enfant et de l'adolescent Vol20(4), Nov 2011, pp315-414 2011 (4):Nov-414.

Abstract: Objective: To review the basic pharmacology and published literature regarding escitalopram and citalopram in child and adolescent depression.

Methods: A literature review was conducted using the search terms: 'escitalopram', 'citalopram', 'depression', 'randomized controlled trial', 'open label trial' and limits set to: Human trials, English Language and All Child (Age 0-18). Additional articles were identified from reference information and poster presentation data. Results: Three prospective, randomized controlled trials (RCT) were found for escitalopram in pediatric depression, and two RCTs were found for citalopram. One RCT each for escitalopram and citalopram showed superiority over placebo on the primary outcome measure. Adverse effects in escitalopram and citalopram trials were generally mild to moderate. Suicidality was not assessed systematically in all RCTs reviewed, but did not appear to be elevated over placebo in escitalopram RCTs. One trial reported numerically higher suicide related events for citalopram compared to placebo (14 vs. 5, $p = 0.06$). Conclusion: At present, escitalopram and citalopram should be considered a second-line option for adolescent depression. The US Food and Drug Administration approval of escitalopram for treatment of adolescent depression was based on a single positive RCT. This is less evidence than typically required for approval of a drug for a new indication. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

36. Cohen D, Deniau E, Maturana A, Tanguy ML, Bodeau N, Labelle R, et al. **Are child and adolescent responses to placebo higher in major depression than in anxiety disorders? A systematic review of placebo-controlled trials.** PLoS ONE [Electronic Resource] 2008;3(7):e2632.

Abstract: BACKGROUND: In a previous report, we hypothesized that responses to placebo were high in child and adolescent depression because of specific psychopathological factors associated with youth major depression. The purpose of this study was to compare the placebo response rates in pharmacological trials for major depressive disorder (MDD), obsessive compulsive disorder (OCD) and other anxiety disorders (AD-non-OCD) METHODOLOGY AND PRINCIPAL FINDINGS: We reviewed the literature relevant to the use of psychotropic medication in children and adolescents with internalized disorders, restricting our review to double-blind studies including a placebo arm. Placebo response rates were pooled and compared according to diagnosis (MDD vs. OCD vs. AD-non-OCD), age (adolescent vs. child), and date of publication. From 1972 to 2007, we found 23 trials that evaluated the efficacy of psychotropic medication (mainly non-tricyclic antidepressants) involving youth with MDD, 7 pertaining to youth with OCD, and 10 pertaining to youth with other anxiety disorders (N = 2533 patients in placebo arms). As hypothesized, the placebo response rate was significantly higher in studies on MDD, than in those examining OCD and AD-non-OCD (49.6% [range: 17-90%] vs. 31% [range: 4-41%] vs. 39.6% [range: 9-53], respectively, ANOVA $F = 7.1$, $p = 0.002$). Children showed a higher stable placebo response within all three diagnoses than adolescents, though this difference was not significant. Finally, no significant effects were found with respect to the year of publication CONCLUSION: MDD in children and adolescents appears to be more responsive to placebo than other internalized conditions, which highlights differential psychopathology. [References: 110]

37. Corrieri S, Heider D, Conrad I, Blume A, Konig HH, Riedel-Heller SG. **School-based prevention programs for depression and anxiety in adolescence: a systematic review.** Health PromotInt 2013.
 Abstract: School-based interventions are considered a promising effort to prevent the occurrence of mental disorders in adolescents. This systematic review focuses on school-based prevention interventions on depression and anxiety disorders utilizing an RCT design, starting from the year 2000. Based on an online search (PubMed, Scirus, OVID, ISI) and bibliographic findings in the eligible articles, 28 studies providing information were reviewed. The search process ended on 2 May 2011. The majority of interventions turn out to be effective, both for depression (65%) and anxiety (73%). However, the obtained overall mean effect sizes calculated from the most utilized questionnaires can be considered rather small (CDI: -0.12; RCMAS: -0.29). The majority of the reviewed school-based interventions shows effectiveness in reducing or preventing mental disorders in adolescents. However, effect size computation revealed only small-scale effectiveness. Future studies have to consider the impact of program implementation variations
38. Cox GR, Callahan P, Churchill R, Hunot V, Merry SN, Parker AG, et al. **Psychological therapies versus antidepressant medication, alone and in combination for depression in children and adolescents.** Cochrane Database of Systematic Reviews 2012;11:CD008324.
 Abstract: BACKGROUND: Depressive disorders are common in children and adolescents and, if left untreated, are likely to recur in adulthood. Depression is highly debilitating, affecting psychosocial, family and academic functioning OBJECTIVES: To evaluate the effectiveness of psychological therapies and antidepressant medication, alone and in combination, for the treatment of depressive disorder in children and adolescents. We have examined clinical outcomes including remission, clinician and self reported depression measures, and suicide-related outcomes SEARCH METHODS: We searched the Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Register (CCDANCTR) to 11 November 2011. This register contains reports of relevant randomised controlled trials (RCTs) from the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1950 to date), EMBASE (1974 to date), and PsycINFO (1967 to date) SELECTION CRITERIA: RCTs were eligible for inclusion if they compared i) any psychological therapy with any antidepressant medication, or ii) a combination of psychological therapy and antidepressant medication with a psychological therapy alone, or an antidepressant medication alone, or iii) a combination of psychological therapy and antidepressant medication with a placebo or 'treatment as usual', or (iv) a combination of psychological therapy and antidepressant medication with a psychological therapy or antidepressant medication plus a placebo. We included studies if they involved participants aged between 6 and 18 years, diagnosed by a clinician as having Major Depressive Disorder (MDD) based on Diagnostic and Statistical Manual (DSM) or International Classification of Diseases (ICD) criteria DATA COLLECTION AND ANALYSIS: Two review authors independently selected studies, extracted data and assessed the quality of the studies. We applied a random-effects meta-analysis, using the odds ratio (OR) to describe dichotomous outcomes, mean difference (MD) to describe continuous outcomes when the same measures were used, and standard mean difference (SMD) when outcomes were measured on different scales MAIN RESULTS: We included ten studies, involving 1235 participants in this review. Studies recruited participants with different severities of disorder and with a variety of comorbid disorders, including anxiety and substance use disorder, therefore limiting the comparability of the results. Regarding

the risk of bias in studies, half the studies had adequate allocation concealment (there was insufficient information to determine allocation concealment in the remainder), outcome assessors were blind to the participants' intervention in six studies, and in general, studies reported on incomplete data analysis methods, mainly using intention-to-treat (ITT) analyses. For the majority of outcomes there were no statistically significant differences between the interventions compared. There was limited evidence (based on two studies involving 220 participants) that antidepressant medication was more effective than psychotherapy on measures of clinician defined remission immediately post-intervention (odds ratio (OR) 0.52, 95% confidence interval (CI) 0.27 to 0.98), with 67.8% of participants in the medication group and 53.7% in the psychotherapy group rated as being in remission. There was limited evidence (based on three studies involving 378 participants) that combination therapy was more effective than antidepressant medication alone in achieving higher remission from a depressive episode immediately post-intervention (OR 1.56, 95% CI 0.98 to 2.47), with 65.9% of participants treated with combination therapy and 57.8% of participants treated with medication, rated as being in remission. There was no evidence to suggest that combination therapy was more effective than psychological therapy alone, based on clinician rated remission immediately post-intervention (OR 1.82, 95% CI 0.38 to 8.68). Suicide-related Serious Adverse Events (SAEs) were reported in various ways across studies and could not be combined in meta-analyses. However suicidal ideation specifically was generally measured and reported using standardised assessment tools suitable for meta-analysis. In one study involving 188 participants, rates of suicidal ideation were significantly higher in the antidepressant medication group (18.6%) compared with the psychological therapy group (5.4%) (OR 0.26, 95% CI 0.09 to 0.72) and this effect appeared to remain at six to nine months (OR 1.27, 95% CI 0.68 to 2.36), with 13.6% of participants in the medication group and 3.9% of participants in the psychological therapy group reporting suicidal ideation. It was unclear what the effect of combination therapy was compared with either antidepressant medication alone or psychological therapy alone on rates of suicidal ideation. The impact of any of the assigned treatment packages on drop out was also mostly unclear across the various comparisons in the review. Limited data and conflicting results based on other outcome measures make it difficult to draw conclusions regarding the effectiveness of any specific intervention based on these outcomes

AUTHORS' CONCLUSIONS: There is very limited evidence upon which to base conclusions about the relative effectiveness of psychological interventions, antidepressant medication and a combination of these interventions. On the basis of the available evidence, the effectiveness of these interventions for treating depressive disorders in children and adolescents cannot be established. Further appropriately powered RCTs are required

39. Cox GR, Fisher CA, De SS, Phelan M, Akinwale OP, Simmons MB, et al. **Interventions for preventing relapse and recurrence of a depressive disorder in children and adolescents.** Cochrane Database of Systematic Reviews 2012;11:CD007504.
- Abstract: **BACKGROUND:** Depressive disorders often begin during childhood or adolescence. There is a growing body of evidence supporting effective treatments during the acute phase of a depressive disorder. However, little is known about treatments for preventing relapse or recurrence of depression once an individual has achieved remission or recovery from their symptoms
- OBJECTIVES:** To determine the efficacy of early interventions, including

psychological and pharmacological interventions, to prevent relapse or recurrence of depressive disorders in children and adolescents

SEARCH METHODS: We searched the Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Register (CCDANCTR) (to 1 June 2011). The CCDANCTR contains reports of relevant randomised controlled trials from The Cochrane Library (all years), EMBASE (1974 to date), MEDLINE (1950 to date) and PsycINFO (1967 to date). In addition we handsearched the references of all included studies and review articles

SELECTION CRITERIA: Randomised controlled trials using a psychological or pharmacological intervention, with the aim of preventing relapse or recurrence from an episode of major depressive disorder (MDD) or dysthymic disorder (DD) in children and adolescents were included. Participants were required to have been diagnosed with MDD or DD according to DSM or ICD criteria, using a standardised and validated assessment tool

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed all trials for inclusion in the review, extracted trial and outcome data, and assessed trial quality. Results for dichotomous outcomes are expressed as odds ratio and continuous measures as mean difference or standardised mean difference. We combined results using random-effects meta-analyses, with 95% confidence intervals. We contacted lead authors of included trials and requested additional data where possible

MAIN RESULTS: Nine trials with 882 participants were included in the review. In five trials the outcome assessors were blind to the participants' intervention condition and in the remainder of trials it was unclear. In the majority of trials, participants were either not blind to their intervention condition, or it was unclear whether they were or not. Allocation concealment was also unclear in the majority of trials. Although all trials treated participants in an outpatient setting, the designs implemented in trials was diverse, which limits the generalisability of the results. Three trials indicated participants treated with antidepressant medication had lower relapse-recurrence rates (40.9%) compared to those treated with placebo (66.6%) during a relapse prevention phase (odds ratio (OR) 0.34; 95% confidence interval (CI) 0.18 to 0.64, $P = 0.02$). One trial that compared a combination of psychological therapy and medication to medication alone favoured a combination approach over medication alone, however this result did not reach statistical significance (OR 0.26; 95% CI 0.06 to 1.15). The majority of trials that involved antidepressant medication reported adverse events including suicide-related behaviours. However, there were not enough data to show which treatment approach results in the most favourable adverse event profile

AUTHORS' CONCLUSIONS: Currently, there is little evidence to conclude which type of treatment approach is most effective in preventing relapse or recurrence of depressive episodes in children and adolescents. Limited trials found that antidepressant medication reduces the chance of relapse-recurrence in the future, however, there is considerable diversity in the design of trials, making it difficult to compare outcomes across studies. Some of the research involving psychological therapies is encouraging, however at present more trials with larger sample sizes need to be conducted in order to explore this treatment approach further

40. David-Ferdon C, Kaslow NJ. **Evidence-based psychosocial treatments for child and adolescent depression (DARE structured abstract)**. *Journal of Clinical Child and Adolescent Psychology* 2008;37:62-104.
Abstract:
41. De HM, Dobbelaere M, Sheridan EM, Cohen D, Correll CU. **Metabolic and endocrine adverse effects of second-generation antipsychotics in**

children and adolescents: A systematic review of randomized, placebo controlled trials and guidelines for clinical practice.

European Psychiatry 2011;26(3):144-158.

Abstract: Second-generation antipsychotics (SGA) are being used more often than ever before in children and adolescents with psychotic and a wide range of non-psychotic disorders. Several SGA have received regulatory approval for some paediatric indications in various countries, but off-label use is still frequent. The aim of this paper was to perform a systematic review and critically evaluate the literature on cardiometabolic and endocrine side-effects of SGA in children and adolescents through a Medline/Pubmed/Google Scholar search of randomized, placebo controlled trials of antipsychotics in children and adolescents (<18 years old) until February 2010. In total, 31 randomized, controlled studies including 3595 paediatric patients were identified. A review of these data confirmed that SGA are associated with relevant cardiometabolic and endocrine side-effects, and that children and adolescents have a high liability to experience antipsychotic induced hyperprolactinaemia, weight gain and associated metabolic disturbances. Only weight change data were sufficiently reported to conduct a formal meta-analysis. In 24 trials of 3048 paediatric patients with varying ages and diagnoses, ziprasidone was associated with the lowest weight gain (-0.04. kg, 95% confidence interval [CI]: -0.38 to +0.30), followed by aripiprazole (0.79. kg, 95% CI: 0.54 to 1.04], quetiapine (1.43. kg, 95% CI: 1.17 to 1.69) and risperidone (1.76. kg, 95% CI: 1.27 to 2.25) were intermediate, and olanzapine was associated with weight gain the most (3.45. kg, 95% CI: 2.93 to 3.97). Significant weight gain appeared to be more prevalent in patients with autistic disorder who were also younger and likely less exposed to antipsychotics previously. These data clearly suggest that close screening and monitoring of metabolic side effects is warranted and that the least cardiometabolically problematic agents should be used first whenever possible. A good collaboration between child- and adolescent psychiatrists, general practitioners and paediatricians is essential to maximize overall outcomes and to reduce the likelihood of premature cardiovascular morbidity and mortality. 2010 Elsevier Masson SAS

42. Gearing RE, Schwalbe CS, Lee R, Hoagwood KE. **THE EFFECTIVENESS OF BOOSTER SESSIONS IN CBT TREATMENT FOR CHILD AND ADOLESCENT MOOD AND ANXIETY DISORDERS.** *DepressAnxiety* 2013.

Abstract: **BACKGROUND:** To investigate the effects of booster sessions in cognitive behavioral therapy (CBT) for children and adolescents with mood or anxiety disorders, whereas controlling for youth demographics (e.g., gender, age), primary diagnosis, and intervention characteristics (e.g., treatment modality, number of sessions). **METHODS:** Electronic databases were searched for CBT interventions for youth with mood and anxiety disorders. Fifty-three (k = 53) studies investigating 1,937 youth met criteria for inclusion. Booster sessions were examined using two case-controlled effect sizes: pre-post and pre-follow-up (6 months) effect sizes and employing weighted least squares (WLSs) regressions. **RESULTS:** Meta-analyses found pre-post studies with booster sessions had a larger effect size $r = .58$ (k = 15; 95% CI = 0.52-0.65; $P < .01$) than those without booster sessions $r = .45$ (k = 38; 95% CI = 0.41-0.49; $P < .001$). In the WLS regression analyses, controlling for demographic factors, primary diagnosis, and intervention characteristics, studies with booster sessions showed larger pre-post effect sizes than those without booster sessions ($B = 0.13$, $P < .10$). Similarly, pre-follow-up studies with booster sessions showed a larger effect size $r = .64$ (k = 10; 95% CI = 0.57-0.70; $P < .10$) than those without booster

sessions $r = .48$ ($k = 20$; 95% CI = 0.42-0.53; $P < .01$). Also, in the WLS regression analyses, pre-follow-up studies showed larger effect sizes than those without booster sessions ($B = 0.08$, $P < .01$) after accounting for all control variables. **CONCLUSIONS:** Result suggests that CBT interventions with booster sessions are more effective and the effect is more sustainable for youth managing mood or anxiety disorders than CBT interventions without booster sessions

43. Gentile S. **Antidepressant use in children and adolescents diagnosed with major depressive disorder: what can we learn from published data?** *Reviews on Recent Clinical Trials* 2010;5(1):63-75.
Abstract: **OBJECTIVE:** The consequences of major depression disorder (MDD) in youths are likely to be devastating for both the patient and his/her family. Thus, this review analyzes systematically the effectiveness of antidepressant drugs (ADDs) in managing such patients **DATA SOURCES:** Medical literature reporting primary data on use of ADDs in children and adolescents was identified through searches (1966-January 2010) of MEDLINE/PubMed, EMBASE, SCOPUS, and The Cochrane Library databases. Additional studies were manually identified from the reference lists of published articles **SEARCH STRATEGY:** Search terms (variously combined) were: children, childhood, adolescents, adolescence, MDD, mood/affective disorders, depression, tricyclic antidepressants (TCAs) SSRIs, Serotonin-Norepinephrine Reuptake inhibitors (SNRIs), noradrenergic/specific serotonergic antidepressants (NaSSA). A separate search was conducted to complete the profile of effectiveness of each single antidepressant agent **DATA SELECTION:** 43 peer-reviewed articles met the inclusion criteria **DATA SYNTHESIS:** Reviewed information does not definitively support the use of antidepressants in children younger than 10 years old. In contrast, robust information suggests that fluoxetine should be considered as first-line agent in depressed adolescents whose clinical conditions require psychopharmacological approach **CONCLUSIONS:** Depressed children should be primarily approached with non-pharmacological interventions that should include the evaluation of potential parental psychiatric disorders. In adolescents with MDD, the decision to use fluoxetine should be associated with specific social and health protocols focused to reinforce self-esteem, improve the quality of relationships with parents and peers, facilitate healthy life-style changes, and identify the potential onset/worsening of suicidality. [References: 112]
44. Hazell P. **Depression in children and adolescents.** *Clinical Evidence* 2009;2009:2009.
Abstract: **INTRODUCTION:** Depression may affect 2-8% of children and adolescents, with a peak incidence around puberty. It may be self-limiting, but about 40% of affected children experience a recurrent attack, a third of affected children will make a suicide attempt, and 3-4% will die from suicide. **METHODS AND OUTCOMES:** We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of pharmacological, psychological, combination, and complementary treatments for depression in children and adolescents? What are the effects of treatments for refractory depression in children and adolescents? We searched: Medline, Embase, The Cochrane Library, and other important databases up to April 2008 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA) **RESULTS:** We found 18

systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions **CONCLUSIONS:** In this systematic review we present information relating to the effectiveness and safety of the following interventions: citalopram, cognitive behavioural therapy (CBT) (individual or group, to prevent relapse), escitalopram, electroconvulsive therapy, family therapy, fluoxetine (alone or with cognitive therapy or CBT), fluvoxamine, group therapeutic support (other than CBT), guided self-help, individual psychodynamic psychotherapy, interpersonal therapy, lithium, mirtazapine, monoamine oxidase inhibitors (MAOIs), omega-3 polyunsaturated fatty acids, paroxetine, sertraline (alone or with CBT), St John's Wort (*Hypericum perforatum*), tricyclic antidepressants, and venlafaxine

45. Hazell P, Mirzaie M. **Tricyclic drugs for depression in children and adolescents.** *CochraneDatabaseSystRev* 2013;6:CD002317.

Abstract: **BACKGROUND:** There is a need to identify effective and safe treatments for depression in children and adolescents. While tricyclic drugs are effective in treating depression in adults, individual studies involving children and adolescents have been equivocal. Prescribing of tricyclic drugs for depression in children and adolescents is now uncommon, but an accurate estimate of their efficacy is helpful as a comparator for other drug treatments for depression in this age group. This is an update of a Cochrane review first published in 2000 and updated in 2002, 2006 and 2010. **OBJECTIVES:** To assess the effects of tricyclic drugs compared with placebo for depression in children and adolescents and to determine whether there are differential responses to tricyclic drugs between child and adolescent patient populations. **SEARCH METHODS:** We conducted a search of the Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Register (CCDANCTR) (to 12 April 2013), which includes relevant randomised controlled trials from the following bibliographic databases: the Cochrane Central Register of Controlled Trials (CENTRAL) (all years), EMBASE (1974-), MEDLINE (1950-) and PsycINFO (1967-). The bibliographies of previously published reviews and papers describing original research were cross-checked. We contacted authors of relevant abstracts in conference proceedings of the American Academy of Child and Adolescent Psychiatry, and we handsearched the Journal of the American Academy of Child and Adolescent Psychiatry (1978 to 1999). **SELECTION CRITERIA:** Randomised controlled trials comparing the efficacy of orally administered tricyclic drugs with placebo in depressed people aged 6 to 18 years. **DATA COLLECTION AND ANALYSIS:** One of two review authors selected the trials, assessed their quality, and extracted trial and outcome data. A second review author assessed quality and checked accuracy of extracted data. Most studies reported multiple outcome measures including depression scales and clinical global impression scales. For each study, we took the best available depression measure as the index measure of depression outcome. We established predetermined criteria to assist in the ranking of measures. Where study authors reported categorical outcomes, we calculated individual and pooled risk ratios for non-improvement in treated compared with control subjects. For continuous outcomes, we calculated pooled effect sizes as the number of standard deviations by which the change in depression scores for the treatment group exceeded those for the control group. **MAIN RESULTS:** Fourteen trials (590 participants) were included. No overall difference was found for the primary outcome of response to treatment compared with placebo (risk ratio (RR) 1.07, 95% confidence interval (CI) 0.91 to 1.26; 9 trials, N = 454). There was a small reduction in depression symptoms (standardised mean difference (SMD) -0.32, 95% CI -0.59 to -

0.04; 13 trials, N = 533), but the evidence was of low quality. Subgroup analyses suggested a small reduction in depression symptoms among adolescents (SMD -0.45, 95% CI -0.83 to -0.007), and negligible change among children (SMD 0.15, 95% CI -0.34 to 0.64). Treatment with a tricyclic antidepressant caused more vertigo (RR 2.76, 95% CI 1.73 to 4.43; 5 trials, N = 324), orthostatic hypotension (RR 4.86, 95% CI 1.69 to 13.97; 5 trials, N = 324), tremor (RR 5.43, 95% CI 1.64 to 17.98; 4 trials, N = 308) and dry mouth (RR 3.35, 95% CI 1.98 to 5.64; 5 trials, N = 324) than did placebo, but no differences were found for other possible adverse effects. Wide CIs and the probability of selective reporting mean that there was very low-quality evidence for adverse events. There was heterogeneity across the studies in the age of participants, treatment setting, tricyclic drug administered and outcome measures. Statistical heterogeneity was identified for reduction in depressive symptoms, but not for rates of remission or response. As such, the findings from analyses of pooled data should be interpreted with caution. We judged none of these trials to be at low risk of bias, with limited information about many aspects of risk of bias, high dropout rates, and issues regarding measurement instruments and the clinical usefulness of outcomes, which were often variously defined across trials. **AUTHORS' CONCLUSIONS:** Data suggest tricyclic drugs are not useful in treating depression in children. There is marginal evidence to support the use of tricyclic drugs in the treatment of depression in adolescents

46. Hetrick SE, McKenzie JE, Cox GR, Simmons MB, Merry SN. **Newer generation antidepressants for depressive disorders in children and adolescents.** Cochrane Database of Systematic Reviews 2012;11:CD004851.

Abstract: **BACKGROUND:** Depressive disorders are common in young people and are associated with significant negative impacts. Newer generation antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), are often used, however evidence of their effectiveness in children and adolescents is not clear. Furthermore, there have been warnings against their use in this population due to concerns about increased risk of suicidal ideation and behaviour **OBJECTIVES:** To determine the efficacy and adverse outcomes, including definitive suicidal behaviour and suicidal ideation, of newer generation antidepressants compared with placebo in the treatment of depressive disorders in children and adolescents **SEARCH METHODS:** For this update of the review, we searched the Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Register (CCDANCTR) to October 2011. The CCDANCTR includes relevant randomised controlled trials from the following bibliographic databases: CENTRAL (the Cochrane Central Register of Controlled Trials) (all years), EMBASE (1974 -), MEDLINE (1950 -) and PsycINFO (1967 -). We searched clinical trial registries and pharmaceutical company websites. We checked reference lists of included trials and other reviews, and sent letters to key researchers and the pharmaceutical companies of included trials from January to August 2011 **SELECTION CRITERIA:** Published and unpublished randomised controlled trials (RCTs), cross-over trials and cluster trials comparing a newer generation antidepressant with a placebo in children and adolescents aged 6 to 18 years old and diagnosed with a depressive disorder were eligible for inclusion. In this update, we amended the selection criteria to include newer generation antidepressants rather than SSRIs only **DATA COLLECTION AND ANALYSIS:** Two or three review authors selected the trials, assessed their quality, and extracted trial and outcome data. We used a random-effects meta-analysis. We used risk ratio (RR) to summarise dichotomous outcomes and mean difference (MD) to summarise continuous measures **MAIN**

RESULTS: Nineteen trials of a range of newer antidepressants compared with placebo, containing 3335 participants, were included. The trials excluded young people at high risk of suicide and many co-morbid conditions and the participants are likely to be less unwell than those seen in clinical practice. We judged none of these trials to be at low risk of bias, with limited information about many aspects of risk of bias, high drop out rates and issues regarding measurement instruments and the clinical usefulness of outcomes, which were often variously defined across trials. Overall, there was evidence that those treated with an antidepressant had lower depression severity scores and higher rates of response/remission than those on placebo. However, the size of these effects was small with a reduction in depression symptoms of 3.51 on a scale from 17 to 113 (14 trials; N = 2490; MD -3.51; 95% confidence interval (CI) -4.55 to -2.47). Remission rates increased from 380 per 1000 to 448 per 1000 for those treated with an antidepressant. There was evidence of an increased risk (58%) of suicide-related outcome for those on antidepressants compared with a placebo (17 trials; N = 3229; RR 1.58; 95% CI 1.02 to 2.45). This equates to an increased risk in a group with a median baseline risk from 25 in 1000 to 40 in 1000. Where rates of adverse events were reported, this was higher for those prescribed an antidepressant. There was no evidence that the magnitude of intervention effects (compared with placebo) were modified by individual drug class

AUTHORS' CONCLUSIONS: Caution is required in interpreting the results given the methodological limitations of the included trials in terms of internal and external validity. Further, the size and clinical meaningfulness of statistically significant results are uncertain. However, given the risks of untreated depression in terms of completed suicide and impacts on functioning, if a decision to use medication is agreed, then fluoxetine might be the medication of first choice given guideline recommendations. Clinicians need to keep in mind that there is evidence of an increased risk of suicide-related outcomes in those treated with antidepressant medications

47. Hetrick SE, Merry S, McKenzie J, Sindahl P, Proctor M. **Cochrane review: Selective serotonin reuptake inhibitors (SSRIs) for depressive disorders in children and adolescents.** Evidence-Based Child Health: A Cochrane Review Journal 2008;3(3):815-894.

Abstract: Background Depressive disorders are common in young people and are associated with significant negative impacts. Selective serotonin reuptake inhibitors (SSRIs) are often used, however, evidence of their effectiveness in children and adolescents is not clear. Furthermore, there have been warnings against their use in this population due to concerns about increased risk of suicidal ideation and behaviour. Objectives To determine the efficacy and adverse outcomes, including definitive suicidal behaviour and suicidal ideation, of SSRIs compared to placebo in the treatment of depressive disorders in children and adolescents. Search strategy We searched the CCDAN Trials Register, MEDLINE, PSYCHINFO and CENTRAL. Reference lists were checked, letters were sent to key researchers and internet databases searched. Selection criteria We included published and unpublished randomised controlled trials. Data collection and analysis Two or three review authors selected the trials, assessed the quality and extracted trial and outcome data. We used a fixed-effect meta-analysis. The relative risk was used to summarise dichotomous outcomes and the mean difference to summarise continuous measures. Main results Twelve trials were eligible for inclusion, with ten providing usable data. At 8-12 weeks, there was evidence that children and adolescents 'responded' to treatment with SSRIs (RR 1.28, 95% CI 1.17 to 1.41). There was also evidence of an increased risk of

suicidal ideation and behaviour for those prescribed SSRIs (RR 1.80, 95% CI 1.19 to 2.72). Fluoxetine was the only SSRI where there was consistent evidence from three trials that it was effective in reducing depression symptoms in both children and adolescents (CDRS-R treatment effect -5.63, 95% CI -7.38 to -3.88), and 'response' to treatment (RR 1.86, 95% CI 1.49 to 2.32). Where rates of adverse events were reported, this was higher for those prescribed SSRIs. Authors' conclusions Caution is required to interpret the results. First, there were methodological issues, including high attrition, issues regarding measurement instruments and clinical usefulness of outcomes, often variously defined across trials. Second, patients seen in clinical practice are likely to be more unwell, and at greater risk of suicide, compared to those in the trials, and it is unclear how this group would respond to SSRIs. This needs to be considered, along with the evidence of an increased risk of suicide related outcomes in those treated with SSRIs. It is unclear what the effect of SSRIs is on suicide completion. While untreated depression is associated with the risk of completed suicide and impacts on functioning, it is unclear whether SSRIs would modify this risk in a clinically meaningful way. Plain language summary Selective serotonin reuptake inhibitors (new generation antidepressants) for depressive disorders in children and adolescents Depressive disorders are common in young people and have significant negative impacts. Selective serotonin reuptake inhibitors (SSRIs) are commonly prescribed for the treatment of depressive disorder in children and adolescents. The review of 12 trials highlighted limitations with the data, making it difficult to answer questions about the effectiveness and safety of SSRIs in clinical practice. Overall, there was evidence of greater reduction in depressive symptoms to a predetermined level deemed a "response" on SSRI compared to placebo. However, response was variously defined across trials making interpretation of this outcome difficult. Fluoxetine was the only SSRI where there was consistent evidence from three trials showing that it was effective in reducing symptoms of depressive disorder in both children and adolescents. Those receiving fluoxetine had a greater improvement, scoring on average 5.63 lower on the Children's Depression Rating Scale-Revised (CDRS-R) scale (range 17-113) than those on placebo. It is unclear whether this small difference is a meaningful outcome for children and adolescents with depressive disorders. Nor is it apparent how children and adolescents with co-morbid conditions and at risk of suicide would respond to SSRIs, given this group were largely excluded from the trials. There is evidence that those prescribed SSRIs are at an increased risk of suicidal ideation and attempts (RR 1.80, 95% CI 1.19 to 2.72) consistent with a number of similar reviews in the area. Additionally, there was an increased risk of other adverse events. It is unclear how this relates to the risk of suicide completion. The trials were not designed to measure any of the suicide related outcomes adequately. At the same time, untreated depression is associated with the risk of completed suicide and impacts on academic and social functioning, however, it is not clear whether treatment with an SSRI will modify this risk in a clinically meaningful way for children and young people. Clinicians need to provide accurate information to children and adolescents and their families about the uncertainties regarding the benefits and risks of SSRI medication for depressive disorders

48. Ipser JC, Stein DJ, Hawkrigde S, Hoppe L. **Cochrane Review: Pharmacotherapy for anxiety disorders in children and adolescents.** Evidence-Based Child Health: A Cochrane Review Journal 2010;5(2):555-628.

Abstract: Background Anxiety disorders are a potentially disabling group of disorders which are prevalent in childhood and adolescence. The recognition of the early onset of anxiety disorders, and their successful treatment with medication in adults, has led to the growing interest in using medication for paediatric anxiety disorders. Objectives To assess the efficacy and tolerability of medication for treating paediatric anxiety disorders. Search strategy We searched the Cochrane Depression, Anxiety & Neurosis Group specialised register (CCDANCTR-Studies), MEDLINE (via PubMed 1966 to August 2008), EMBASE (1966 to August 2008), and PsycINFO (1972 to August 2008). Various electronic registers were searched for unpublished studies. Reference lists of retrieved articles were searched for additional studies. Selection criteria All randomised controlled trials (RCTs) of pharmacotherapy in childhood/adolescent anxiety disorders. Data collection and analysis Two raters independently assessed RCTs for inclusion in the review, collated trial data, and assessed trial quality. Investigators were contacted to obtain missing data. Summary statistics were stratified by medication class, and by medication agent for the selective serotonin reuptake inhibitors (SSRIs). Dichotomous and continuous measures were calculated using a random effects model, heterogeneity was assessed, and subgroup/sensitivity analyses were undertaken. Main results 22 short-term (≤ 16 weeks) RCTs were included in the analysis (2519 participants). The majority of the trials assessed the efficacy of the SSRIs ($N = 15$). Medication and placebo response occurred in 58.1% and 31.5% of patients, respectively (Number of studies (N) = 14, Number needed to treat (NNT) = 4). Medication was more effective than placebo in reducing overall symptom severity in OCD in a post-hoc comparison ($N = 7$, Weighted Mean Difference (WMD) = -4.45, 95%CI = -5.94, -2.97, $n = 765$). Medication was less well tolerated than placebo overall, though the absolute proportion of participants who withdrew due to drug-related adverse events was low (4.9%). Authors' conclusions Medication treatments can be effective in paediatric anxiety disorders, acting to reduce core symptoms, and should be considered as part of the treatment of these disorders. The greatest number of trials showing efficacy to date have assessed the SSRIs in treating paediatric OCD. There is no clear evidence to show that any particular class of medication is more effective or better tolerated than any other. As quantitative data was only available for the SSRIs and venlafaxine the routine use of benzodiazepines cannot be recommended, especially given concerns of dependency and treatment-related emergent adverse events associated with this class of drugs. Future RCTs could help identify potential clinical moderators of treatment efficacy. Studies of the long-term efficacy of medication treatment, optimal dosage, as well as direct comparisons of pharmacotherapy and psychotherapy are also warranted.

Plain Language Summary A systematic review and meta-analysis of randomised controlled trials of medication in treating anxiety disorders in children and adolescents Anxiety disorders are a potentially disabling group of disorders which frequently occur in childhood and adolescence. Increasing recognition of the early onset of anxiety disorders and of the effectiveness of medication in treating adult anxiety disorders has contributed to a growing interest in the use of medication in treating paediatric patients. This systematic review of randomised controlled trials (RCTs) of pharmacotherapy of anxiety disorders in children and adolescents identified 22 short-term (≤ 16 weeks) randomised controlled trials which were eligible for inclusion (2519 participants). Treatment response was significantly greater after treatment with medication (58.1%) than with placebo (31.5%) in 14 trials. Medication was more effective than placebo in reducing overall symptom severity across all of the anxiety disorders (number of studies (N) = 9). The greatest number

o trials were for obsessive compulsive disorder (OCD), for which treatment efficacy in reducing symptom severity was also observed. The greatest number of trials showing efficacy to date have used the selective serotonin reuptake inhibitors (SSRIs). No controlled evidence could be found for the effectiveness of benzodiazepines, despite their continued prescription for paediatric anxiety disorders. Medication was less well tolerated than placebo, as indicated by the significant proportion of children and adolescents who dropped out due to adverse effects during the short term trials. Furthermore, while few incidences of suicidal behaviour/ideation in the included trials were attributed to study medication, it is important to be aware of the need for careful monitoring after initiation of SSRIs in treating this population. In conclusion, medication should be considered as part of the treatment of paediatric anxiety disorders over the short-term. Additional research into the optimal dose and duration of medication treatment, as well as the effects of age on the efficacy and tolerability of medication is warranted

49. James AC, James G, Cowdrey FA, Soler A, Choke A. **Cognitive behavioural therapy for anxiety disorders in children and adolescents.** CochraneDatabaseSystRev 2013;6:CD004690.

Abstract: **BACKGROUND:** A previous Cochrane review (James 2005) showed that cognitive behavioural therapy (CBT) was effective in treating childhood anxiety disorders; however, questions remain regarding (1) the relative efficacy of CBT versus non-CBT active treatments; (2) the relative efficacy of CBT versus medication and the combination of CBT and medication versus placebo; and (3) the long-term effects of CBT. **OBJECTIVES:** To examine (1) whether CBT is an effective treatment for childhood and adolescent anxiety disorders in comparison with (a) wait-list controls; (b) active non-CBT treatments (i.e. psychological placebo, bibliotherapy and treatment as usual (TAU)); and (c) medication and the combination of medication and CBT versus placebo; and (2) the long-term effects of CBT. **SEARCH METHODS:** Searches for this review included the Cochrane Central Register of Controlled Trials (CENTRAL) and the Cochrane Depression, Anxiety and Neurosis Group Register, which consists of relevant randomised controlled trials from the bibliographic databases The Cochrane Library (1970 to July 2012), EMBASE, (1970 to July 2012) MEDLINE (1970 to July 2012) and PsycINFO (1970 to July 2012). **SELECTION CRITERIA:** All randomised controlled trials (RCTs) of CBT versus waiting list, active control conditions, TAU or medication were reviewed. All participants must have met the criteria of the Diagnostic and Statistical Manual (DSM) or the International Classification of Diseases (ICD) for an anxiety diagnosis, excluding simple phobia, obsessive-compulsive disorder, post-traumatic stress disorder and elective mutism. **DATA COLLECTION AND ANALYSIS:** The methodological quality of included trials was assessed by three reviewers independently. For the dichotomous outcome of remission of anxiety diagnosis, the odds ratio (OR) with 95% confidence interval (CI) based on the random-effects model, with pooling of data via the inverse variance method of weighting, was used. Significance was set at $P < 0.05$. Continuous data on each child's anxiety symptoms were pooled using the standardised mean difference (SMD). **MAIN RESULTS:** Forty-one studies consisting of 1806 participants were included in the analyses. The studies involved children and adolescents with anxiety of mild to moderate severity in university and community clinics and school settings. For the primary outcome of remission of any anxiety diagnosis for CBT versus waiting list controls, intention-to-treat (ITT) analyses with 26 studies and 1350 participants showed an OR of 0.13 (95% CI 0.09 to 0.19, $Z = 10.26$, $P < 0.0001$), but with evidence of moderate heterogeneity ($P = 0.04$, $I(2) = 33\%$). The number needed to treat (NNT) was

6.0 (95% CI 7.5 to 4.6). No difference in outcome was noted between individual, group and family/parental formats. ITT analyses revealed that CBT was no more effective than non-CBT active control treatments (six studies, 426 participants) or TAU in reducing anxiety diagnoses (two studies, 88 participants). The few controlled follow-up studies (n = 4) indicate that treatment gains in the remission of anxiety diagnosis are not statistically significant. **AUTHORS' CONCLUSIONS:** Cognitive behavioural therapy is an effective treatment for childhood and adolescent anxiety disorders; however, the evidence suggesting that CBT is more effective than active controls or TAU or medication at follow-up, is limited and inconclusive

50. Kelvin R. **Review: antidepressants are of limited efficacy in juvenile depression.** Evidence Based Mental Health 2009;12(1):11-11.
- Abstract:** **QUESTION** Question: What is the efficacy of antidepressants in children and adolescents with depression? **Outcomes:** Responder rate, defined as the proportion of the study sample reaching a study specified level of improvement in clinical ratings, typically a 50% or greater reduction in depressive symptoms **METHODS** Design: Systematic review with meta-analysis. Data sources: MEDLINE, PsycINFO, EMBASE, Cochrane Library, PsiTri and ClinicalTrials.gov were searched from inception to May 2006 for randomised controlled trials (RCTs). Reference lists of identified studies were hand searched. Trial authors and experts in the field were consulted for unpublished information. Websites of pharmaceutical companies, the UK Committee on Safety of Medicines and the US FDA were also searched. **Study selection and analysis:** Two reviewers appraised the studies and selected RCTs comparing antidepressants with placebo in children and adolescents aged 20 years or less with major depression, dysthymia or depression not otherwise specified (DSM-III or later); depressive disorder (ICD-9/ 10); or depression diagnosed by clinical or structured diagnostic interview. Two reviewers assessed the quality of the RCTs. Included trials had to be double blind with random assignment to parallel antidepressant or placebo groups. Responder rates had to be reported as the number of participants responding rather than just as a percentage change in a symptom score. Continuous measures of clinical symptom rating scales were converted to a uniform percentage scale of clinical severity. Doses across agents and studies were compared using standardised imipramine equivalent (IMleq) daily doses. Selected potency ratios were based on median doses estimated from the manufacturer's recommendations, textbook summaries, clinical studies and clinical experience with adults. Fixed effect meta-analyses were conducted using Intercooled Stata software. Separate meta-analyses were carried out for antidepressants as a whole, individual antidepressants type (tricyclic antidepressants (TCAs), serotonin uptake inhibitors (SRIs) or other) and for each age group. Heterogeneity was investigated using I^2 and τ^2 statistics. Publication bias was investigated with a funnel plot. **Main results:** Twenty-nine RCTs met the inclusion criteria. One trial included three arms (placebo vs TCA vs SRI) so there were 30 drug-placebo comparisons pooled in the metaanalysis (mean age 15.5 years, median age 14.5, range 6-20). Antidepressants improved response rates compared with placebo (30 comparisons, 3069 participants; RR 1.22, 95% CI 1.15 to 1.31; see online table). SRIs produced a greater improvement in response rate than TCAs but overlapping CIs indicated a lack of statistical difference between the different drug types (SRI vs placebo RR 1.23, 95% CI 1.14 to 1.33; TCAs vs placebo: RR 1.15, 95% CI 0.98 to 1.34). For children younger than 12 years, there was no difference in response rate between antidepressants and placebo (RR 1.11, 95% CI 0.75 to 1.64). For adolescents, antidepressants improved response rates compared with placebo (RR 1.27, 95% CI 1.15 to 1.40) **CONCLUSIONS**

Antidepressants show some clinical efficacy in adolescents but are not effective in children. Different classes of antidepressant showed limited difference in response rate

51. Maag JW, Swearer SM, Toland MD. **Cognitive-behavioral interventions for depression in children and adolescents: Meta-analysis, promising programs, and implications for school personnel.** Mayer, Matthew J [Ed]; Lochman, John E [Ed]; Van Acker, Richard [Ed](2009)Cognitive-behavioral interventions for emotional and behavioral disorders: School-based practice(pp235-265)xii, 420 ppNew York, NY, US: Guilford Press; US 2009 (2009):420.
Abstract: (from the chapter) Depression is a mood (affective) disorder that affects approximately 2% of children and adolescents in the general population. Once considered exclusively the domain of psychiatry, depressive disorders can and should be considered by school personnel in identification, assessment, and treatment. Students with emotional and behavioral disorders (EBD) and learning disabilities (LD) may be particularly at risk for developing depression. Beck's cognitive therapy for depression is perhaps the most widely used treatment approach—either as a main therapy or adjunctive therapy to pharmacological approaches. Clients are taught to identify dysfunctional thoughts and maladaptive assumptions—either through recall or imagined situations—that may be contributing to feelings of depression. Virtually all effective cognitive therapies with youngsters include behavioral components. This approach encompasses techniques for promoting emotional and behavioral change by teaching children to change thoughts and cognitive processing in an overt, active, and problem-oriented way. The purpose of this chapter is threefold. First, a meta-analysis of all published studies in refereed journals is presented. This restriction was imposed to eliminate doctoral dissertations and data appearing in book chapters that may not have been subjected to the rigor of blind peer review in order to determine whether cognitive behavior intervention (CBI) was statistically significant for ameliorating depression in children and adolescents. Second, the most promising CBI programs for treating childhood and adolescent depression are described. Third, implications for school personnel using CBIs are discussed within a collaborative framework involving school psychologists, counselors, and special educators. (PsycINFO Database Record (c) 2012 APA, all rights reserved)
52. Merry SN. **Review: psychotherapy for adolescents with depression: initial but no sustainable benefits.** Evidence Based Mental Health 2008;11(2):49-49.
Abstract: Question: Is psychotherapy an effective way to treat children and adolescents with depression? Outcomes: Risk of response, defined as score below the threshold for diagnosis of depression on whichever scale the study used—"operationalized criteria" or "a validated depression severity measure". Secondary outcomes were cost and safety of treatment METHODS Design: Systematic review with meta-analysis Data sources: Cochrane CENTRAL, MEDLINE, CINAHL, PsycINFO, EMBASE, PSYINDEX, LILACS, conference proceedings and hand searches of journals; performed by searching the Cochrane Collaboration Depression, Anxiety and Neurosis Registers on 17 December 2004. Additional supplementary search of CENTRAL, MEDLINE, PsycINFO and EMBASE was carried out, and from the selected papers, reference lists were examined and lead authors contacted for further data on other trials Study selection and analysis: Individual or cluster randomised controlled trials of any psychotherapy (PT) versus no treatment, attention-placebo, waiting-list control, or treatment as usual, in adolescents (aged 6-18

years) with depression or dysthymia. Attention-placebo was defined as interventions that involved time spent with the patient but which did not focus on depressive symptoms (for example, psycho-drama or art therapy). Exclusions: psychotherapy that did not focus specifically on the individual--for example, family therapy, counselling. Standardised data extraction forms were used and methodological quality assessed using the Quality Rating Scale. Results from individual studies were combined and number needed to treat and relative risk of response (primary outcome) were calculated using a random effects model. Intracluster correlation coefficients were used, where available, to estimate effect size in cluster randomised trials. Subgroup analysis was planned a priori to assess the effect of psychotherapy type, control condition used, severity of depression, and age. Dropouts were included in intention-to-treat analysis (ITT) MAIN RESULTS Twenty seven studies involving 35 randomised comparisons (3 cluster) and 1744 patients, met the inclusion criteria. Psychotherapy (25 trials investigating cognitive behavioural therapy (CBT), 2 cognitive therapy (CT), 3 behavioural therapy (BT), 2 interpersonal therapy (IPT), 1 problem solving therapy (PST), 1 supportive therapy (ST), and 1 other) were compared to treatment as usual (TAU; used in 3 comparisons and included any non-study mental health care), attention-placebo (8 comparisons; including health education and psychodrama), waiting list control (18 comparisons), and no treatment (6 comparisons). Psychotherapy improved post-treatment response compared to control overall: 450/907 (49.6%) of the PT group had responded at study completion compared to 267/767 (34.8%) of the control groups (RR response: 1.39, 95% CI 1.18 to 1.65; $p = 0.0001$). Estimated NNT was 4.3. In analyses specifically looking at 1-6 month follow-up and 6-12 month follow-up, there were no differences between psychotherapy and the control conditions ($p > 0.15$ for both). For subgroup analyses see online notes CONCLUSIONS Psychotherapy improves post-treatment response for children and adolescents with depression compared to control, with most evidence for CBT. However, adding PT to usual treatment for depression does not improve response above usual treatment alone. Benefit is greatest for those in the 12-18 age group. Benefit over control is not sustained at longer-term follow-up

53. Merry SN, Hetrick SE, Cox GR, Brudevold-Iversen T, Bir JJ, McDowell H. **Psychological and educational interventions for preventing depression in children and adolescents.** Cochrane Database of Systematic Reviews 2011 (12):CD003380.

Abstract: BACKGROUND: Depression is common in young people, has a marked negative impact and is associated with self-harm and suicide. Preventing its onset would be an important advance in public health OBJECTIVES: To determine whether psychological or educational interventions, or both, are effective in preventing the onset of depressive disorder in children and adolescents SEARCH METHODS: The Cochrane Depression, Anxiety and Neurosis Review Group's trials registers (CCDANCTR) were searched at the editorial base in July 2010. Update searches of MEDLINE, EMBASE, PsycINFO and ERIC were conducted by the authors in September 2009. Conference abstracts, reference lists of included studies and reviews were searched and experts in the field contacted SELECTION CRITERIA: Randomised controlled trials of psychological or educational prevention programmes, or both, compared with placebo, any comparison intervention, or no intervention for young people aged 5 to 19 years-old, who did not currently meet diagnostic criteria for depression or who were below the clinical range on standardised, validated, and reliable rating scales of depression, or both, were included

DATA COLLECTION AND ANALYSIS: Two authors independently assessed studies for inclusion and rated their quality. Sample sizes were adjusted to take account of cluster designs and multiple comparisons. We contacted study authors for additional information where needed.

MAIN RESULTS: Fifty-three studies including 14,406 participants were included in the analysis. There were only six studies with clear allocation concealment, participants and assessors were mostly not blind to the intervention or blinding was unclear so that the overall risk of bias was moderately high. Sixteen studies including 3240 participants reported outcomes on depressive diagnosis. The risk of having a depressive disorder post-intervention was reduced immediately compared with no intervention (15 studies; 3115 participants risk difference (RD) -0.09; 95% confidence interval (CI) -0.14 to -0.05; $P < 0.0003$), at three to nine months (14 studies; 1842 participants; RD -0.11; 95% CI -0.16 to -0.06) and at 12 months (10 studies; 1750 participants; RD -0.06; 95% CI -0.11 to -0.01). There was no evidence for continued efficacy at 24 months (eight studies; 2084 participant; RD -0.01; 95% CI -0.04 to 0.03) but limited evidence of efficacy at 36 months (two studies; 464 participants; RD -0.10; 95% CI -0.19 to -0.02). There was significant heterogeneity in all these findings. There was no evidence of efficacy in the few studies that compared intervention with placebo or attention controls.

AUTHORS' CONCLUSIONS: There is some evidence from this review that targeted and universal depression prevention programmes may prevent the onset of depressive disorders compared with no intervention. However, allocation concealment is unclear in most studies, and there is heterogeneity in the findings. The persistence of findings suggests that this is real and not a placebo effect

54. Merry SN, Hetrick SE, Cox GR, Brudevold-Iversen T, Bir JJ, McDowell H. **Cochrane Review: Psychological and educational interventions for preventing depression in children and adolescents.** Evidence-Based Child Health: A Cochrane Review Journal 2012;7(5):1409-1685.
- Abstract: Background Depression is common in young people, has a marked negative impact and is associated with self-harm and suicide. Preventing its onset would be an important advance in public health. Objectives To determine whether psychological or educational interventions, or both, are effective in preventing the onset of depressive disorder in children and adolescents. Search methods The Cochrane Depression, Anxiety and Neurosis Review Group's trials registers (CCDANCTR) were searched at the editorial base in July 2010. Update searches of MEDLINE, EMBASE, PsycINFO and ERIC were conducted by the authors in September 2009. Conference abstracts, reference lists of included studies and reviews were searched and experts in the field contacted. Selection criteria Randomised controlled trials of psychological or educational prevention programmes, or both, compared with placebo, any comparison intervention, or no intervention for young people aged 5 to 19 years-old, who did not currently meet diagnostic criteria for depression or who were below the clinical range on standardised, validated, and reliable rating scales of depression, or both, were included. Data collection and analysis Two authors independently assessed studies for inclusion and rated their quality.- Sample sizes were adjusted to take account of cluster designs and multiple comparisons. We contacted study authors for additional information where needed.- Main results Fifty-three studies including 14,406 participants were included in the analysis. There were only six studies with clear allocation concealment, participants and assessors were mostly not blind to the intervention or blinding was unclear so that the overall risk of bias was moderately high. Sixteen studies including 3240 participants reported outcomes on depressive

diagnosis.- The risk of having a depressive disorder post-intervention was reduced immediately compared with no intervention (15 studies; 3115 participants risk difference (RD) -0.09; 95% confidence interval (CI) -0.14 to -0.05; $P < 0.0003$), at three to nine months (14 studies; 1842 participants; RD -0.11; 95% CI -0.16 to -0.06) and at 12 months (10 studies; 1750 participants; RD -0.06; 95% CI -0.11 to -0.01). There was no evidence for continued efficacy at 24 months (eight studies; 2084 participant; RD -0.01; 95% CI -0.04 to 0.03) but limited evidence of efficacy at 36 months (two studies; 464 participants; RD -0.10; 95% CI -0.19 to -0.02). There was significant heterogeneity in all these findings. There was no evidence of efficacy in the few studies that compared intervention with placebo or attention controls. Authors' conclusions There is some evidence from this review that targeted and universal depression prevention programmes may prevent the onset of depressive disorders compared with no intervention. However, allocation concealment is unclear in most studies, and there is heterogeneity in the findings.- The persistence of findings suggests that this is real and not a placebo effect.- Plain Language Summary Psychological and educational interventions for preventing depression in children and adolescents Depressive disorder is common and has a major impact on the functioning of young people. The aim of this review was to assess the effectiveness of programmes designed to prevent its onset. We found that, compared with no intervention, psychological depression prevention programmes were effective in preventing depression with a number of studies showing a decrease in episodes of depressive illness over a year. There were some problems with the way the studies were done but despite this the results are encouraging. We found data to support both targeted and universal programmes, which is important as universal programmes are likely to be easier to implement. We recommend that further research be undertaken to identify the most effective programmes and to test these in the real world

55. Mychailyszyn MP. **School-based interventions for anxious and depressed youth: A meta-analysis of outcomes.** Dissertation Abstracts International: Section B: The Sciences and Engineering Vol72(8-B),2012, pp5004 2012 (8-B):2012, pp.
- Abstract: Objective: Conduct a meta-analysis of school-based interventions for anxious and depressed youth to evaluate the findings according to QUORUM guidelines. Method: A search of the literature was conducted using PubMed, PsycINFO, and manual searches, supplemented by contact with leading researchers. The present meta-analysis used 63 studies and investigated 8,225 participants receiving CBT and 6,986 participants in comparison conditions. Results: Mean pre-post effect size estimates indicate that anxiety-focused school-based CBT was moderately effective at improving symptomatology of anxiety (Hedge's $g = 0.501$) and depression-focused school-based CBT was mildly effective at improving depression symptomatology (Hedge's $g = 0.298$) for youth receiving active interventions as compared to those in anxiety intervention control conditions (Hedge's $g = 0.193$) and depression intervention controls (Hedge's $g = 0.091$). Moderators and mediators of treatment outcome were explored. Conclusions: School-based CBT interventions for youth anxiety and for youth depression hold considerable promise, though further investigation is still needed to identify features that optimize service delivery and outcome. (PsycINFO Database Record (c) 2012 APA, all rights reserved)
56. Mychailyszyn MP, Brodman DM, Read KL, Kendall PC. **Cognitive-behavioral school-based interventions for anxious and depressed**

youth: A meta-analysis of outcomes. Clinical Psychology: Science and Practice Vol19(2), Jun 2012, pp129-153 2012 (2):Jun-153.

Abstract: A meta-analysis of school-based interventions for anxious and depressed youth using QUORUM guidelines was conducted. Studies were located by searching electronic databases, manual effort, and contact with expert researchers. Analyses examined 63 studies with 8,225 participants receiving cognitive-behavioral therapy (CBT) and 6,986 in comparison conditions. Mean pre-post effect sizes indicate that anxiety-focused school-based CBT was moderately effective in reducing anxiety (Hedge's $g = 0.501$) and depression-focused school-based CBT was mildly effective in reducing depression (Hedge's $g = 0.298$) for youth receiving interventions as compared to those in anxiety intervention control conditions (Hedge's $g = 0.193$) and depression intervention controls (Hedge's $g = 0.091$). Predictors of outcome were explored. School-based CBT interventions for youth anxiety and for youth depression hold considerable promise, although investigation is still needed to identify features that optimize service delivery and outcome. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

57. Neil AL, Christensen H. **Efficacy and effectiveness of school-based prevention and early intervention programs for anxiety.** Clinical Psychology Review 2009;29(3):208-215.

Abstract: A systematic review was conducted of school-based prevention and early intervention programs for anxiety. The aim of the review was to identify and describe the programs available, and to evaluate their effectiveness in reducing symptoms of anxiety. Twenty-seven outcome trials, describing 20 individual programs, were identified through the Cochrane Library, PsycInfo and PubMed databases. Results of the review indicated that most universal, selective and indicated prevention programs are effective in reducing symptoms of anxiety in children and adolescents, with effect sizes ranging from 0.11 to 1.37. Most programs targeted adolescents (59%), were aimed at reducing the symptoms of nonspecific anxiety (67%), and delivered cognitive behavioural therapy (CBT; 78%). Further quality school-based research is required that involves longer-term follow-up, the use of attention control conditions and evaluates teacher delivery

58. Nevo GA, Manassis K. **Outcomes for treated anxious children: a critical review of Long-Term-Follow-Up studies.** Depression and Anxiety 2009;26(7):650-660.

Abstract: BACKGROUND: Anxiety disorders are the most common psychiatric disorders of childhood, generating significant distress in the individual and an economic burden to society. They are precursors to diverse psychiatric illnesses and have an impact on development. Childhood anxiety's reach into the future accentuates the importance of studying the long-term effect of treatment. The purpose of this paper is to examine existing Long-Term-Follow-Up (LTFU) studies' capacity to inform us on the impact of anxiety treatment on development METHOD: Medline, PsycInfo, SciSearch, SocScisearch, Cinhal, Embase, and the Cochrane library were searched. Bibliographies of relevant book chapters and review articles and information from colleagues with expertise in anxiety were also a source of information. The search produced more than a thousand citations. Only eight studies met inclusion criteria: follow-up of a cohort of treated anxious youth for more than 2 years RESULTS: follow-up ranged from 2 to 7.4 years. The studies were methodologically rigorous and, in general, showed maintenance of or improvement in acute treatment gains. The studies reviewed could not outline course of recovery or control for pivotal confounding variables such

as maturation. Seven of the eight studies employed a Cognitive Behavioral intervention and one employed a manualized, time-limited, psychodynamic intervention. No LTFU trial for medication was found CONCLUSION: ample evidence exists for the short-term benefit of pediatric anxiety treatment, but evidence is still lacking for the understanding of treatment's role in the facilitation of healthy development into adulthood. Recommendations for future research are proposed. [References: 53]

59. Nilsen TS, Eisemann M, Kvernmo S. **Predictors and moderators of outcome in child and adolescent anxiety and depression: a systematic review of psychological treatment studies.** *European Child and Adolescent Psychiatry* 2013;22(2):69-87.

Abstract: The aim of this literature review was to examine pre-treatment child and adolescent characteristics as predictors and moderators of outcome in psychotherapy treatment trials of anxiety and depressive disorders. A literature search was conducted using several databases and resulted in 45 published studies (32 anxiety studies and 13 depression studies) meeting predefined methodological criteria. Ten client demographic (age, gender, ethnicity, IQ) and clinical factors (duration, type of diagnosis, pre-treatment severity, comorbidity) were examined across studies. The majority of findings showed non-significant associations between demographic factors (gender and age) with treatment outcome for both the anxiety and the depression treatment trials. Some important differences between the results of the anxiety and depression treatment trials were found. The majority of findings for the anxiety studies suggest that there are no demographic or clinical factors that predict or moderate treatment outcome. For the depression studies, however, the findings suggest that baseline symptom severity and comorbid anxiety may impact on treatment response. Overall, existing studies of pre-treatment patient variables as predictors and moderators of anxiety and depression treatment outcome provide little consistent knowledge concerning for what type of patients and under what conditions treatments work. Suggestions for future research are discussed

60. Offidani E, Fava GA, Tomba E, Baldessarini RJ. **Excessive mood elevation and behavioral activation with antidepressant treatment of juvenile depressive and anxiety disorders: a systematic review.** *Psychotherapy and Psychosomatics* 2013;82(3):132-141.

Record no: 10

Abstract: BACKGROUND: The prevalence, characteristics and implications of excessive arousal-activation in children and adolescents treated with antidepressants for specific illnesses have not been systematically examined METHODS: We compared reports of antidepressant trials (n = 6,767 subjects) in juvenile depressive (n = 17) and anxiety disorders (n = 25) for consensus-based indications of psychopathological mood elevation or behavioral activation RESULTS: Rates of excessive arousal-activation during treatment with antidepressants were at least as high in juvenile anxiety (13.8%) as depressive (9.79%) disorders, and much lower with placebos (5.22 vs. 1.10%, respectively; both p < 0.0001). The antidepressant/placebo risk ratio for such reactions in paired comparisons was 3.50 (12.9/3.69%), and the meta-analytically pooled rate ratio was 1.7 (95% confidence interval: 1.2-2.2; both p <= 0.001). Overall rates for 'mania or hypomania', specifically, were 8.19% with and 0.17% without antidepressant treatment, with large drug/placebo risk ratios among depressive (10.4/0.45%) and anxiety (1.98/0.00%) disorder patients CONCLUSIONS: Risks of excessive mood elevation during antidepressant treatment, including mania-hypomania, were much greater than with placebo, and similar in juvenile anxiety and

depressive disorders. Excessive arousal-activation in children or adolescents treated with antidepressants for anxiety as well as depressive disorders calls for particular caution and monitoring for potential risk of future bipolar disorder. Copyright 2013 S. Karger AG, Basel

61. Poirier M, Marcotte D, Joly J. **Depression in adolescents: a review of prevention programs and intervention (Provisional abstract).** *Revue Francophone de Clinique Comportementale et Cognitive* 2010;15:15-29.
62. Reynolds S, Wilson C, Austin J, Hooper L. **Effects of psychotherapy for anxiety in children and adolescents: a meta-analytic review.** *Clinical Psychology Review* 2012;32(4):251-262.
Abstract: This paper provides a comprehensive quantitative review of high quality randomized controlled trials of psychological therapies for anxiety disorders in children and young people. Using a systematic search for randomized controlled trials which included a control condition and reported data suitable for meta-analysis, 55 studies were included. Eligible studies were rated for methodological quality and outcome data were extracted and analyzed using standard methods. Trial quality was variable, many studies were underpowered and adverse effects were rarely assessed; however, quality ratings were higher for more recently published studies. Most trials evaluated cognitive behavior therapy or behavior therapy and most recruited both children and adolescents. Psychological therapy for anxiety in children and young people was moderately effective overall, but effect sizes were small to medium when psychological therapy was compared to an active control condition. The effect size for non-CBT interventions was not significant. Parental involvement in therapy was not associated with differential effectiveness. Treatment targeted at specific anxiety disorders, individual psychotherapy, and psychotherapy with older children and adolescents had effect sizes which were larger than effect sizes for treatments targeting a range of anxiety disorders, group psychotherapy, and psychotherapy with younger children. Few studies included an effective follow-up. Future studies should follow CONSORT reporting standards, be adequately powered, and assess follow-up. Research trials are unlikely to address all important clinical questions around treatment delivery. Thus, careful assessment and formulation will remain an essential part of successful psychological treatment for anxiety in children and young people. Copyright 2012 Elsevier Ltd. All rights reserved
63. Richardson T, Stallard P, Velleman S. **Computerised cognitive behavioural therapy for the prevention and treatment of depression and anxiety in children and adolescents: a systematic review.** *Clinical Child and Family Psychology Review* 2010;13(3):275-290.
Abstract: Research has shown that computerised cognitive behaviour therapy (cCBT) can be effective in the treatment of depression and anxiety in adults, although the outcomes with children and adolescents are unclear. The aim of the study is to systematically review the literature on the effectiveness of cCBT for the prevention and treatment of depression and anxiety in children and adolescents. EMBASE, PsychInfo and Pubmed were searched using specific terms and inclusion criteria for cCBT studies involving young people under the age of 18. A hand search was also conducted, and the authors were contacted to identify additional papers. Ten studies met the inclusion criteria. These included case series and randomised controlled trials concerned with both treatment and prevention. Six different software packages were described that varied in length and the nature and extent of

professional contact and supervision. All studies reported reductions in clinical symptoms and also improvements in variables such as behaviour, self-esteem and cognitions. Satisfaction with treatment was moderate to high from both children and parents, though levels of drop out and non-completion were often high. Additional randomised controlled trials are required, as the literature is currently limited. However, preliminary evidence suggests that cCBT is an acceptable and effective intervention for this age group

64. Rickwood D, Bradford S. **The role of self-help in the treatment of mild anxiety disorders in young people: an evidence-based review (Provisional abstract)**. Database of Abstracts of Reviews of Effects 2012;25-36.
65. Segool NK, Carlson JS. **Efficacy of cognitive-behavioral and pharmacological treatments for children with social anxiety**. Depression and Anxiety 2008;25(7):620-631.
Abstract: Childhood social anxiety is associated with significant social and academic impairment. The purpose of this study was to compare and contrast the efficacy of two major treatments for social anxiety disorders in children: cognitive-behavioral therapy and selective serotonin reuptake inhibitor (SSRI) drug treatment. Treatment studies in the literature were evaluated using meta-analytic techniques to compare pre- and post-treatment measures of social anxiety symptoms, general anxiousness, social competency, and impairment. Results indicate that the core symptoms of social anxiety and impairment were reduced by both cognitive-behavioral treatment (ES=0.86 and 1.56) and SSRI treatment (ES=1.30 and 2.29), respectively. Similarly, peripheral symptoms of general anxiousness were reduced by both cognitive-behavioral treatment (ES=0.75) and SSRI treatment (ES=1.29). Finally, both cognitive-behavioral (ES=0.68) and SSRI treatment (ES=0.68) resulted in moderate improvements in social competence. Implications and the limitations of these meta-analytic findings are discussed with respect to the evidence-based intervention movement
66. Stallard P. **Review: school based prevention and early intervention programmes reduce anxiety**. Evidence Based Mental Health 2009;12(4):116-116.
Abstract: Question: Do school based prevention and early intervention programmes effectively reduce symptoms of anxiety? Outcomes: Anxiety symptoms; diagnosis of anxiety. Methods Design: Systematic review. Data sources: PsycINFO, Cochrane Library and PubMed were searched from 1987 to February 2008 for randomised controlled trials (RCTs). Reference lists of identified studies were hand searched. Study selection and analysis: The primary author appraised studies and selected RCTs of structured school based programmes with a primary outcome of building resilience to anxiety symptoms, reducing or preventing anxiety symptoms in children (aged 5 -- 12 years) and adolescents (aged 13 -- 19 years). Studies had to be published in English language peer reviewed journals to be included. Two reviewers rated study quality and extracted data. Standardised effect size (ES) estimates were calculated using Cohen's d or phi (for dichotomous outcomes) to compare the efficacy and effectiveness of the early intervention and prevention programmes. A Cohen's d ES of 0.8 is considered large, 0.5 is considered moderate and 0.2 small. For phi, an ES of 0.5 is considered large, 0.3 moderate and 0.1 small. A formal meta-analysis was not performed owing to the poor quality of the studies. The efficacy trials conducted by mental health researchers could not accurately be compared with the

effectiveness trials conducted by classroom teachers. Main results Twenty-seven RCTs met the inclusion criteria. Programmes were targeted at adolescents in 59% of trials. Sixteen RCTs were universal programmes presented to all students, three were selective programmes targeted at students at risk of developing anxiety symptoms and eight were indicated programmes delivered to students with mild or early anxiety symptoms. Cognitive behavioural therapy formed the basis for most programmes (78%). Overall, the programmes reduced anxiety symptoms at either post-test or follow-up or both (21 of 27 trials, 78%, ES range 0.11 to 1.37). The remaining six trials had a non-significant ES. Of the 21 studies, 17 programmes significantly reduced anxiety symptoms (ES 0.11 to 1.37) post-test while four reduced anxiety symptoms at follow-up (ES 0.22 to 0.81). Eleven of 16 universal programmes significantly improved anxiety symptoms compared with control at post-test (ES 0.31 to 1.37). Of six trials with reported follow-up, three programmes significantly improved anxiety symptoms compared with control at follow-up (ES 0.22 to 0.70). Two of these 16 trials demonstrated significant differences between intervention and control at both post-test and follow-up. Two of three selective programmes significantly improved anxiety symptoms compared with control at post-test (ES 0.11 and 0.39). One trial reported on follow-up but there were no significant differences between the groups. None of the selective programme trials demonstrated significant differences between intervention and control at both post-test and follow-up. Four of eight indicated programmes significantly improved anxiety symptoms compared with control at post-test (ES 0.20 to 0.76). Of six trials with reported follow-up, five programmes significantly improved anxiety symptoms compared with control at follow-up (ES 0.19 to 1.03). Two of these eight trials demonstrated significant differences between intervention and control at both post-test and follow-up. Conclusions School based anxiety prevention and early intervention programmes lead to small to moderate reductions in anxiety symptoms

67. Teubert D, Pincus M. **A meta-analytic review on the prevention of symptoms of anxiety in children and adolescents.** *Journal of Anxiety Disorders* Vol25(8), Dec 2011, pp1046-1059 2011 (8):Dec-1059.
 Abstract: Anxiety disorders are the most frequent psychiatric disorders in children and adolescents and have adverse effects on their psychosocial functioning. An increasing number of studies are aimed at its prevention. This meta-analysis included 65 studies on anxiety prevention. We found small but significant effects on anxiety at posttest (symptoms: $g = .22$, diagnosis: $g = .23$; SD units) and follow-up (symptoms: $g = .19$, diagnosis: $g = .32$). Intervention effects at posttest varied by type of prevention: Indicated/selective prevention programs showed larger effect sizes than universal programs. At follow-up, smaller effects were found in samples with higher percentages of girls and stronger effect size for programs focusing primarily on anxiety prevention. We conclude: Anxiety prevention programs produce effects size of practical relevance. More efforts are needed for assessing the long-term program effects on the risk for developing anxiety disorders and for improving long-term prevention effects on girls.
 (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)
68. Townsend E, Walker DM, Sargeant S, Vostanis P, Hawton K, Stocker O, et al. **Systematic review and meta-analysis of interventions relevant for young offenders with mood disorders, anxiety disorders, or self-harm.** *Journal of Adolescence* 2010;33(1):9-20.

Abstract: Background Mood and anxiety disorders, and problems with self-harm are significant and serious issues that are common in young people in the Criminal Justice System. Aims To examine whether interventions relevant to young offenders with mood or anxiety disorders, or problems with self-harm are effective. Method Systematic review and meta-analysis of data from randomised controlled trials relevant to young offenders experiencing these problems. Results An exhaustive search of the worldwide literature (published and unpublished) yielded 10 studies suitable for inclusion in this review. Meta-analysis of data from three studies (with a total population of 171 individuals) revealed that group-based Cognitive Behaviour Therapy (CBT) may help to reduce symptoms of depression in young offenders. Conclusions These preliminary findings suggest that group-based CBT may be useful for young offenders with such mental health problems, but larger high quality RCTs are now needed to bolster the evidence-base. Copyright (c) 2009 The Association for Professionals in Services for Adolescents. Published by Elsevier Ltd. All rights reserved. [References: 39]

69. Tsapakis EM, Soldani F, Tondo L, Baldessarini RJ. **Efficacy of antidepressants in juvenile depression: meta-analysis.** British Journal of Psychiatry 2008;193(1):10-17.

Abstract: BACKGROUND: The safety of antidepressants in children and adolescents is being questioned and the efficacy of these drugs in juvenile depression remains uncertain AIMS: To assess antidepressant efficacy in juvenile depression METHOD: Systematic review and meta-analysis of randomised controlled trials (RCTs) comparing responses to antidepressants, overall and by type, v. placebo in young people with depression RESULTS: Thirty drug-placebo contrasts in RCTs lasting 8 weeks (median) involved 3069 participants (512 person-years) of average age 13.5 years. Meta-analysis yielded a modest pooled drug/placebo response rate ratio (RR=1.22, 95% CI 1.15-1.31), with little separation between antidepressant types. Findings were similar for response rate differences and corresponding number needed to treat (NNT): overall NNT=9; tricyclic antidepressants NNT=14 > serotonin reuptake inhibitors NNT=9 > other antidepressants NNT=8. Numbers needed to treat decreased with increasing age: children (NNT=21) > mixed ages (NNT=10) > adolescents (NNT=8) CONCLUSIONS: Antidepressants of all types showed limited efficacy in juvenile depression, but fluoxetine might be more effective, especially in adolescents. Studies in children and in severely depressed, hospitalised or suicidal juvenile patients are needed, and effective, safe and readily accessible treatments for juvenile depression are urgently required. [References: 81]

70. Ulloa-Flores RE, de la Pena-Olvera F, Nogaies-Imoca I. **The multimodal treatment for children and adolescents with depression.** Salud Mental Vol34(5), Sep-Oct 2011, pp403-407 2011 (5):Sep-Oct.

Abstract: Major Depressive Disorder (MDD) in children and adolescents is a common and impairing condition that is both recurrent and persistent into adulthood. In this article, a review of the literature regarding multimodal treatment is presented. The literature review process for this article included adolescents, ((children)), ((depression)), ((treatment)), ((antidepressants)) and ((psychotherapy)) as key words. The initial Medline search covered a 10 year period dating back to 2001. Double blind randomized and meta-analysis studies were considered as gold standard to be included in the revision, but also experts' consensus were incorporated. Regarding pharmacological treatment, tricyclic-antidepressants did not show better efficacy against placebo in double blind controlled studies; selective serotonin reuptake

inhibitors showed better efficacy against placebo in controlled studies, specifically fluoxetine and escitalopram, both approved to be used in pediatric population with MDD. Norodrenalin and serotonin reuptake inhibitors like venlafaxine or mirtazapine had not shown superior response than placebo. Comorbidity needs to be taken into account in the decisions of the pharmacological treatment; attention deficit hyperactivity disorder is the most frequent associated disorder and requires to add specific drug treatment like stimulants; if psychotic symptoms are present, atypical antipsychotics should be added. Regarding psychosocial treatment, psychoeducation is the first step in this treatment approach. Psychotherapy aims include decreasing symptoms severity by improving self esteem, increasing frustration tolerance and autonomy, as well as the ability to enjoy doily life activities, and establishing good relations with peers. Interpersonal and cognitive behavioral therapies are good options as psychotherapy for this age group. It is important to monitor patients to prevent relapses and complications of depression and suicidal behavior. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

71. Usala T, Clavenna A, Zuddas A, Bonati M. **Randomised controlled trials of selective serotonin reuptake inhibitors in treating depression in children and adolescents: a systematic review and meta-analysis.**

European Neuropsychopharmacology 2008;18(1):62-73.

Abstract: To evaluate the efficacy of selective serotonin reuptake inhibitors (SSRIs) in children and adolescents with depressive disorder, the main electronic databases and the reference lists of retrieved articles and reviews were searched up to January 2007. Randomized controlled studies (RCT) were assessed for methodological quality, taking into consideration the specific diagnostic and severity evaluation tools used, and a meta-analysis on the efficacy of SSRIs compared placebo was undertaken. In all, 13 studies were included, covering a total of 2530 children and adolescents. Eleven studies met the criteria for inclusion in the meta-analysis. The pooled odds ratio was 1.57 (95% C.I. 1.29-1.91). Only fluoxetine appeared to offer a moderately significant benefit profile (OR=2.39). All studies differed in diagnostic tools and primary efficacy measures. SSRI treatment, especially with fluoxetine, may be effective on child and adolescent depression. Nevertheless, additional RCTs with sound methodological designs, validated diagnostic instruments, large sample sizes, and consistent outcomes are necessary to determine the role of SSRIs, alone or in combination with psychological interventions in the treatment of depression in children and adolescents. [References: 93]

72. Uthman OA, Abdulmalik J. **Comparative efficacy and acceptability of pharmacotherapeutic agents for anxiety disorders in children and adolescents: a mixed treatment comparison meta-analysis.** Current Medical Research and Opinion 2010;26(1):53-59.

Abstract: OBJECTIVE: to compare efficacy and acceptability of different pharmacotherapeutic agents for treating anxiety disorders in children and adolescents METHODS: A recently conducted Cochrane Review on pharmacotherapy for anxiety disorders in children and adolescents was updated. A mixed treatment comparison meta-analysis using Bayesian Markov Chain Monte Carlo simulation was used to perform the indirect comparison. We calculated relative risk ratios (RR) with 95% credible interval (CrI) using placebo as the common comparator RESULTS: Data were combined from 16 clinical trials that randomized children to six different treatment strategies, including placebo. Fluoxetine, fluvoxamine, paroxetine, sertraline, and venlafaxine were more efficacious than placebo.

Venlafaxine was significantly less efficacious than fluvoxamine (RR = 0.60; 95% CrI 0.35-0.95) and paroxetine (RR = 0.65; 95% CrI 0.44-0.93). Fluoxetine, fluvoxamine, paroxetine, and sertraline had higher acceptability profile than placebo. Venlafaxine was less tolerated than fluvoxamine (RR = 0.16; 95% CrI 0.01-0.64), paroxetine (RR = 0.21; 95% CrI 0.05-0.59), and sertraline (RR = 0.31; 95% CrI 0.08-0.83). Fluvoxamine had a higher rate of clinical response and acceptability compared to other treatments in the network, with probability of 47.5% and 50.6% of being the most efficacious and well-tolerated treatment, respectively. CONCLUSION: Clinically important differences exist between commonly prescribed pharmacotherapeutic agents for treating anxiety among children in terms of both efficacy and acceptability in favor of fluvoxamine. Fluvoxamine might be the best choice when starting treatment for anxiety disorders among children and adolescents because it has the most favorable balance between benefits and acceptability.

73. Walkup JT, Compton S. **Review: pharmacotherapy increases response and reduces symptom severity in paediatric anxiety disorders.**

Evidence Based Mental Health 2010;13(1):19-19.

Abstract: Question: What is the efficacy and tolerability of pharmacotherapy for paediatric anxiety disorders? Outcomes: Response (score of 1 or 2 (much or very much improved) on the Clinical Global Impressions-Improvement scale); symptom severity or investigator defined response on closely related measures; symptom severity (clinician rated DSM based anxiety scales such as the Child Yale-Brown Obsessive-Compulsive Scale); adverse events. Methods Design: Systematic review and meta-analysis. Data sources: Cochrane Depression, Anxiety and Neurosis Group specialised register (CCDANCTR-Studies), MEDLINE (from 1966), EMBASE (from 1966) and PsycINFO (from 1972) were searched in August 2008. Reference lists of retrieved articles were hand searched; ongoing and unpublished studies were identified through electronic registers and contact with experts. Study selection and analysis: Placebo controlled randomised controlled trials (RCTs) of pharmacotherapy in children and adolescents (aged <18 years) with primary diagnoses of anxiety disorders (DSM-III or later). Studies where participants were receiving psychotherapy or pharmacotherapy for secondary psychiatric disorders were excluded. Authors were contacted if required. Two reviewers decided on the inclusion of studies. Meta-analyses were stratified by drug class and also by individual selective serotonin reuptake inhibitors (SSRIs). Random effects models were used for meta-analyses, and heterogeneity assessed using the χ^2 test and I^2 statistic. Publication bias was assessed using a funnel plot. Main results 22 RCTs (2519 participants; mean age 12 years) met the inclusion criteria. The most common condition treated was obsessive-compulsive disorder (OCD; 11 RCTs). Fifteen RCTs assessed SSRIs, five assessed serotonin-norepinephrine reuptake inhibitors, two benzodiazepines and one a tricyclic antidepressant. The trials had follow-up of 16 weeks or less. Pharmacotherapy increased response compared with placebo (14 RCTs of SSRIs and a serotonin/norepinephrine reuptake inhibitor (SNRI), n=2102; absolute risk 58.1% with pharmacotherapy vs 31.8% with placebo; relative risk (RR) 1.9, 95% CI 1.6 to 2.26). This analysis showed significant heterogeneity (I^2 p=0.01; I^2 =52%) which did not seem to be explained by differences between the individual SSRIs or between SSRI and SNRI trials. Post-hoc analyses showed that pharmacotherapy increased response to treatment in OCD and non-OCD anxiety disorders (OCD: five RCTs, n=654; RR 1.65, 95% CI 1.32 to 2.06; non-OCD: 9 RCTs, n=1448; RR 2.01, 95% CI 1.59 to 2.55). There was only heterogeneity in the analysis of non-OCD disorders (χ^2

$p < 0.01$, $I^2 = 66\%$). Pharmacotherapy was more effective than placebo in reducing overall symptom severity (nine RCTs of SSRIs and an SNRI, $n = 810$; standardised mean difference -0.69 , 95% CI -0.94 to -0.44). There was also heterogeneity in this analysis ($x^2 p < 0.01$, $I^2 = 62\%$) which appeared to be at least partly due to heterogeneity among non-OCD disorders trials ($x^2 p < 0.01$, $I^2 = 78\%$). Dropouts due to drug related adverse events were significantly more frequent with pharmacotherapy than placebo (12 RCTs, $n = 1997$; RR 1.91, 95% CI 1.2 to 3.05). There was no significant heterogeneity in this analysis ($p = 0.38$, $I^2 = 7\%$). Conclusions Pharmacotherapy can be effective for reducing symptoms of anxiety disorders in children and adolescents in the short term. Most trials thus far have assessed the effects of SSRIs for OCD. No trials on the use of benzodiazepines were identified that provided quantitative data, and therefore their routine use cannot be recommended

74. Weersing VR, Walker PN. **Review: cognitive behavioural therapy for adolescents with depression.** Evidence Based Mental Health 2008;11(3):76-76.

Abstract: Question: How effective is cognitive behavioural therapy (CBT) for adolescent depression and what factors explain the observed changes in meta-analytic effect sizes over time? Outcomes: Effectiveness of CBT; differences in estimates of efficacy of cognitive behavioural therapy for adolescents; moderator variables (treatment duration, nature of sample, type of control group, setting, methodological rigor, therapist vocation, severity of depression at baseline). METHODS Design: Systematic review with meta-analysis. Data sources: Medical and psychological databases (PsycINFO and MEDLINE) were searched from January 1980 to September 2006. A hand search of reference lists of studies of CBT was also carried out. Study selection and analysis: Published, peer-reviewed randomised controlled trials (RCTs) of CBT in people aged 12DS18 years with depression (DSM-III or later, Researcher Diagnostic Criteria, Bellevue Index of Depression Criteria). RCTs had to compare CBT with a control group (for example, waiting list control) or an alternative psychotherapy group (for example, non-directive supportive therapy). Effect sizes were calculated for each study (by dividing the post-therapy difference between depression score means in CBT and control groups divided by their pooled standard deviation, corrected for small sample bias where necessary) and pooled through a random effects meta-analytic model. Cumulative meta-analyses were conducted to evaluate changes in effect of CBT over time. To examine effects of different variables on modification of effect sizes, ANOVA was conducted for the following coded variables: treatment duration (more or less than 867 treatment minutes), sample size, type of control group (active or inactive), setting (clinical or non-clinical), methodological rigour (fulfilling more or less than 17 of 22 CONSORT criteria), vocation of the therapist (clinicians or research assistants/graduate students) and severity of depression. MAIN RESULTS Eleven randomised studies met criteria for inclusion. Overall, CBT reduced symptoms of depression in adolescents at the end of treatment (mean weighted effect size of CBT: 0.53, 95% CI 0.24 to 0.82; random effects analysis). There was significant heterogeneity between studies. At follow-up CBT also reduced symptoms (mean weighted effect size (0.59, 95% CI 0.14 to 1.05; random effects analysis). Cumulative meta-analysis demonstrated a steady decrease in effect size over time and narrowing of the confidence intervals. Factors contributing to this decline were: improvements in study quality (that is, studies fulfilling more CONSORT criteria had smaller effect sizes; studies using intention to treat analyses had smaller effect sizes), use of active comparator (that is, studies using active comparators had smaller

effect sizes), and treatment in clinical settings (that is, studies in clinical settings had smaller effect sizes) (see online table). CONCLUSIONS Pooling of studies to date suggests that CBT is an effective treatment for adolescents with depression. Methodological differences between early and more recent investigations may be responsible for differences in estimates over time of efficacy of CBT for depressed adolescents. ABSTRACTED FROM Klein JB, Jacobs RH, Reinecke MA. Cognitive-behavioral therapy for adolescent depression: a meta-analytic investigation of changes in effect-size estimates. *J Am Acad Child Adolesc Psychiatry* 2007;46:1403-13

Søkestrategier

Søk: Malene W. Gundersen

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Dato: 28.06.2013

Antall treff: 558

#	Searches	Results
1	Anxiety/	50743
2	exp Anxiety Disorders/	65085
3	Anxiety, Separation/	1830
4	Depression/	72541
5	Depressive Disorder, Major/	18084
6	depressive disorder/	57424
7	Dysthymic Disorder/	974
8	seasonal affective disorder/	1061
9	(anxiety or anxiousness or depression or depressive or depressed).tw.	342161
10	or/1-9	423756
11	exp Child/	1514131
12	Adolescent/	1572892
13	Pediatrics/	38945
14	(child\$ or adolescen\$ or pediatric\$ or paediatric\$).tw.	1143713
15	(boy\$1 or girl\$1 or kid\$1 or juvenil\$ or under?age\$ or teen\$ or minor\$ or pubescen\$ or young people or young person\$ or youth\$).tw.	484541

16	or/11-15	2906470
17	10 and 16	97464
18	limit 10 to "all child (0 to 18 years)"	84784
19	17 or 18	100515
20	exp Therapeutics/	3281961
21	th.xs.	5369326
22	(treatment* or therap* or interven*).tw.	4268234
23	or/20-22	8322768
24	19 and 23	52733
25	limit 24 to (yr="2008 -Current" and "reviews (maximizes specificity)")	497
26	(guideline* or guidance).ti.	56949
27	(guideline or practice guideline).pt.	24318
28	26 or 27	70938
29	24 and 28	205
30	limit 29 to yr="2008 -Current"	69
31	25 or 30	558

Database: Embase 1974 to 2013 June 27

Dato: 28.06.2013

Antall treff: 572

#	Searches	Results
1	anxiety/	109201
2	exp anxiety disorder/	136778
3	exp depression/	294708
4	(anxiety or anxiousness or depression or depressive or depressed).tw.	435056
5	or/1-4	625961
6	exp child/	1751197
7	exp adolescent/	1251941
8	pediatrics/	55990
9	(child\$ or adolescenc\$ or pediatric\$ or paediatric\$).tw.	1414700
10	(boy\$1 or girl\$1 or kid\$1 or juvenil\$ or under?age\$ or teen\$ or minor\$ or pubescen\$ or young people or young person\$ or youth\$).tw.	588308
11	or/6-10	3084756
12	5 and 11	109838
13	limit 5 to (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	74770
14	12 or 13	109838
15	exp therapy/	5949574
16	(dt or pc or th or rh or su).fs.	5530424
17	(treatment* or therap* or interven*).tw.	5418616
18	or/15-17	10721313
19	14 and 18	63409
20	limit 19 to ("reviews (maximizes specificity)" and yr="2008 -Current")	456
21	(guideline* or guidance).ti.	72017
22	19 and 21	260
23	limit 22 to yr="2008 -Current"	122
24	20 or 23	572

Database: PsycINFO 1806 to June Week 1 2013

Dato: 28.06.2013

Antall treff: 405

#	Searches	Results
1	exp anxiety/	47892
2	exp anxiety disorders/	57515
3	exp major depression/	86419
4	atypical depression/	145
5	seasonal affective disorder/	871
6	"depression (emotion)"/	20906
7	(anxiety or anxiousness or depression or depressive or depressed).tw.	283097
8	or/1-7	315922
9	limit 8 to (100 childhood <birth to age 12 yrs> or 200 adolescence <age 13 to 17 yrs>)	52700
10	pediatrics/	13267
11	(child\$ or adolescen\$ or pediatric\$ or paediatric\$).tw.	615030
12	(boy\$1 or girl\$1 or kid\$1 or juvenil\$ or under?age\$ or teen\$ or minor\$ or pubescen\$ or young people or young person\$ or youth\$).tw.	214972
13	or/10-12	716812
14	8 and 13	68725
15	9 or 14	80339
16	exp treatment/	549273
17	(treatment* or therap* or interven*).tw.	741019
18	or/16-17	924125
19	15 and 18	32810
20	limit 19 to ("reviews (maximizes specificity)" and yr="2008 -Current")	342
21	treatment guidelines/	3854
22	(guideline* or guidance).ti.	10894
23	or/21-22	13230
24	19 and 23	193

25	limit 24 to yr="2008 -Current"	66
26	20 or 25	405

Database: Cinahl

Dato: 28.06.2013

Antall treff: 209

#	Query	Re- sults
S1	(MH "Anxiety+")	14,497
S2	(MH "Anxiety Disorders+")	14,787
S3	(MH "Depression+")	41,359
S4	(MH "Seasonal Affective Disorder")	367
S5	TI ((anxiety or anxiousness or depression or depressive or depressed) OR AB ((anxiety or anxiousness or depression or depressive or depressed))	56,816
S6	S1 OR S2 OR S3 OR S4 OR S5	83,302
S7	(MH "Child+")	277,64 0
S8	(MH "Adolescence+")	188,20 7
S9	(MH "Pediatrics+")	6,496
S10	TI ((child* or adolescen* or pediatric* or paediatric*) OR AB ((child* or adolescen* or pediatric* or paediatric*))	213,86 7
S11	TI ((boy# or girl# or kid# or juvenil* or under#age or teen# or minor# or pubescen* or young people or young person* or youth*) OR AB ((boy# or girl# or kid# or juvenil* or under#age or teen# or minor# or pubescen* or young people or young person# or youth*))	54,917
S12	S7 OR S8 OR S9 OR S10 OR S11	446,56 8

S13	S6 AND S12	20,567
S14	S1 OR S2 OR S3 OR S4 OR S5 Limiters - Age Groups: All Child	16,879
S15	S13 OR S14	20,567
S16	(MH "Therapeutics+")	665,079
S17	MW "DH" or "DT" or "PC" or "SU" or "TU" or "TH"	746,671
S18	TI ((treatment* or therap* or interven*) OR AB ((treatment* or therap* or interven*))	457,788
S19	S16 OR S17 OR S18	1,292,138
S20	S15 AND S19	11,663
S21	S15 AND S19 Limiters - Clinical Queries: Review - High Specificity; Published Date from: 20080101-20131231	129
S22	S15 AND S19 Limiters - Publication Type: Practice Guidelines; Published Date from: 20080101-20131231	12
S23	(MH "Practice Guidelines")	30,008
S24	TI (guideline* or guidance)	21,557
S25	S23 OR S24	41,943
S26	S20 AND S25 Limiters - Published Date from: 20080101-20131231	79
S27	S22 OR S26	84
S28	S21 OR S27	209

Database: Cochrane Database of Systematic Reviews : Issue 6 of 12, June 2013; Database of Abstracts of Reviews of Effect : Issue 2 of 4, April 2013; Cochrane Methodology Register : Issue 2 of 4, April 2013; Health Technology Assessment Database : Issue 2 of 4, April 2013; NHS Economic Evaluation Database : Issue 2 of 4, April 2013

Dato: 28.06.2013

Antall treff: 372 (CDSR: 140; DARE: 140; CMR: 26; HTA: 7; EED: 59)

ID	Search	Results
#1	MeSH descriptor: [Anxiety] this term only	4347
#2	MeSH descriptor: [Anxiety Disorders] explode all trees	4406
#3	MeSH descriptor: [Anxiety, Separation] this term only	51
#4	MeSH descriptor: [Depression] this term only	4702
#5	MeSH descriptor: [Depressive Disorder, Major] this term only	2066
#6	MeSH descriptor: [Depressive Disorder] this term only	4417
#7	MeSH descriptor: [Dysthymic Disorder] this term only	129
#8	MeSH descriptor: [Seasonal Affective Disorder] this term only	136
#9	(anxiety or anxiousness or depression or depressive or depressed):ti,ab,kw	43022
#10	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9	44467
#11	MeSH descriptor: [Child] explode all trees	71
#12	MeSH descriptor: [Adolescent] this term only	70256
#13	MeSH descriptor: [Pediatrics] this term only	442
#14	(child* or adolescen* or pediatric* or paediatric*):ti,ab,kw	124396
#15	(boy* or girl* or kid* or juvenil* or underage* or (under next age*) or teen* or minor* or pubescen* or (young next people) or (young next person*) or youth*):ti,ab,kw	34787
#16	#11 or #12 or #13 or #14 or #15	148653
#17	#10 and #16	9255
#18	MeSH descriptor: [Therapeutics] explode all trees	220388
#19	Any MeSH descriptor with qualifier(s): [Diet therapy - DH, Prevention & control - PC, Rehabilitation - RH, Surgery - SU, Therapy - TH]	165947
#20	(treatment* or therap* or interven*):ti,ab,kw	409843
#21	#18 or #19 or #20	496316

#22	#17 and #21 in Cochrane Reviews (Reviews and Protocols), Other Reviews, Methods Studies, Technology Assessments and Economic Evaluations	372
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Database: G-I-N

Dato: 28.06.2013

Antall treff: 4 + 28

Publication Type Guideline OR Systematic Review

Search Text (child* AND depress*) OR (child* AND anxi*) OR (adolescen* AND depress*) OR (adolescen* AND anxi*)

Search Type basic

Search Results: 4 (2008-)

Publication Types Guideline

MeSH Terms Depressive Disorder (F03.600.300)

Anxiety Disorders (F03.080)

Search Type advanced

Search Results: 28 (2008-)

Database: National Guidelines Clearingshouse

Dato: 28.06.2013

Antall treff: 196

Keyword: (anxiety or depression)

Age of Target Population: Adolescent (13 to 18 years), Child (2 to 12 years), Infant (1 to 23 months)

Guideline Category: Assessment of Therapeutic Effectiveness, Treatment

Publication Year: 2008, 2009, 2010, 2011, 2012, 2013

Database: TRIP

Dato: 28.06.2013

Antall treff: 71

((title:child* or adolescent*) AND (title:anxiety or depression)) from:2008 to:2013 – begrenset til Secondary Evidence.

Database: BMJ Clinical Evidence
Dato: 25.06.2013
Antall treff: 198 + 35

child* [anxiety depress*]
adolescen* [anxiety depress*]

Database: Up-To-Date
Dato: 25.06.2013
Antall treff: Ca. de første 150 treff (relevansrangert)

Depression – begrenset til Pediatric
Anxiety – begrenset til Pediatric

Database: NHS
Dato: 01.07.2013
Antall treff: 484
Kommentar: Begrenset til de siste tre årene på grunn av begrensninger i databasens søkefunksjonalitet

((child* OR adolescen*) AND (anxiety OR depress*))
Begrenset til Guideline eller SR samt behandling.

Database: PubMed
Dato: 01.07.2013
Antall treff: 60

Search	Query	Items
#64	Search (#62 and #63)	60
#63	Search pubstatusaheadofprint	162828
#62	Search (#60 and #61)	10144
#61	Search (guideline* or guidance or meta-analys* or "meta analys*" or review* or search* or pubmed or medline[Title/Abstract])	2759870

Search	Query	Items
#60	Search (#50 and #59)	54698
#59	Search (#53 or #57 or #58)	8076210
#50	Search (#48 or #49)	104829
#58	Search (treatment* or therap* or interven*[Title/Abstract])	4748995
#57	Search "therapy" [Subheading]	5212762
#53	Search "Therapeutics"[Mesh]	3151184
#49	Search (#32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40) Filters: Child: birth-18 years	83705
#48	Search (#41 and #47)	102705
#41	Search (#32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40)	457210
#47	Search (#42 or #43 or #44 or #45 or #46)	3112922
#46	Search (boy* or girl* or kid* or juvenil* or underage* or "under age*" or teen* or minor* or pubescen* or "young people" or "young person*" or youth*[Title/Abstract])	548824
#45	Search (child* or adolescen* or pediatric* or paediatric*[Title/Abstract])	2831672
#44	Search "Pediatrics"[Mesh:NoExp]	38249
#43	Search "Adolescent"[Mesh:NoExp]	1523223
#42	Search "Child"[Mesh]	1476392
#32	Search "Anxiety"[Mesh:NoExp]	48923
#33	Search "Anxiety Disorders"[Mesh]	62730
#34	Search "Anxiety, Separation"[Mesh:NoExp]	1807
#35	Search "Depression"[Mesh:NoExp]	69329
#36	Search "Depressive Disorder, Major"[Mesh:NoExp]	16783
#37	Search "Depressive Disorder"[Mesh:NoExp]	55785
#38	Search "Dysthymic Disorder"[Mesh:NoExp]	932
#39	Search "Seasonal Affective Disorder"[Mesh:NoExp]	1043
#40	Search (anxiety or anxiousness or depression or depressive or de-	429969

Search	Query	Items
	pressed[Title/Abstract]	

Tidsskrift: Evidence-Based Child Health

Dato: 01.07.2013

Antall treff: 101

((child* or adolescent*) AND (anxiet* or depress*)) in Evidence-Based Child Health: A Cochrane Review Journal

Referanser

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2. Clinical Practice Guideline on Major Depression in Childhood and Adolescence. GuiaSalud 2009.
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6. Anxiety and Depression in Children and Youth - Diagnosis and Treatment. Clinical Practice Guidelines and Protocols in British Columbia 2010.
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