

# Best Evidence Summaries of Topics in Mental Healthcare

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

## Question

“In adults exposed to traumatic events how effective are pharmacological interventions compared to a placebo for the prevention of post-traumatic stress disorder (PTSD)?”

## Clarification of question using PICO structure

*Patients:* Adults exposed to traumatic events  
*Intervention:* Any pharmacological intervention  
*Comparator:* Placebo  
*Outcome:* Post-traumatic stress disorder (PTSD)

## Clinical and research implications

One, well conducted Cochrane systematic review found some very limited evidence that hydrocortisone may be effective in preventing the development of post-traumatic stress disorder in adults exposed to various traumatic experiences. Evidence was derived from four small randomised controlled trials with a total of 165 participants and some methodological weaknesses.

As noted by the review authors, further research is needed to adequately assess the efficacy of hydrocortisone and other pharmacotherapies in preventing PTSD. Further research is therefore needed to adequately assess the efficacy of various pharmacotherapies in preventing PTSD.

### What does the evidence say?

#### *Number of included studies/reviews (number of participants)*

We identified one systematic review which was considered relevant to this evidence summary. The review included nine small placebo-controlled, randomised controlled trials (RCTs), assessing the effectiveness of various pharmacological interventions for the prevention of post-traumatic stress disorder (PTSD) in adults exposed to traumatic events. Seven of the studies included in the review were conducted in younger adults with mixed trauma sources typically including traffic accidents (driver or pedestrian), work accidents and assaults. The remaining two studies were conducted in older adults following medical trauma, septic shock and cardiac surgery respectively. No studies were conducted in people with combat-related trauma.

#### *Main Findings*

There was some evidence to indicate that hydrocortisone may be effective in preventing PTSD: RR 0.17 (95% CI: 0.05 to 0.56), 4 studies with 165 participants, i.e. between 7 and 13 people would need to be treated in order to prevent one case of PTSD. Despite variation in the intervention regimens and clinical characteristics of participants, between-study statistical heterogeneity was low. However, sample sizes were small and three of the four studies were rated as high risk of bias.

The summary estimate from three trials of propranolol and individual estimates from single trials of escitalopram, temazepam and gabapentin indicated that these interventions had no significant effect on the development of PTSD.

There was no evidence of a significant effect of any treatment on any other outcome measure assessed.

#### *Authors Conclusions*

“There is moderate quality evidence for the efficacy of hydrocortisone for the prevention of PTSD development in adults. We found no evidence to support the efficacy of propranolol, escitalopram, temazepam and gabapentin in preventing PTSD onset. The findings, however, are based on a few small studies with multiple limitations. Further research is necessary in order to determine the efficacy of pharmacotherapy in preventing PTSD and to identify potential moderators of treatment effect.”

#### *Reliability of conclusions/Strength of evidence*

All of the evidence included in this summary was derived from a high quality Cochrane systematic review. As noted by the review authors, their findings were based on a few small studies with methodological limitations. Further research is therefore needed to adequately assess the efficacy of various pharmacotherapies in preventing PTSD.

### **What do guidelines say?**

Neither National Institute for Health and Care Excellence (NICE) nor Scottish Intercollegiate Guidelines Network (SIGN) guidelines comment upon the use of pharmacological interventions for the prevention of post-traumatic stress disorder (PTSD).

**Date question received:** 23/01/2015

**Date searches conducted:** 23/01/2015

**Date answer completed:** 16/02/2015

### **References**

Amos, T., Stein, D. J., & Ipser, J. C. (2014). Pharmacological interventions for preventing post-traumatic stress disorder (PTSD). *Cochrane Database of Systematic Reviews*, Issue 7. Art. No.: CD006239. DOI: 10.1002/14651858.CD006239.pub2.

## Results

### Systematic Reviews

Author (year)	Search Date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Amos et al. (2014)	The main searches were completed 04/2012. Up-date searches were completed in 2013 and 2014 for specialist Cochrane registers.	<p><i>Participants:</i> Adult participants (18 years and older) who have been exposed to any traumatic events, but who did not meet the diagnostic criteria for post-traumatic stress disorder at study recruitment. Studies of people with acute stress disorder or co-morbid psychopathological disorders were excluded.</p> <p><i>Intervention:</i> Any pharmacological intervention, grouped as: antipsychotics; benzodiazepines; beta-blockers; selective serotonin reuptake inhibitors (SSRIs); serotonin and norepinephrine reuptake inhibitors (SNRIs); Tricyclic antidepressants (TCAs); mono-amine oxidase inhibitors (MAOIs); other medications.</p> <p><i>Comparator:</i> Placebo</p>	9 studies (n=365 participants)	<p>This systematic review aimed to assess the effectiveness of pharmacological interventions for the prevention of post-traumatic stress disorder (PTSD) in adults exposed to traumatic events.</p> <p>The review included nine small RCTs, of which seven were conducted in younger adults (mean age 29 to 38 years) with mixed trauma sources typically including traffic accidents (driver or pedestrian), work accidents and assaults. The remaining two studies were conducted in older adults mean age 52 and 68.5 years following medical trauma, septic shock and cardiac surgery respectively. No studies were conducted in people with combat-related trauma.</p> <p>Four studies, including the two medical trauma studies, assessed hydrocortisone with varying dose and duration, three studies assessed propranolol (one of which also assessed gabapentin), and one study</p>	<p>A clear research objective was stated and appropriate inclusion criteria were defined.</p> <p>Searches included an appropriate range of bibliographic databases and attempts to identify additional and un-published studies through reference screening and contact with researchers. Full search strategies were reported.</p> <p>The review process</p>


		<p><i>Outcome:</i>  Primary outcomes - Treatment efficacy as determined by the number of people who developed PTSD (DSM-IV criteria); and treatment acceptability.  Secondary outcomes - PTSD symptoms; comorbidities (e.g. depression and anxiety); quality of life; functional disability; and side effects.</p> <p><i>Study design:</i>  Randomised controlled trials (RCTs)</p>	<p>each assessed temazepam and escitalopram. Intervention durations were short (maximum 19 days) and follow-up ranged from duration was most commonly 3 months (up to a maximum of 49 months in one study).</p> <p>The summary estimate derived from the four trials (n=165 participants) of hydrocortisone (RR 0.17 (95% CI: 0.05 to 0.56)) indicated that hydrocortisone may be effective in preventing PTSD (median follow-up duration 4.5 months). Despite variation in the intervention regimens and clinical characteristics of participants, between-study statistical heterogeneity was low. Three of the four studies were rated as high risk of bias.</p> <p>The summary estimate from three trials of propranolol and individual estimates from single trials of escitalopram, temazepam and gabapentin indicated that these interventions had no significant effect on the development of PTSD.</p> <p>There was no evidence of a significant effect of any treatment on any other outcome measure assessed.</p>	<p>included measures to minimise error and/or bias (involvement of two reviewers throughout).</p> <p>The methodological quality of included studies was assessed using the Cochrane risk of bias tool.</p> <p>The meta-analyses presented were appropriate.</p>
--	--	---	--	---


**Risk of Bias:**

**SRs**

Author (year)	RISK OF BIAS				
	Inclusion criteria	Searches	Review Process	Quality assessment	Synthesis
Amos et al. (2014)					

 Low Risk

 High Risk

 Unclear Risk

## Search Details

Source	Search Strategy	Number of hits	Relevant evidence identified
<b>SRs and Guidelines</b>			
NICE	prevent* AND (PTSD OR post-traumatic stress disorder)	68	0
<b>Primary studies</b>			
CENTRAL	<p>#1 (seroton* or norepinephrine or noradrenaline or dopamin* or neurotransmitter) next (uptake or reuptake or re-uptake) 4726</p> <p>#2 5-hydroxytryptophan or acetylcarnitine or alaproclate or alprazolam or amersergide or amiflamine or amineptine or amitriptyline or amoxapine or anticonvulsant* or antidepress* or antipsychotic* or anxiolytic* 22071</p> <p>#3 (befloxadone or benactyzine or benzodiazepine* or brofaromine or bupropion or butriptyline) 6118</p> <p>#4 caroxazone or cck-4 or chlorimipramine or chlorphenamidine or chlorpoxiten or cilosamine or cimoxatone or citalopram or clomipramine or clonidine or clorgyline or clovoxamine or cyproheptadine or d-cycloserine 5936</p> <p>#5 deanol or demexiptiline or deprenyl or desipramine or desvenlafaxine or dibenzipin or diclofensine or divalproex or dopamin* or dosulepin or dothiepin or doxepin or duloxetine 8475</p> <p>#6 escitalopram or etoperidone or femoxetine or fenfluramine or flumazenil or fluotracen or fluoxetine or fluparoxan or fluphenazine or fluvoxamine or furazolidone 5961</p> <p>#7 haloperidol or harmaline or harmine or hydrocortisone or idazoxan or imipramine or inositol or iprindole or iproniazid or isocarboxazid or lamotrigine 12720</p> <p>#8 (lithium carbonate or lithium compounds or litoxetine or lofepramine) 878</p> <p>#9 maoi* or maprotiline or medicat* or medifoxamine or melitracen or metapramine or metyrapone or mianserin or milnacipran or minaprine or mirtazapine or moclobemide or monoamine oxidase inhibitor* 46086</p> <p>#10 naloxone or naltrexone or nefazodone or nialamide or nomifensine or noradrenerg* or norfenfluramine or nortriptyline or noxiptiline or olanzapine or opipramol or oxaflozane or oxaprotiline 7222</p> <p>#11 pargyline or paroxetine or pharmacother* or phenelzine or pheniprazine or piribedil or pirlindole or</p>	130	0

	<p>pivagabine or pizotyline or prazosin or procaine or propranolol or prosulpride or protriptyline or psychotropic* 15393</p> <p>#12 quetiapine or quinupramine or quipazine or reboxetine or risperidone or ritanserlin or rolipram 3461</p> <p>#13 selegiline or seroto* or sertraline or setiptiline or snri* or ssri* or sulpiride 10939</p> <p>#14 teniloxine or tetrindole or thiazesim or thozalinone or tiagabine or tianeptine or toloxatone or tomoxetine or topiramate or tranylcypromine or trazodone or tricyclic* or trimipramine or tryptophan 4999</p> <p>#15 venlafaxine or viloxazine or viqualine or yohimbine or zimeldine 1796</p> <p>#16 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 101289</p> <p>#17 MeSH descriptor: [Stress Disorders, Post-Traumatic] explode all trees 957</p> <p>#18 (post-traumatic or post traumatic or posttraumatic) and disorder* 2387</p> <p>#19 ptsd 1374</p> <p>#20 #17 or #18 or #19 2702</p> <p>#21 #16 and #20</p>		
Embase	<p>1. EMBASE; (((seroton* OR norepinephrine OR noradrenaline OR dopamin* OR neurotransmitter) adj1 (uptake OR reuptake OR re-uptake))).ti,ab; 21426 results.</p> <p>2. EMBASE; (5-hydroxytryptophan OR acetylcarnitine OR alaproclate OR alprazolam OR amersergide OR amiflamine OR amineptine OR amitriptyline OR amoxapine OR anticonvulsant* OR antidepress* OR antipsychotic* OR anxiolytic*).ti,ab; 136332 results.</p> <p>3. EMBASE; (befloxatone OR benactyzine OR benzodiazepine* OR brofaromine OR bupropion OR butriptyline).ti,ab; 40916 results.</p> <p>4. EMBASE; (caroxazone OR cck-4 OR chlorimipramine OR chlorphenamidine OR chlorpoxiten OR cilosamine OR cimoxatone OR citalopram OR clomipramine OR clonidine OR clorgyline OR clovoxamine OR cyproheptadine OR d-cycloserine).ti,ab; 27841 results.</p> <p>5. EMBASE; (deanol OR demexiptiline OR deprenyl OR desipramine OR desvenlafaxine OR dibenzipin OR diclofensine OR divalproex OR dopamin* OR dosulepin OR dothiepin OR doxepin OR duloxetine).ti,ab; 150454 results.</p> <p>6. EMBASE; (escitalopram OR etoperidone OR femoxetine OR fenfluramine OR flumazenil OR fluotracen OR fluoxetine OR fluparoxan OR fluphenazine OR fluvoxamine OR furazolidone).ti,ab; 25277 results.</p> <p>7. EMBASE; (haloperidol OR harmaline OR harmine OR hydrocortisone OR idazoxan OR imipramine OR inositol OR iprindole OR iproniazid OR isocarboxazid OR lamotrigine).ti,ab; 84025 results.</p> <p>8. EMBASE; (lithium AND carbonate OR lithium AND compounds OR litoxetine OR lofepramine).ti,ab; 1789</p>	243	0



	<p>results.</p> <p>9. EMBASE; (maoi* OR maprotiline OR medicat* OR medifoxamine OR melitracen OR metapramine OR metyrapone OR mianserin OR milnacipran OR minaprine OR mirtazapine OR moclobemide OR monoamine AND oxidase AND inhibitor*).ti,ab; 7352 results.</p> <p>10. EMBASE; (naloxone OR naltrexone OR nefazodone OR nialamide OR nomifensine OR noradrenerg* OR norfenfluramine OR nortriptyline OR noxiptiline OR olanzapine OR opipramol OR oxaflozane OR oxaprotiline).ti,ab; 56902 results.</p> <p>11. EMBASE; (pargyline OR paroxetine OR pharmacother* OR phenelzine OR pheniprazine OR piribedil OR pirlindole OR pivagabine OR pizotyline OR prazosin OR procaine OR propranolol OR prosulpride OR protriptyline OR psychotropic*).ti,ab; 103689 results.</p> <p>12. EMBASE; (quetiapine OR quinupramine OR quipazine OR reboxetine OR risperidone OR ritanserin OR rolipram).ti,ab; 18510 results.</p> <p>13. EMBASE; (selegiline OR seroto* OR sertraline OR setiptiline OR snri* OR ssri* OR sulpiride).ti,ab; 110250 results.</p> <p>14. EMBASE; (teniloxine OR tetrindole OR thiazesim OR thozalinone OR tiagabine OR tianeptine OR toloxatone OR tomoxetine OR topiramate OR tranylcypromine OR trazodone OR tricyclic* OR trimipramine OR tryptophan).ti,ab; 65364 results.</p> <p>15. EMBASE; (venlafaxine OR viloxazine OR viqualine OR yohimbine OR zimeldine).ti,ab; 12151 results.</p> <p>16. EMBASE; 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15; 617058 results.</p> <p>17. EMBASE; POSTTRAUMATIC STRESS DISORDER/; 36615 results.</p> <p>18. EMBASE; ((post-traumatic OR post traumatic OR posttraumatic) AND disorder*).ti,ab; 23191 results.</p> <p>19. EMBASE; ptsd.ti,ab; 16909 results.</p> <p>20. EMBASE; 17 OR 18 OR 19; 40923 results.</p> <p>21. EMBASE; CLINICAL TRIAL/; 837391 results.</p> <p>22. EMBASE; RANDOMIZED CONTROLLED TRIAL/; 356075 results.</p> <p>23. EMBASE; RANDOMIZATION/; 64185 results.</p> <p>24. EMBASE; SINGLE BLIND PROCEDURE/; 19250 results.</p> <p>25. EMBASE; DOUBLE BLIND PROCEDURE/; 116908 results.</p> <p>26. EMBASE; CROSSOVER PROCEDURE/; 41027 results.</p> <p>27. EMBASE; "Randomi?ed controlled trial\$.ti,ab; 107148 results.</p> <p>28. EMBASE; rct.ti,ab; 15502 results.</p>		
--	---	--	--

	<p>29. EMBASE; "Random allocation".ti,ab; 1355 results.</p> <p>30. EMBASE; "Randomly allocated".ti,ab; 21256 results.</p> <p>31. EMBASE; ((allocated adj2 random)).ti,ab; 720 results.</p> <p>32. EMBASE; "Single blind\$.ti,ab; 15025 results.</p> <p>33. EMBASE; "Double blind\$.ti,ab; 145845 results.</p> <p>34. EMBASE; (treble ADJ blind\$.ti,ab; 0 results.</p> <p>35. EMBASE; (triple ADJ blind\$.ti,ab; 410 results.</p> <p>36. EMBASE; Placebo\$.ti,ab; 206020 results.</p> <p>37. EMBASE; PROSPECTIVE STUDY/; 270436 results.</p> <p>38. EMBASE; 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 47 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37; 1407163 results.</p> <p>39. EMBASE; "case report".ti,ab; 270970 results.</p> <p>40. EMBASE; ABSTRACT REPORT/; 71432 results.</p> <p>41. EMBASE; LETTER/; 839280 results.</p> <p>42. EMBASE; 60 OR 39 OR 40 OR 41; 1205188 results.</p> <p>43. EMBASE; 38 not 42; 1368726 results.</p> <p>44. EMBASE; 16 AND 20 AND 43; 1042 results.</p> <p>45. EMBASE; 44 [Limit to: Publication Year 2012-2015]; 243 results.</p>		
Medline	<p>1. MEDLINE; (((serotonin OR norepinephrine OR noradrenaline OR dopamine OR neurotransmitter) adj1 (uptake OR reuptake OR re-uptake))).ti,ab; 16964 results.</p> <p>2. MEDLINE; ((antiadrenergic OR anti-adrenergic)).ti,ab; 593 results.</p> <p>3. MEDLINE; (5-hydroxytryptophan OR Acetylcarnitine OR Alaproclate OR alprazolam OR Amersergide OR Amiflamine OR Amineptine OR Amitriptyline OR Amoxapine OR anticonvulsant* OR Antidepress* OR antipsychotic* OR anxiolytic* OR Aripiprazole).ti,ab; 103559 results.</p> <p>4. MEDLINE; (Befloxatone OR Benactyzine OR Benzodiazepine* OR Brofaromine OR Bupropion OR Butriptyline).ti,ab; 31909 results.</p> <p>5. MEDLINE; (Carbazepine OR Caroxazone OR cck-4 OR Chlorimipramine OR Chlorphenamidine OR Chlorpoxiten OR Cilosamine OR Cimoxatone OR Citalopram OR Clomipramine OR clonidine OR Clorgyline OR Clovoxamine OR Cyproheptadine OR d-Cycloserine).ti,ab; 24528 results.</p> <p>6. MEDLINE; (Deanol OR Demexiptiline OR Deprenyl OR Desipramine OR Desvenlafaxine OR Dibenzipin OR Diclofensine OR divalproex OR dopamin* OR Dosulepin OR Dothiepin OR Doxazosin OR Doxepin OR Duloxetine).ti,ab; 132818 results.</p>	428	0

	<p>7. MEDLINE; (Escitalopram OR Etoperidone OR Femoxetine OR Fenfluramine OR flumazenil OR Fluotracen OR fluoxetine OR Fluparoxan OR fluphenazine OR Fluvoxamine OR Furazolidone OR Guanfacine).ti,ab; 21456 results.</p> <p>8. MEDLINE; (haloperidol OR Harmaline OR Harmine OR hydrocortisone OR Idazoxan OR Imipramine OR inositol OR Iprindole OR Iproniazid OR Isocarboxazid OR lamotrigine).ti,ab; 77583 results.</p> <p>9. MEDLINE; (Lithium AND carbonate OR Lithium AND compounds OR Litoxetine OR Lofepamine).ti,ab; 1454 results.</p> <p>10. MEDLINE; (MAOI* OR Maprotiline OR medicat* OR Medifoxamine OR Melitracen OR Metapramine OR Metyrapone OR Mianserin OR Milnacipran OR Minaprine OR Mirtazapine OR Moclobemide OR Monoamine AND Oxidase AND Inhibitor*).ti,ab; 6954 results.</p> <p>11. MEDLINE; (Naloxone OR Naltrexone OR Nefazodone OR Nialamide OR Nomifensine OR noradrenerg* OR Norfenfluramine OR Nortriptyline OR Noxiptiline OR Olanzapine OR Opipramol OR Oxaflozane OR Oxaprotiline OR Oxcarbazepine).ti,ab; 51533 results.</p> <p>12. MEDLINE; N-METHYL-3,4-METHYLENEDIOXYAMPHETAMINE/; 3330 results.</p> <p>13. MEDLINE; (Pargyline OR Paroxetine OR pharmacother* OR Phenelzine OR Pheniprazine OR Piribedil OR Pirlindole OR Pivagabine OR Pizotyline OR Prazosin OR Pregabalin OR Procaine OR Propranolol OR Prosulpride OR Protriptyline OR psychotropic*).ti,ab; 88740 results.</p> <p>14. MEDLINE; (Quetiapine OR Quinupramine OR Quipazine OR Reboxetine OR Risperidone OR Ritanserin OR Rolipram).ti,ab; 13199 results.</p> <p>15. MEDLINE; (Selegiline OR seroto* OR Sertraline OR Setiptiline OR SNRI* OR SSRI* OR Sulpiride).ti,ab; 94534 results.</p> <p>16. MEDLINE; (Teniloxine OR Tetrindole OR Thiazesim OR Thozalinone OR Tiagabine OR Tianeptine OR Toloxatone OR Tomoxetine OR Topiramate OR Tranylcypramine OR Trazodone OR tricyclic* OR Trimipramine OR Tryptophan).ti,ab; 58349 results.</p> <p>17. MEDLINE; (Venlafaxine OR Viloxazine OR Viqualine OR Yohimbine OR Zimeldine).ti,ab; 10234 results.</p> <p>18. MEDLINE; exp STRESS DISORDERS, TRAUMATIC/; 24016 results.</p> <p>19. MEDLINE; 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18; 556298 results.</p> <p>20. MEDLINE; exp STRESS DISORDERS, TRAUMATIC/; 24016 results.</p> <p>21. MEDLINE; ((post-traumatic OR post traumatic OR posttraumatic) AND disorder*).ti,ab; 18616 results.</p> <p>22. MEDLINE; PTSD.ti,ab; 13101 results.</p> <p>23. MEDLINE; 20 OR 21 OR 22; 30492 results.</p>		
--	--	--	--

	<p>24. MEDLINE; RANDOMIZED CONTROLLED TRIALS AS TOPIC/; 94675 results.</p> <p>25. MEDLINE; RANDOMIZED CONTROLLED TRIAL/; 381907 results.</p> <p>26. MEDLINE; RANDOM ALLOCATION/; 81648 results.</p> <p>27. MEDLINE; DOUBLE-BLIND METHOD/; 126837 results.</p> <p>28. MEDLINE; SINGLE-BLIND METHOD/; 19669 results.</p> <p>29. MEDLINE; CLINICAL TRIAL/; 488227 results.</p> <p>30. MEDLINE; "clinical trial, phase i".pt; 14422 results.</p> <p>31. MEDLINE; "clinical trial, phase ii".pt; 23287 results.</p> <p>32. MEDLINE; "clinical trial, phase iii".pt; 9305 results.</p> <p>33. MEDLINE; "clinical trial, phase iv".pt; 973 results.</p> <p>34. MEDLINE; "controlled clinical trial".pt; 88467 results.</p> <p>35. MEDLINE; "randomized controlled trial".pt; 381907 results.</p> <p>36. MEDLINE; "clinical trial".pt; 488227 results.</p> <p>37. MEDLINE; exp CLINICAL TRIALS AS TOPIC/; 282845 results.</p> <p>38. MEDLINE; (single\$ ADJ blind\$).ti,ab; 11914 results.</p> <p>39. MEDLINE; (doubl\$ ADJ blind\$).ti,ab; 117919 results.</p> <p>40. MEDLINE; (treb\$ ADJ blind\$).ti,ab; 0 results.</p> <p>41. MEDLINE; (trip\$ ADJ blind\$).ti,ab; 365 results.</p> <p>42. MEDLINE; (single\$ ADJ mask\$).ti,ab; 319 results.</p> <p>43. MEDLINE; (doub\$ ADJ mask\$).ti,ab; 2682 results.</p> <p>44. MEDLINE; (treb\$ ADJ mask\$).ti,ab; 0 results.</p> <p>45. MEDLINE; (trip\$ ADJ mask\$).ti,ab; 40 results.</p> <p>46. MEDLINE; PLACEBOS/; 32470 results.</p> <p>47. MEDLINE; placebo\$.ti,ab; 162200 results.</p> <p>48. MEDLINE; "randomly allocated".ti,ab; 17833 results.</p> <p>49. MEDLINE; (allocated adj2 random\$).ti,ab; 20457 results.</p> <p>50. MEDLINE; 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37; 955832 results.</p> <p>51. MEDLINE; 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49; 240437 results.</p> <p>52. MEDLINE; 50 OR 51; 1003904 results.</p> <p>53. MEDLINE; "case report".ti,ab; 213077 results.</p> <p>54. MEDLINE; LETTER/; 858114 results.</p>		
--	--	--	--

	55. MEDLINE; HISTORICAL ARTICLE/; 304942 results. 56. MEDLINE; 53 OR 54 OR 55; 1364215 results. 57. MEDLINE; 52 not 56; 976327 results. 58. MEDLINE; 19 AND 23 AND 57; 1751 results. 59. MEDLINE; 58 [Limit to: Publication Year 2012-2015]; 428 results.		
<b>Summary</b>	<b>NA</b>	<b>NA</b>	

## **Disclaimer**

BEST in MH answers to clinical questions are for information purposes only. BEST in MH does not make recommendations. Individual health care providers are responsible for assessing the applicability of BEST in MH answers to their clinical practice. BEST in MH is not responsible or liable for, directly or indirectly, any form of damage resulting from the use/misuse of information contained in or implied by these documents. Links to other sites are provided for information purposes only. BEST in MH cannot accept responsibility for the content of linked sites.