BEST in Mental Health

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Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

Is there strong evidence to prove that medication is more effective than therapeutic interventions in improving psychological wellbeing in children and young adults in mental health services?

Clarification of question using PICO structure

Patients:	Children and adolescents in mental health services
Intervention:	Any pharmacological treatment
Comparator:	Any psychological/therapeutic (or no) intervention
Outcome:	All patient outcomes

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Clinical and research implications

Evidence from one high quality systematic review and mixed treatment meta-analysis indicated that fluoxetine in combination with cognitive behavioural therapy (CBT) was the most effective treatment option for improving symptoms in children and adolescents with major depressive disorder. However when safety (rates of suicidal ideation and suicide attempts) and acceptability were taken into consideration, sertraline and mirtazapine were the optimal treatment options. There was no evidence on the relative effectiveness of antidepressants (other than fluoxetine) in combination with CBT. Evidence on the effects of antidepressant treatment on quality of life was inconsistent. One small, poor quality randomised controlled trial suggested that group CBT and sertraline may be similarly effective in reducing obsessive and compulsive symptoms, but that post-treatment relapse rates may be higher in this treated with sertraline, however, this finding requires confirmation by larger, high quality studies.

There appears to be a lack of research comparing the effectiveness of psychological and pharmacological interventions in children and adolescents with mental health problems other than depression.

What does the evidence say?

Number of included studies/reviews (number of participants)

We identified two systematic reviews,[1,2] and one additional randomised controlled trial (RCT)[3] which were relevant to this evidence summary. The first systematic review compared the efficacy and safety of various therapeutic regimens, including pharmacological therapies, psychotherapies and combination treatments, for the acute treatment of major depressive disorder (MDD) in children and adolescents.[1] The second systematic review assessed the effectiveness of antidepressants in children and adolescents with depression and anxiety disorders and focussed on Quality of Life (QoL) outcomes.[2] The additional RCT was conducted in Brazil and included only children and adolescents referred for previously un-treated obsessive compulsive disorder (OCD).[3] The study compared sertraline to a group cognitive behavioural therapy (GCBT) intervention, over a 12 week treatment period; post-treatment relapse rates and nine-months follow-up data for those participants who did not relapse were also reported.[3]

Main findings

The first systematic review included a total of 21 RCTs and the results of mixed treatment meta-analysis indicated that fluoxetine + CBT was the most effective treatment option, followed by fluoxetine alone and mirtazapine.[1] However, treatment regimens which included fluoxetine were associated with a significantly greater risk of suicidal ideation/suicide attempts.[1] Thus the review authors concluded that sertraline and mirtazapine were the optimal treatments, when considering the balance between efficacy, safety and tolerability.[1] The second systematic review included three RCTs (of which two were also included in the first review) and two observational studies.[2] The findings of this systematic review did not add significantly to those of the first review; evidence about the effects of antidepressants on quality of life was inconclusive.[2]

The results of this trial indicated that both sertraline and the GCBT intervention were associated with significant reductions in obsessive and compulsive symptoms during the treatment period (Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) and US National Institute of Mental Health Global Obsessive Compulsive Scale (NIMH-GOCS)), and there appeared to be no clear difference in effectiveness between the two treatments.[3] However, participants in the sertraline treatment group experienced a significantly greater rate of post-treatment relapse (10/18) than

those in the GCBT group (1/19). It should also be noted that only sertraline had a significant effect in reducing depressive symptoms (Children's Depression Inventory (CDI)); this was maintained post-treatment in those participants who did not experience relapse. Neither treatment had any significant effect on anxiety (Multidimensional Anxiety Scale for Children (MASC)).[3]

Authors conclusions

Ma 2014 – Sertraline and mirtazapine exhibited optimally balanced efficacy, acceptability, and safety for first-line acute treatment of child and adolescent MDD.

Stevanovic 2014 – This systematic review found inconclusive evidence that antidepressant treatments improve QOL among children and adolescents with depressive or anxiety disorders.

Asbahr 2005 – The authors concluded that treatment with GCBT may be effective in decreasing obsessive-compulsive symptoms in childhood obsessive-compulsive disorder and should be considered as an alternative to either individual cognitive-behavioural therapy or a medication, such as sertraline. They further stated that their results support the effectiveness and the maintenance of gains of GCBT in the treatment of youngsters with obsessive-compulsive disorder.

Reliability of conclusions/Strength of evidence

The evidence included in this summary was derived from one high quality systematic review and mixed treatment meta-analysis,[1] one moderate quality systematic review[2] and one very small randomised controlled trial,[3] the methodological quality of which could not be adequately assessed due to limitations in the reporting of methods and results. It should also be noted that, as the trial was conducted in Brazil, findings may have limited applicability to UK settings.[3] The evidence on the relative effectiveness of various options for the acute treatment of MDD in children and adolescents, derived from the high quality systematic review, is likely to be reliable.[1] The second systematic review[2] did not add significantly to the findings of the first. The evidence on the relative effectiveness of sertraline and GCBT for the treatment of obsessive compulsive disorder was weak and it should also be noted that, as the trial was conducted in Brazil, findings may have limited applicability to UK settings.[3]

What do guidelines say?

Neither NICE or SIGN guidelines, comment on whether medication is better than psychological/ therapeutic interventions in treating mental health issues in children and young people.

Date question received: 07/12/15
Date searches conducted: 08/12/15
Date answer completed: 04/01/16

References

Systematic Reviews

1. Ma, D., Zhang, Z., Zhang, X., & Li, L. (2014). Comparative efficacy, acceptability, and safety of medicinal, cognitive-behavioral therapy, and placebo treatments for acute major depressive disorder in children and adolescents: a multiple-treatments meta-analysis. Current Medical Research & Opinion, 30(6), 971-995.

2. Stevanovic, D., Tadic, I., & Knez, R. (2014). Are antidepressants effective in quality of life improvement among children and adolescents? A systematic review. *CNS Spectr*, 19(2), 134-141.

RCTs

3. Asbahr, F. R., Castillo, A. R., Ito, L. M., de Oliveira Latorre, M. R. D., Moreira, M. N., & Lotufo-Neto, F. (2005). Group cognitive-behavioral therapy versus sertraline for the treatment of children and adolescents with obsessive-compulsive disorder. *Journal of the American Academy of Child & Adolescent Psychiatry,* 44(11), 1128-1136.

Results

Systematic Reviews

Author (year)	Search Date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Ma et. al. (2014)	March 2013	***Participants*:** Children and adolescents (6-18 years old) with Major Depressive Disorder (MDD) ***Intervention*:** Acute treatment (8-12 weeks) with new-generation antidepressants (citalopram, escitalopram, fluoxetine, mirtazapine, paroxetine, sertraline, venlafaxine), cognitive behavioural therapy (CBT) alone, CBT + fluoxetine, or placebo. ***Comparator*:** As for intervention. ***Outcomes*:** Treatment efficacy (response rate as indicated by an end of treatment rating of 'much improved' or 'very much improved' on the Clinical Global	21 studies (n=4969 participants)	This review aimed to compare the efficacy and safety of various therapeutic regimens, including pharmacological therapies, psychotherapies and combination treatments, for the acute treatment of major depressive disorder (MDD) in children and adolescents. The mean duration of the included studies was 9.8 weeks (range 8 to 12 weeks), and mean sample size was 237 (range: 40 to 439). Twenty of the 21 included studies reported CGI as the primary outcome measure. Sixteen of the 21 included studies were conducted in the USA or the USA and Canada, and 13 were industry funded. Where reported, the mean duration of illness of study participants ranged from 3 to 26 months. Combined fluoxetine + CBT exhibited the highest efficacy (significantly higher response rates than all other interventions assessed, ORs ranging from 1.33 vs. fluoxetine alone to 3.33 vs,	The research objective of the review was clearly stated and appropriate inclusion criteria were defined. Nine bibliographic databases were searched for relevant studies and search terms were reported. Additional studies were sought through reference screening, hand searching of

		Impression (CGI) scale) , acceptability (dropout rate), and safety (suicidal ideation/suicide attempts). ***Study Design:*** Randomised controlled trials		placebo). Fluoxetine alone was associated with a higher response rate than CBT (OR 1.89 (95% CI: 1.41 to 2.63)), paroxetine (OR 1.64 (95% CI: 1.03 to 2.63)), sertraline (OR 1.67 (95% CI: 1.06 to 2.70)), citalopram (OR 2.44 (95% CI: 1.47 to 4.35)), escitalopram (OR 1.59 (95% CI: 1.02 to 2.63)), and placebo treatment (OR 2.56 (95% CI: 1.92 to 3.57)). Sertraline (OR 0.32 (95% CI: 0.19 to 0.63)), paroxetine (OR 0.40 (95% CI: 0.22 to 0.78)), escitalopram (OR 0.37 (95% CI: 0.21 to 0.78)), and venlafaxine (OR 0.41 (95% CI: 0.21 to 0.91)) all had significantly lower dropout rates than fluoxetine; results were similar for combined fluoxetine + CBT. CBT was associated with lower rates of suicidal ideation/suicide attempts than fluoxetine (OR 0.52 (95% CI: 0.38 to 0.70)), but did not differ significantly from other pharmacological interventions. Based on cumulative probabilities derived from a Markov Chain Monte Carlo model, combined fluoxetine + CBT (95.2%), fluoxetine (2.2%), and mirtazapine (1.2%) were the most effective treatments. Sertraline (50%), escitalopram (18.9%), venlafaxine (12.2%), and paroxetine (11.8%) were better tolerated than all other treatments. Mirtazapine (78.4%) and venlafaxine (19.9%) were the safest medications. However, it should be noted that results about mirtazapine	conference proceedings and trail registries, regulatory reports, and contact with individual investigators and pharmaceutical companies. The review process included measures to minimise error and bias and the risk of bias in included studies was assessed using the Cochrane risk of bias tool. Robust meta-analytic methods were used to generate

				and venlafaxine were obtained from only one study each	summary effect estimates and ranking of the effectiveness of various interventions. There were some errors in the labelling of results tables and graphs.
Stevanovic et. al. (2014)	Feb 2013	***Participants*:** Children and adolescents (≤18 years old) with a depressive or anxiety disorder diagnosis. ***Intervention*:** AT least one antidepressant medication – included studies evaluated fluoxetine (2 studies), sertraline (2 studies), and escitalopram (1 study). ***Comparator*:** No inclusion criteria were specified for the comparator – included randomised controlled trials (RCTs) compared: fluoxetine to fluoxetine +	5 studies (n=1239 participants)	This review aimed to assess whether antidepressants improve quality of Life in children with depressive or anxiety disorders. The review included 2 RCTs of fluoxetine in adolescents with MDD; one trial compared fluoxetine alone to fluoxetine + CBT (also included in the Ma 2014 review, see above) and the other compared fluoxetine alone to CBT alone, fluoxetine + CBT and placebo. The review also included one placebo-controlled RCT (also included in the Ma 2014 review, see above) and one observational study of sertraline in children and adolescents with MDD. The remaining study was an observational study of escitalopram in children and adolescents with social anxiety disorder (SAD). Treatment durations ranged from	The research objective of the review was clearly stated. Inclusion criteria were partially defined; no inclusion criteria for study design or comparator were reported. Five bibliographic databases were searched for relevant studies.

		CBT; fluoxetine to CBT alone, fluoxetine + CBT and placebo; sertraline to placebo. Two of the included studies were observational studies (no control group). ***Outcomes*:** Included studies were required to report a Quality of Life (QoL) instrument as an outcome measure. Other outcomes reported were: <u>Depression;</u> - Children's Depression Rating Scale – Revised (CDRS-R) <u>Anxiety;</u> - Screen for Child and Anxiety Related Emotional Disorders (SCARED) <u>Quality of life;</u> - Minimum Standard Checklist for Evaluating Health-Related Quality of Life Outcomes. - Euro quality of life questionnaire (EQ-5D) - Paediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q) - Youth Quality of Life Instrument – Research Version (Y-QOL-R)		10 to 28 weeks across the 5 included studies. QoL instruments were a secondary outcome measure in all studies. The Children's Depression Rating Scale—Revised (CDRS-R) was the primary outcome measure in all four MDD studies and the Screen for Child and Anxiety Related Emotional Disorders (SCARED) was the primary outcome measure in the SAD study. All treatment groups (antidepressant, CBT, antidepressant + CBT and placebo) in all studies showed significant improvements in QoL measures from baseline; an improvement was also observed for depression and anxiety outcomes. Studies of fluoxetine reported inconsistent results. One trial found that fluoxetine + CBT was associated with significantly greater improvements in QoL than placebo, fluoxetine alone or CBT alone and significantly greater improvements in depression than placebo or CBT alone. The same trial found that fluoxetine alone was more effective than CBT alone or placebo in improving depressive symptoms, but not QoL. The second trial found no significant difference in depression or QoL outcomes between fluoxetine + CBT and fluoxetine alone.	Searches were supplemented by reference screening and searching of clinical trials registries and pharmaceutical company's websites. Search terms were reported and no language restrictions were applied. The review process included measures to minimise error and bias. The methodological quality of included studies was assessed only in terms of the

		Study Design: The inclusion criteria for the review did not specify study design; the review included 3 RCTs and 2 open-label observational studies.		The sertraline trial found that sertraline was associated with significantly greater improvements in QoL and depression measures than placebo.	methodology of QoL assessment. The use of a narrative synthesis was appropriate, but numerical results for between group comparisons were poorly reported.

RCTs

Author (year)	**Inclusion criteria**	**Number of participants**	**Summary of results**	**Risk of bias**
Asbahr et. al. 2005	***Participants*:** Young people between the age of 9 – 17 years with a DSM IV diagnosis of OCD. Participants were required to have had OCD for at least six months and to have received no previous CBT or drug treatment for OCD. All participants had significant symptoms (score ≥7 on the NIMH Global Obsessive Compulsive Scale (NIMH-GOCS). People with significant co-	n=40 (GCBT group n=20, sertraline group n=20)	This trial aimed to compare the effectiveness of group cognitive behavioural therapy (GCBT) to sertraline for the treatment of obsessive-compulsive disorder. The study was conducted in children and adolescents who were referred to the Anxiety Disorders in Children and Adolescents Program of the Department of Psychiatry of the University of Sao Paulo Medical School, Brazil. Age and gender distribution, symptom duration, OCD severity and all other outcome measures were similar, at baseline, in the	No details of randomisation or allocation concealment procedures were reported. The nature of the

	existing psychiatric disorders were excluded. ***Intervention*:** Group Cognitive Behavioural Therapy (GCBT): 12 weekly, 90 minute sessions based on an individual CBT protocol that had been adapted for groups. The main elements in the treatment protocol included psychoeducation about OCD, cognitive training, exposure and response prevention (E/RP), and family sessions. Sessions were administered by a child and adolescent psychiatrist and a clinical psychologist. ***Comparator*:** Sertraline: Sertraline hydrochloride was given over 12 weeks. A single 2.5mg dose was given in week one, which was titrated every 4 days up to a 200mg maximum daily dose or as much as could be tolerated. The mean dose of sertraline received by study participants was 137.5±57.1 mg/day. ***Outcome*:** **Primary Outcome** Severity of OCD symptoms:		GCBT and sertraline groups. Post-treatment outcomes: After 12 weeks of treatment, both groups showed significant reductions in OCD severity, as measured by CY-BOCS and obsessive and compulsive sub-scores. Both groups also showed significant reductions in the CGAS, CGI and NIMH-GOCS scales. No comparative data were presented, but graphical representations appeared to show similar reductions in the two groups. For measures of depression and anxiety, only the sertraline group showed a significant reduction in depressive symptoms (CDI) and neither group showed any significant change in anxiety (MASC). Post-treatment outcomes: During a nine month follow-up period, 1/19 participants from the GCBT group relapsed and 10/18 participants from the sertraline group relapsed, p=0.02; relapse was defined as the return of obsessions and compulsions following treatment. When only participants who had not relapsed were considered (n=18 from the GCBT group and n=8 from the sertraline group), the significant effects observed post treatment were maintained at nine months follow-up in the sertraline group (with the exception of compulsive sub-scores of the CY-BOCS, CGI and NIMH-GOCS); significant post-treatment effects observed in the GCBT group were not maintained at nine months follow-up for any outcome measure.	intervention and comparator precluded the blinding of participants and study personnel. Outcomes were assessed independently by evaluators who were blind to treatment group. One participant was withdrawn from the sertraline group because they exhibited symptoms consistent

	- Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) - US National Institute of Mental Health Global Obsessive Compulsive Scale (NIMH-GOCS) - Clinical Global Impressions Scale (CGI) **Secondary Outcomes** Anxiety and depression: - Multidimensional Anxiety Scale for Children (MASC) - Childrens Depression Inventory (CDI) Adaptive Functioning: - Children's Global Assessment Scale (CGAS)			with hypomania. The post-treatment analysis therefore included 20 participants in the CGBT group and 19 in the sertraline group. The follow-up analysis excluded participants who relapsed during the nine month follow-up period, because these participants required re-introduction of other interventions. However,

				relapse rates were reported. Results were reported for all specified outcome measures. However, no statistical between group comparisons were reported.

Risk of bias:

Systematic reviews

Author (year)	RISK OF BIAS				
	Inclusion criteria	Searches	Review process	Quality assessment	Synthesis
Ma 2014	☺	☺	☺	☺	☺
Stevanovic 2014	☹	☺	☺	?	?

RCTs

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Asbahr 2005	?	?	☹	☺	☺	?

☺ Low risk ☹ High risk ? Unclear risk

Search details

Source	Search Strategy		Number of hits	Relevant evidence identified
NICE & SIGN	Psychological and pharmacological interventions in CAMHS Psychological and pharmacological interventions for OCD in CAMHS		26 8	0 0
Systematic Reviews				
Medline			113	0
Embase	1	exp Child/ or exp Adolescent/	2931543	219	1
	2	exp Adolescent Psychiatry/ or exp Adolescent Health Services/ or exp Mental Health Services/ or exp Community Mental Health Services/	134213		
	3	"child*".ab,ti.	1366548		
	4	youth.ab,ti.	49467		
	5	teenager.ab,ti.	2762		
	6	(young adj (Person or people or adult)).ab,ti.	52235		
	7	"Adolescen*".ab,ti.	253004		
	8	1 or 3 or 4 or 5 or 6 or 7	3343952		
	9	2 and 8	81347		
	10	((pharmacological or pharmaceutical, or drug or medication) adj3 (Treatment or intervention* or therap*)).ab,ti.	189091		
	11	exp Psychotherapy/	205748		
	12	exp Cognitive Therapy/	39653		

	13 (psycho* adj (treatment or intervention or therap*)).ab,ti.	18364		
	14 11 or 12 or 13	215096		
	15 9 and 10 and 14	219		
PsycINFO	1 exp Adolescent Psychiatry/ or exp Adolescent Health Services/ or exp Mental Health Services/ or exp Community Mental Health Services/	35451	70	1
	2 "child*".ab,ti.	431519		
	3 youth.ab,ti.	56524		
	4 teenager.ab,ti.	932		
	5 (young adj (Person or people or adult)).ab,ti.	27136		
	6 "Adolescen*".ab,ti.	159726		
	7 ((pharmacological or pharmaceutical, or drug or medication) adj3 (Treatment or intervention* or therap*)).ab,ti.	28521		
	8 exp Psychotherapy/	147756		
	9 exp Cognitive Therapy/	11111		
	10 (psycho* adj (treatment or intervention or therap*)).ab,ti.	18536		
	11 exp Child Psychotherapy/ or exp Child Psychiatry/	10964		
	12 2 or 3 or 4 or 5 or 6	557120		
	13 1 or 11	43748		
	14 12 and 13	17692		
	15 8 or 9 or 10	163610		

	16 7 and 14 and 15 70		
Central	#1 MeSH descriptor: [Child] explode all trees 240 #2 MeSH descriptor: [Adolescent] explode all trees 78006 #3 child 83869 #4 adolescen* 101417 #5 youth 2963 #6 teen* 1598 #7 young adj (person or people or adult) 620 #8 #1 or #2 or #3 or #4 or #5 or #6 or #7 150841 #9 MeSH descriptor: [Child Psychiatry] explode all trees 17 #10 MeSH descriptor: [Adolescent Psychiatry] explode all trees 24 #11 MeSH descriptor: [Mental Health Services] explode all trees 4759 #12 MeSH descriptor: [Community Mental Health Services] explode all trees 664 #13 #9 or #10 or #11 or #12 4791 #14 #8 and #13 1494 #15 ((pharmacological or pharmaceutical, or drug or medication) adj3 (Treatment or intervention* or therap*)) 1839 #16 ((psycho* or cognitive or therap*) adj3 (treatment or intervention or therap*)) 2064 #17 CBT 3311 #18 #16 or #17 5267 #19 #14 and #15 and #18 in Trials 9	9	

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