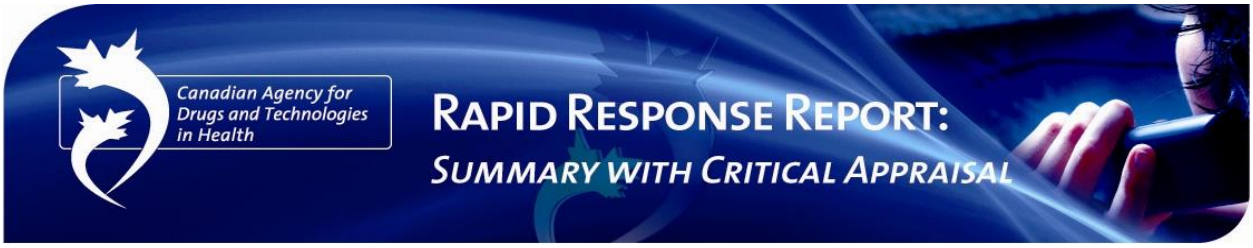

TITLE: Treatment for Post-Traumatic Stress Disorder, Operational Stress Injury, or Critical Incident Stress: A Review of Guidelines

DATE: 27 April 2015

CONTEXT AND POLICY ISSUES

Critical incidents are events where individuals witness or experience tragedy, death, serious injuries, or threatening situations, which may have strong emotional impact.[1] Emergency service workers and law enforcement workers are often affected by critical incident stress (CIS), which may or may not develop a post-traumatic stress disorders (PTSD) after a critical incident or traumatic event.[1] The signs and symptoms of CIS can be physical (e.g., fatigue, headache, dizziness), cognitive (e.g., confusion, nightmares, poor attention and concentration), emotional (e.g., fear, guilt, anger, depression, chronic anxiety) and behavioral (e.g., restlessness, withdrawal, increased alcohol consumption).[1] Tools for the management of CIS include demobilization, crisis management briefings, defusing, and debriefing.[2]

Operational stress injury (OSI) is a non-medical term describing a broad range of medical conditions including anxiety, depression, PTSD, and other less severe conditions.[3] OSI is usually associated with warfare, where intense combat can cause severe psychiatric symptoms, leading to substance abuse, depression, anxiety, and amnesia.[3] PTSD is one of the most common OSIs.[3]

PTSD is characterized by intrusive or distressing thoughts, nightmares, and flashbacks of past exposure to traumatic events, including sudden death of loved ones, accidents, natural disasters, sexual assault, combat injury, and torture.[4] The lifetime prevalence of PTSD in Canada was estimated to be 9.2%, with one month prevalence rates of 2.4%.[5] Women in general are more likely to develop PTSD than men after exposure to traumatic events.[6] PTSD has been associated with high rates of chronic pain, sleep problems, and sexual and cognitive dysfunction, leading to a significant decrease in quality of life.[5] PTSD has been associated with an increased cost of health care due to more often and longer hospitalizations.[1] There is a paucity of convincing evidence that both the psychological and pharmacological strategies can be successfully used in the prevention or early intervention of PTSD. On the other hand, patients with established PTSD can be managed using later pharmacological and/or psychological interventions. There are numerous types of drugs and psychotherapy approaches that may or may not have good clinical evidence for efficacy in treating PTSD.[7,8]

The aim of this report is to review the guidelines regarding treatment for PTSD, OSI, or CIS.

RESEARCH QUESTIONS

1. What are the evidence-based guidelines regarding treatment of patients with PTSD?
2. What are the evidence-based guidelines regarding treatment of patients with operational stress injury?
3. What are the evidence-based guidelines regarding treatment of patients with critical incident stress?

KEY FINDINGS

Selective serotonin reuptake inhibitors (SSRIs; fluoxetine, paroxetine and sertraline), and serotonin norepinephrine reuptake inhibitor (SNRI; venlafaxine) are recommended as first-line pharmacological treatment of PTSD, while cognitive behavioral therapy (CBT), stress management therapy, and eye movement desensitization and reprocessing (EMDR) are recommended as psychological approaches for PTSD. There are no guidelines that have specific recommendations for OSI or CIS.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2015, Issue 03), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to guidelines. The results of a second focused search (with main concepts appearing in the title or subject heading) were also included. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, and meta-analyses. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2008 and March 27, 2015.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection, according to selection criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults with PTSD, operational stress injury or critical incident stress
Intervention	Any treatment
Comparator	Not applicable
Outcomes	Guidelines and recommendations
Study Designs	Health technology assessments, systematic reviews, meta-analyses, and guidelines

Exclusion Criteria

Studies were excluded if they did not satisfy the selection criteria in Table 1, if they were published prior to 2008, duplicate publications of the same guidelines, or older guidelines from the same guideline society or institute.

Critical Appraisal of Individual Studies

The Appraisal of Guidelines Research & Evaluation (AGREE II) instrument was used to evaluate the quality of the included guideline.[9] For the critical appraisal of studies, a numeric score was not calculated. Instead, the strength and limitations of the studies were described.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 634 citations. Upon screening titles and abstracts, 24 potential relevant articles were retrieved for full-text review. Four additional relevant reports were retrieved from other sources. Of the 28 potentially relevant articles, six reports[10-15] were included in this review presenting guidelines and recommendations for treatment of patients with PTSD. No evidence-based guidelines were identified for treatment of patients with OSI or CIS. The study selection process is outlined in a PRISMA flowchart (Appendix 1).

Summary of Study Characteristics

Of the six evidence-based guidelines, one was from Canada (Canadian Anxiety Guidelines Initiative Group [CAGIG] 2014[10]), one from the UK (British Association for Psychopharmacology [BAP] 2014[11]), one from the World Health Organization (WHO) 2013,[12] two from the USA (Veterans Health Administration, Department of Defence [VA/DoD] 2010,[13] American Academy of Sleep Medicine [AASM] 2010[14]) and one from multiple countries (World Federation of Societies of Biological Psychiatry [WFSBP] 2008[15]). All included guidelines provided recommendations for treatment of patients with PTSD only and no recommendations for treatment of patients with OSI or CIS.

All guidelines are evidence based. The methodology of guideline development and evaluation of the science were described in all guidelines. The strength of the recommendations in five guidelines[10,11,13-15] was graded according to the level of evidence in a hierarchical manner where meta-analysis and randomized controlled trials were ranked highest and expert opinions were ranked lowest. The WHO guideline[12] used GRADE system to rank the level of evidence, based on which the recommendation was either classified as “strong” or “standard”. Appendix 2 presents the grading of recommendations and levels of evidence of the included guidelines.

Summary of Critical Appraisal

Strengths and limitations of the included guidelines were assessed using the AGREE II instrument and are presented in Appendix 3.

With respect to scope and purpose, all guidelines clearly stated the objectives, the health questions covered by the guidelines, and the target patient population. For stakeholder involvement, relevant professional groups including members of the steering group, research team and clinical experts were involved in the development of the guidelines. For rigour of development, all guidelines used systematic methods to search for the evidence, and clearly described the criteria for selecting the evidence, the strengths and limitations of the body of

evidence, and methods of formulating the recommendations. In addition, the health benefits, side effects, and risks were discussed and considered in formulating the recommendations. However, three guidelines[10,11,14] did not provide a procedure for updating the guidelines. For clarity, the recommendations of all guidelines were specific, unambiguous, and easy to identify. The different options for management of the condition were clearly presented. Four guidelines[10,11,14,15] had limitations in the applicability, in which advice and/or tools on how the recommendations can be put into practice, facilitators and barriers to their application, potential resource implications of applying the recommendations, and monitoring and/or audit criteria were not provided. For editorial independence, four guidelines[10,13-15] did not report whether or not the content of the guideline were influenced by the funding body.

Overall, all guidelines clearly stated the scope and purpose, stakeholder involvement, rigour of development, and clarity of recommendation. Some guidelines had limitations in applicability and editorial independence.

Summary of Findings

Recommendations for treatment of PTSD from six identified guidelines, including evidence levels and strength of recommendation, are presented in Appendix 4.

The Canadian guideline (CAGIG 2014)[10] had recommendations for the management of anxiety disorders, PTSD, and obsessive-compulsive disorders. For PTSD, the guideline only provided recommendations for pharmacotherapy for core symptoms of PTSD, although it had discussion about prevention and early intervention, psychological treatment, and combined psychological and pharmacological treatment. Selective serotonin re-uptake inhibitors (SSRIs) such as fluoxetine, paroxetine and sertraline, and serotonin norepinephrine re-uptake inhibitors (SNRIs), especially venlafaxine were recommended as first-line treatment of PTSD. A number of other drugs were recommended for second-line, third-line, adjunctive therapy or not recommended based on the level of evidence. There were no recommendations for psychological treatment in this guideline.

The British guideline (BAP 2014)[11] had recommendations for pharmacological treatment of anxiety disorders, PTSD, and obsessive-compulsive disorders. Recommendations for managing patients with PTSD included detection and diagnosis, prevention of post-traumatic symptoms, acute treatment of chronic PTSD, long-term treatment, combination of drug and psychological treatment, and treatments when initial therapy fail. Both pharmacological and psychological treatments were considered in this guideline. Selective serotonin re-uptake inhibitors (SSRIs) were recommended as first-line acute treatment of PTSD. Psychological treatment included cognitive behavioral therapy (CBT) and eye movement desensitization or reprocessing (EMDR). Combination of pharmacological and psychological treatment was not recommended for initial treatment. It was recommended for consideration when the initial therapy fails.

The WHO guideline 2013[12] was developed to provide recommendations for managing problems and disorders related to stress in post-conflict and natural disaster settings. It had recommendations for management of acute traumatic stress symptoms (re-experiencing, avoidance, hyperarousal), insomnia, dissociative disorders, and hyperventilation after a potential traumatic recent event. It also had recommendations for treatment of PTSD. Both pharmacological and non-pharmacological treatments were considered in the guideline. CBT and relaxation techniques were suggested for the management of symptoms after a potential traumatic recent event, while benzodiazepines and antidepressants were not recommended. Individual or group CBT was recommended for treatment of PTSD, while SSRIs and tricyclic antidepressants (TCAs) were not recommended to be used as first-line treatment. SSRIs and TCAs were recommended only when CBT or EMDR had failed or had been not available.

The US guideline (VA/DoD 2010)[13] had recommendations for early interventions to prevent PTSD and treatment of PTSD. For early interventions to prevent PTSD, psychotherapy such as CBT was recommended for patients with significant early symptom levels. No pharmacological therapy was recommended at this stage, due to a lack of evidence. For treatment of PTSD, both psychotherapy and pharmacotherapy could be considered as first-line treatment, providing that the therapy must be evidence-based and the selection of therapy should be driven by patient and provider preferences. Exposure-based therapy, CBT, and EMDR are psychotherapy interventions, the choice of which was recommended to be based on the severity of symptoms, clinician expertise and patient preference. Other psychological methods included relaxation techniques, imagery rehearsal therapy, brief psychodynamic therapy, and hypnotic techniques. For pharmacotherapy, SSRIs (fluoxetine, paroxetine, or sertraline) or SNRIs (venlafaxine) were strongly recommended as first-line monotherapy treatment for PTSD. A number of other drugs including TCAs and monoamine oxidase inhibitors were also recommended for treatment of PTSD. The guideline also had recommendations for adjunctive pharmacotherapy and adjunctive services such as psychological rehabilitation techniques. Acupuncture was recommended as somatic treatment for patients with PTSD. Complementary and alternative medicine was not recommended as first-line treatment for PTSD, but it could be used in an adjunctive approach.

The US guideline (AASM SPC 2010)[14] had specific recommendations for the management of PTSD-associated nightmares using both pharmacological and non-pharmacological approaches. Prazosin, clonidine, and a number of other drugs were recommended for treatment of PTSD-associated nightmares, while venlafaxine and clonazepam were not. Recommended non-pharmacological approaches included CBT (image rehearsal therapy, lucid treatment therapy, exposure, relaxation and rescripting therapy, sleep dynamic therapy, self-exposure therapy, systematic desensitization), deep muscle relaxation, hypnosis, EMDR, and the testimony method. Many of those approaches were based on low-grade evidence.

The multi-country guideline (WFSBP 2008)[15] had recommendations for the pharmacological treatment of anxiety disorders, obsessive-compulsive disorders and PTSD. For the treatment of PTSD, SSRIs (fluoxetine, paroxetine, sertraline) and the SNRI venlafaxine were recommended as first-line treatments for PTSD. A number of other drugs with lower quality of evidence were also recommended. CBT and repetitive transcranial magnetic stimulation appeared to be effective as non-pharmacological treatment for PTSD while debriefing was contraindicated.

Limitations

The Canadian guideline CAGIC 2014[10] clearly stated the recommendations for pharmacotherapy for PTSD, but did not provide recommendations for prevention and early intervention, psychological treatment, and combined psychological and pharmacological treatment, although these topics were discussed. All guidelines, except the WHO guideline,[12] appear to agree with first-line pharmacotherapy, where SSRIs had strongest support for the treatment of PTSD. Recommendations for second-line, third-line and adjunctive therapy for both pharmacotherapy and psychotherapy were not clearly described in many guidelines. Recommendations for psychotherapy varied among guidelines, although CBT appears to be the best option. The US guideline VA/DoD 2010[13] provided more detailed recommendations for non-pharmacological treatment for PTSD compared to other guidelines.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Six evidence-based guidelines were identified which had recommendations for pharmacological and/or psychological treatment of PTSD. There are no guidelines that have specific recommendations for OSI or CIS. The BAP,[11] WHO[12] and VA/DoD[13] guidelines had recommendations for prevention of PTSD in individuals who had been recently exposed to traumatic events, which may be relevant to the treatment of CIS. Those guidelines also provided detailed recommendations for treatment of PTSD. Except the WHO guideline,[12] there is a consistent agreement across guidelines that SSRIs (fluoxetine, paroxetine and sertraline), and SNRI (venlafaxine) should be used as first-line pharmacological treatment of PTSD. In the WHO guideline, CBT, EMDR or stress management was recommended for adult with PTSD, while SSRIs and TCAs were not recommended as first-line treatment. It was unclear why the WHO recommendations differed from those in the rest of the guidelines with to respect to drug therapy. One possible explanation is that the WHO guideline used GRADE to assess the quality of evidence, which was rated not study by study, but across studies for specific clinical outcomes. The Canadian guideline[10] listed drugs for second-line, third-line, adjunctive therapy and those that are not recommended. Of the psychological approaches, CBT, stress management therapy and EMDR are the recommended options. One guideline[11] did not recommend the combination of drug and psychological approaches as initial treatment for PTSD, while the rest of the guidelines did not mention combination therapy.

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REFERENCES

1. Kulbarsh P. Critical incident stress. Officer com [Internet]. 2007 Oct 15 [cited 2015 Apr 10]. Available from: http://www.officer.com/article/10249385/critical-incident-stress

2. Critical incident stress debriefing (powerful event group support) [Internet]. In: Placer County law enforcement chaplaincy: training manual. Placer County (CA): Placer County Law Enforcement Chaplaincy; 2007 Sep. p. 4-1-4-16. Chapter 4 [cited 2015 Apr 10]. Available from: http://www.placerchaplains.com/Documents/Chapter%204_Critical%20Incident%20Stress%20Debriefing.pdf.

3. Operational stress injury social support [Internet]. Ottawa: Department of National Defence. Official definition of an OSI; 2006 [cited 2015 Apr 10]. Available from: http://www.osiss.ca/engraph/def_e.asp?sidecat=1

4. Ciechanowski P. Posttraumatic stress disorder: epidemiology, pathophysiology, clinical manifestations, course, and diagnosis. 2014 Dec 30 [cited 2015 Apr 1]. In: UpToDate [Internet]. Waltham (MA): UpToDate; 1992 - . Available from: www.uptodate.com Subscription required.

5. Van Ameringen M, Mancini C, Patterson B, Boyle MH. Post-traumatic stress disorder in Canada. CNS Neurosci Ther. 2008;14(3):171-81.

6. Pietrzak RH, Goldstein RB, Southwick SM, Grant BF. Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. J Anxiety Disord [Internet]. 2011 Apr [cited 2015 Oct 24];25(3):456-65. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3051041

7. Bandelow B, Sher L, Bunevicius R, Hollander E, Kasper S, Zohar J, et al. Guidelines for the pharmacological treatment of anxiety disorders, obsessive-compulsive disorder and posttraumatic stress disorder in primary care. Int J Psychiatry Clin Pract [Internet]. 2012 Jun [cited 2015 Mar 31];16(2):77-84. Available from: http://www.wfsbp.org/fileadmin/user_upload/Treatment_Guidelines/Bandelow_et_al_01.pdf

8. Rothbaum BO. Psychotherapy for posttraumatic stress disorder [cited 2015 Apr 1]. In: UpToDate [Internet]. Waltham (MA): UpToDate; 1992 - . Available from: www.uptodate.com Subscription required.

9. Brouwers M, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in healthcare. CMAJ [Internet]. 2010 Dec [cited 2015 Apr 9];182(18):E839-E842. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3001530/pdf/182e839.pdf

10. Katzman MA, Bleau P, Blier P, Chokka P, Kjernisted K, Van AM, et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. BMC Psychiatry [Internet]. 2014 [cited 2015 Mar 30];14 Suppl 1:S1. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4120194

11. Baldwin DS, Anderson IM, Nutt DJ, Allgulander C, Bandelow B, den Boer JA, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. J Psychopharmacol. 2014 May;28(5):403-39.

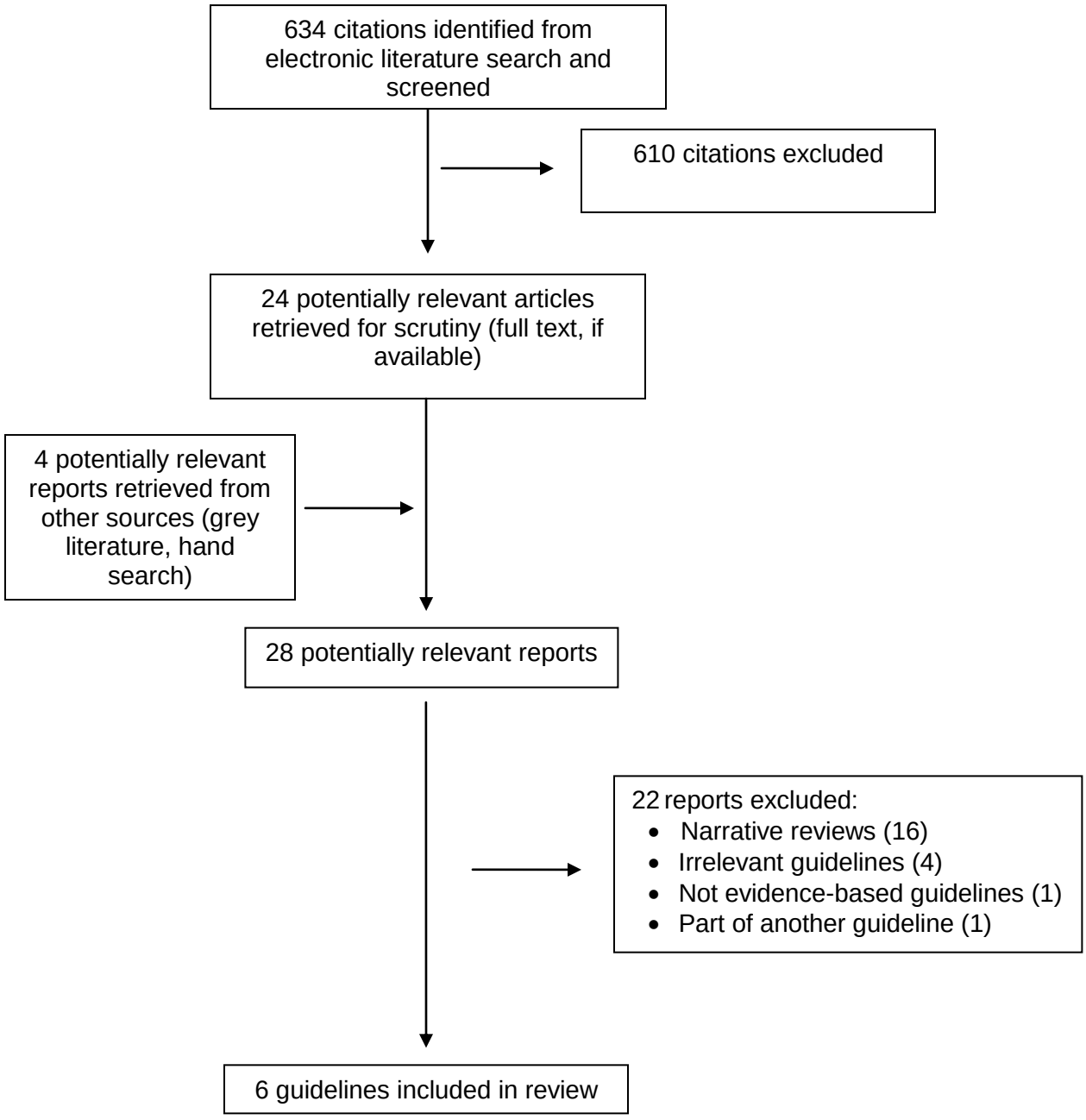
12. Guidelines for the management of conditions specifically related to stress [Internet]. Geneva: World Health Organization; 2013. [cited 2015 Apr 7]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK159725/pdf/TOC.pdf

13. Management of post-traumatic stress [Internet]. 2.0. Washington (DC): Department of Veterans Affairs, Department of Defense; 2010. [cited 2015 Apr 2]. (VA/DoD clinical practice guideline). Available from: http://www.healthquality.va.gov/PTSD-Full-2010c.pdf

14. Aurora RN, Zak RS, Auerbach SH, Casey KR, Chowdhuri S, Karippot A, et al. Best practice guide for the treatment of nightmare disorder in adults. J Clin Sleep Med [Internet]. 2010 Aug 15 [cited 2015 Mar 31];6(4):389-401. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2919672

15. Bandelow B, Zohar J, Hollander E, Kasper S, Moller HJ, WFSBP Task Force, et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders. World J Biol Psychiatry. 2008;9(4):248-312.

APPENDIX 1: Selection of Included Studies



APPENDIX 2: Grading of Recommendations and Levels of Evidence

Guideline Society or Institute, Year, Country	Recommendation Grade	Level of Evidence
CAGIG[10] 2014 Canada	**First-line**: Level 1 or Level 2 evidence plus clinical support for efficacy and safety **Second-line**: Level 3 evidence or higher plus clinical support for efficacy and safety **Third-line**: Level 4 evidence or higher clinical support for efficacy and safety **Not recommended**: Level 1 or Level 2 evidence for lack of efficacy	**1** Meta-analysis or at least 2 randomized controlled trials (RCTs) that included a placebo condition **2** At least 1 RCT with placebo or active comparison condition **3** Uncontrolled trial with at least 10 subjects **4** Anecdotal reports or expert opinions
BAP[11] 2014 UK	**A** Directly based on category I evidence (either I [M] or I [PCT] **B** Directly based on category II evidence or an extrapolated recommendation from category I evidence **C** Directly based on category III evidence or an extrapolated recommendation from category I or II evidence **D** Directly based on category IV evidence or an extrapolated recommendation from other categories **S** Standard of clinical care	**I** [M] Evidence from meta-analysis of randomized double-blind placebo-controlled trials **I** [PCT] Evidence from at least one randomized double-blind placebo-controlled trial **II** Evidence from at least one randomized double-blind comparator-controlled trial (without placebo) **III** Evidence from non-experimental descriptive studies **IV** Evidence from expert committee reports or opinions and/or clinical experience of respected authorities
WHO[12] 2013	**"Strong"**: meaning that the GDG agreed that the quality of the evidence combined with certainty about the values, preferences, benefits and feasibility of this recommendation meant it should be followed in all or almost all circumstances **"Standard"**: meaning that there was less certainty about the combined quality of evidence and values, preferences, benefits and feasibility of this recommendation, thus there may be circumstances in which it will not apply. The word "standard" (rather than "weak" or "conditional") was chosen to be in line with early WHO mhGAP guidelines and to avoid the negative connotations of the word "weak", which could have risked biasing GDG members towards	**GRADE system**: **High**: High confidence that the true effect lies close to that of the estimate of the effect **Moderate**: Moderate confidence in the effect of estimate: the true effect is likely to be close to the estimate of the effect, but there was a possibility that it is substantially different **Low**: Limited confidence in the effect estimate: the true effect may be substantially different from the estimate of the true effect **Very low**: Very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect

Guideline Society or Institute, Year, Country	Recommendation Grade	Level of Evidence
	"strong" recommendations.	
VA/DoD[13] 2010 USA	**A** A strong recommendation that the clinicians provide the intervention to eligible patients. *Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.* **B** A recommendation that clinicians provide (the service) to eligible patients. *A least fair evidence was found that the intervention improves health outcomes and concludes that benefit outweigh harm*. **C** No recommendation for or against the routine provision of the intervention is made. *At least fair evidence was found that the intervention can improve health outcomes, but concludes that the balance of benefits and harms is too close to justify a general recommendation*. **D** Recommendation is made against routinely providing the intervention to asymptomatic patients. *At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.* **I** The conclusion is that evidence is insufficient to recommend for or against routinely providing the intervention. *Evidence that the intervention is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined*.	**I** At least one properly done randomized controlled trial (RCT) **II-1** Well-designed controlled trial without randomization **II-2** Well-designed cohort or case-controlled analytic study, preferably from more than one source **II-3** Multiple time series evidence with/without intervention, dramatic results of uncontrolled experiment **III** Opinion of respected authorities, descriptive studies, case reports, and expert committees **Overall Quality** **Good** High grade evidence (I or II-1) directly linked to health outcome **Fair** High grade evidence (I or II-1) linked to intermediate outcome or moderate grade evidence (II-2 or II-3) directly linked to health outcome **Poor** Level III evidence or no linkage of evidence to health outcome
AASM SPC[14] 2010 USA	**A** Assessment supported by a substantial amount of high quality (Level 1 or 2) evidence and/or based on a consensus of clinical judgment **B** Assessment supported by sparse high grade (Level 1 or 2) data or a substantial amount of low-grade (Level 3 or 4) data and/or clinical	**1** High quality randomized clinical trials with narrow confidence intervals **2** Low quality randomized clinical trials or high quality cohort studies **3** Case-control studies **4** Case series or poor case-control studies or poor cohort studies or case reports

Guideline Society or Institute, Year, Country	Recommendation Grade	Level of Evidence
	consensus by the task force **C** Assessment supported by low grade data without the volume to recommend more highly and likely subject to revision with further studies	
WFSBP[15] 2008 Multi countries	**1** Category A evidence *and* good risk-benefit ratio **2** Category A evidence *and* moderate risk-benefit ratio **3** Category B evidence **4** Category C evidence **5** Category D evidence	**A** Full evidence from controlled studies **B** Limited positive evidence from controlled studies **C** Evidence from uncontrolled studies (C1), case reports (C2), or expert opinion (C3) **D** Inconsistent results **E** Negative evidence **F** Lack of evidence

BAP = The British Association for Psychopharmacology; CAGIG = Canadian Anxiety Guidelines Initiative Group; GDG = guideline development group; mhGAP = mental health GAP Action Program; VA/DoD = Veterans Health Administration, Department of Defense; WFSBP = World Federation of Society of Biological Psychiatry

APPENDIX 3: Summary of Study Strengths and Limitations – Guidelines

First Author, Publication Year	Strengths	Limitations
CAGIG[10] 2014 Canada	Scope and purpose • Objectives and target patients population were explicit • The health question covered by the guidelines is specifically described • The population to whom the guidelines is meant to apply is specifically described Stakeholder involvement • The guideline development group includes individuals from all relevant professional groups • The views and preferences of the target population have been sought • The target users of the guideline are clearly defined Rigour of development • Systematic methods were used to search for evidence • The criteria for selecting the evidence are clearly described • The strengths and limitations of the body of evidence are clearly described • The methods of formulating the recommendations are clearly described • The health benefits, side effects, and risks have been considered in formulating the recommendations • There is an explicit link between the recommendations and the supporting evidence • The guideline has been externally reviewed by experts prior to its publication Clarity of recommendation • The recommendations are specific and unambiguous • The different options for management of the condition or health issue are clearly presented • Key recommendations are easily identified Editorial independence • Competing interests of guideline development group members have been recorded and addressed	Rigour of development • A procedure for updating the guideline is not provided Applicability • The guidelines does not provide advice and/or tools on how the recommendations can be put into practice • The guideline does not describes facilitators and barriers to its application • The potential resource implications of applying the recommendations have not been considered • The guideline does not present monitoring and/or auditing criteria Editorial independence • It is unclear if the views of the funding body have influenced the content of the guideline

First Author, Publication Year	Strengths	Limitations
BAP[11] 2014 UK	Scope and purpose • Objectives and target patients population were explicit • The health question covered by the guidelines is specifically described • The population to whom the guidelines is meant to apply is specifically described Stakeholder involvement • The guideline development group includes individuals from all relevant professional groups • The views and preferences of the target population have been sought • The target users of the guideline are clearly defined Rigour of development • Systematic methods were used to search for evidence • The criteria for selecting the evidence are clearly described • The strengths and limitations of the body of evidence are clearly described • The methods of formulating the recommendations are clearly described • The health benefits, side effects, and risks have been considered in formulating the recommendations • There is an explicit link between the recommendations and the supporting evidence • The guideline has been externally reviewed by experts prior to its publication Clarity of recommendation • The recommendations are specific and unambiguous • The different options for management of the condition or health issue are clearly presented • Key recommendations are easily identified Editorial independence • The views of the funding body have not influenced the content of the guideline • Competing interests of guideline development group members have been recorded and addressed	Rigour of development • A procedure for updating the guideline is not provided Applicability • The guidelines does not provide advice and/or tools on how the recommendations can be put into practice • The guideline does not describes facilitators and barriers to its application • The potential resource implications of applying the recommendations have not been considered • The guideline does not present monitoring and/or auditing criteria

First Author, Publication Year	Strengths	Limitations
WHO[12] 2013	Scope and purpose • Objectives and target patients population were explicit • The health question covered by the guidelines is specifically described • The population to whom the guidelines is meant to apply is specifically described Stakeholder involvement • The guideline development group includes individuals from all relevant professional groups • The views and preferences of the target population have been sought • The target users of the guideline are clearly defined Rigour of development • Systematic methods were used to search for evidence • The criteria for selecting the evidence are clearly described • The strengths and limitations of the body of evidence are clearly described • The methods of formulating the recommendations are clearly described • The health benefits, side effects, and risks have been considered in formulating the recommendations • There is an explicit link between the recommendations and the supporting evidence • The guideline has been externally reviewed by experts prior to its publication • A procedure for updating the guideline is provided Applicability • The guidelines provides advice and/or tools on how the recommendations can be put into practice • The guideline describes facilitators and barriers to its application • The potential resource implications of applying the recommendations have been considered • The guideline presents monitoring and/or auditing criteria Clarity of recommendation • The recommendations are specific	

First Author, Publication Year	Strengths	Limitations
	and unambiguous • The different options for management of the condition or health issue are clearly presented • Key recommendations are easily identified <u>Editorial independence</u> • The views of the funding body have not influenced the content of the guideline • Competing interests of guideline development group members have been recorded and addressed	
VA/DoD[13] 2010 USA	<u>Scope and purpose</u> • Objectives and target patients population were explicit • The health question covered by the guidelines is specifically described • The population to whom the guidelines is meant to apply is specifically described <u>Stakeholder involvement</u> • The guideline development group includes individuals from all relevant professional groups • The views and preferences of the target population have been sought • The target users of the guideline are clearly defined <u>Rigour of development</u> • Systematic methods were used to search for evidence • The criteria for selecting the evidence are clearly described • The strengths and limitations of the body of evidence are clearly described • The methods of formulating the recommendations are clearly described • The health benefits, side effects, and risks have been considered in formulating the recommendations • There is an explicit link between the recommendations and the supporting evidence • The guideline has been externally reviewed by experts prior to its publication • A procedure for updating the guideline is provided	<u>Editorial independence</u> • It is unclear if the views of the funding body have influenced the content of the guideline • Competing interests of guideline development group members have not been recorded and addressed

First Author, Publication Year	Strengths	Limitations
	Applicability • The guidelines provides advice and/or tools on how the recommendations can be put into practice • The guideline describes facilitators and barriers to its application • The potential resource implications of applying the recommendations have been considered • The guideline presents monitoring and/or auditing criteria Clarity of recommendation • The recommendations are specific and unambiguous • The different options for management of the condition or health issue are clearly presented • Key recommendations are easily identified	
AASM SPC[14] 2010 USA	Scope and purpose • Objectives and target patients population were explicit • The health question covered by the guidelines is specifically described • The population to whom the guidelines is meant to apply is specifically described Stakeholder involvement • The guideline development group includes individuals from all relevant professional groups • The views and preferences of the target population have been sought • The target users of the guideline are clearly defined Rigour of development • Systematic methods were used to search for evidence • The criteria for selecting the evidence are clearly described • The strengths and limitations of the body of evidence are clearly described • The methods of formulating the recommendations are clearly described • The health benefits, side effects, and risks have been considered in formulating the recommendations • There is an explicit link between the recommendations and the	Rigour of development • A procedure for updating the guideline is not provided Applicability • The guidelines does not provide advice and/or tools on how the recommendations can be put into practice • The guideline does not describes facilitators and barriers to its application • The potential resource implications of applying the recommendations have not been considered • The guideline does not present monitoring and/or auditing criteria Editorial independence • It is unclear if the views of the funding body have influenced the content of the guideline

First Author, Publication Year	Strengths	Limitations
	supporting evidence • The guideline has been externally reviewed by experts prior to its publication <u>Clarity of recommendation</u> • The recommendations are specific and unambiguous • The different options for management of the condition or health issue are clearly presented • Key recommendations are easily identified <u>Editorial independence</u> • Competing interests of guideline development group members have been recorded and addressed	
WFSBP[15] 2008 Multi countries	<u>Scope and purpose</u> • Objectives and target patients population were explicit • The health question covered by the guidelines is specifically described • The population to whom the guidelines is meant to apply is specifically described <u>Stakeholder involvement</u> • The guideline development group includes individuals from all relevant professional groups <u>Rigour of development</u> • Systematic methods were used to search for evidence • The criteria for selecting the evidence are clearly described • The strengths and limitations of the body of evidence are clearly described • The methods of formulating the recommendations are clearly described • The health benefits, side effects, and risks have been considered in formulating the recommendations • There is an explicit link between the recommendations and the supporting evidence • The guideline has been externally reviewed by experts prior to its publication <u>Clarity of recommendation</u> • The recommendations are specific and unambiguous • The different options for	<u>Stakeholder involvement</u> • The views and preferences of the target population have not been sought • The target users of the guideline are not clearly defined <u>Rigour of development</u> • A procedure for updating the guideline is not provided <u>Applicability</u> • The guidelines does not provide advice and/or tools on how the recommendations can be put into practice • The guideline does not describes facilitators and barriers to its application • The potential resource implications of applying the recommendations have not been considered • The guideline does not present monitoring and/or auditing criteria <u>Editorial independence</u> • It is unclear if the views of the funding body have influenced the content of the guideline

First Author, Publication Year	Strengths	Limitations
	management of the condition or health issue are clearly presented • Key recommendations are easily identified <u>Editorial independence</u> • Competing interests of guideline development group members have been recorded and addressed	

APPENDIX 4: Guideline Recommendations

Summary of Recommendations from Included Guidelines for PTSD Treatment	
Guideline Society or Institute, Year, Country	**Recommendations [grade of recommendation]**
CAGIG[10] 2014 Canada	• SSRIs (fluoxetine, paroxetine and sertraline), and SNRI (venlafaxine XR) are recommended as first-line treatment of PTSD • A number of other drugs are recommended as second-line, third-line and adjunctive therapy, or not recommended
BAP[11] 2014 UK	• For prevention of PTSD after major trauma, preventive treatment with propranolol or sertraline [A] or trauma-focussed CBT [A] is recommended, but not routine single- or multiple-session “debriefing” [A] • For acute treatment of PTSD, SSRIs (paroxetine, sertraline), and SNRI (venlafaxine) are recommended as pharmacological treatment [A], and trauma-focussed individual CBT as psychological treatment [A] • Drug treatment should be continued at least 12 months in patients responding to treatment [A] • Combination of drug and psychological approaches is not recommended for initial treatment [A] • When initial therapy fail, consider increase dosage [D], switch to other evidence-based treatment [D], combining evidence-based treatments [S], combining evidence-based pharmacological and psychological treatments [A], addition of antidepressants (olanzapine [A], risperidone [A], or prazosin [A]) or referral to regional or national specialist services [S].

WHO[12]
 	
2013
	• After a potential traumatic recent event,
	  ○ CBT is recommended for treatment of acute traumatic stress symptoms [standard].
	  ○ No specific recommendation about stand-alone problem solving counselling, EMDR, relaxation or psycho-education [not applicable].
	  ○ Benzodiazepines [strong] and antidepressants [standard] are not recommended
	  ○ Relaxation techniques, and advice about sleep hygiene are recommended for patients with acute insomnia [standard]
	  ○ Benzodiazepines are not recommended for adults with insomnia [standard]
	  ○ There is no specific recommendation for dissociative (conversion) disorders [not applicable]
	  ○ There is no specific recommendation for hyperventilation [not applicable]
	• For PTSD,
	  ○ Individual or group CBT with trauma focus, EMDR, or stress management are recommended [standard]
	  ○ SSRIs and TCAs are not recommended as first-line treatment. They should be considered if stress management or EMDR have failed or are not available, or there is concurrent moderate-to-severe depression [standard]

VA/DoD[13]
 	
2010
 	
USA
	• After exposure to traumatic event,
	  ○ CBT is recommended as early intervention to prevent PTSD [A]
	  ○ Routine psychotherapy intervention for asymptomatic individuals is not recommended [D]
	  ○ Individual Psychological Debriefing is not recommended [D]
	  ○ Voluntary multiple group sessions may be effective [I]
	  ○ Pharmacological therapy is not recommended [I]
	• For psychotherapy interventions of PTSD,
	  ○ CBT or EMDR is recommended as psychotherapy [A]
	  ○ Relaxation techniques [C], Imagery Rehearsal Therapy (IRT) [C], and Brief Psychotic Therapy [C], hypnotic techniques [C], and group therapy [C] and augmentation therapy can be considered for symptoms-associated with PTSD
	  ○ There is no specific recommendation about Dialectical Behavioral Therapy (DBT) [I], Family or Couples Therapy [I] as first-line treatment
	  ○ Supportive psychotherapy is not considered
	• For pharmacological interventions of PTSD,
	  ○ SSRIs (fluoxetine, paroxetine and sertraline), and SNRI (venlafaxine XR) are strongly recommended as monotherapy [A]
	  ○ Mirtazapine, nefazodone, TCAs (amitriptyline, imipramine), or monoamine oxidase inhibitors (phenelzine) are also recommended [B]
	  ○ The use of benzodiazepines, guanfacine, anticonvulsants (tiagabine, topiramate, valproate) is not recommended [D]
	  ○ There is no recommendation for the use of prazosin, bupropione, trazodone, anticonvulsants (lamotrigine, gabapentin), or atypical antipsychotic [I]
	  ○ Atypical antipsychotics (risperidone or olanzapine [B], or quetiapine [C]), and prazosin for nightmares [B] are recommended as adjunctive therapy
	  ○ There is no recommendation for a sympatholytic or an anticonvulsant as adjunctive therapy [I]
	• For somatic treatment of PTSD,
	  ○ Acupuncture may be considered [B]
	• For complementary and alternative medicine (CAM) of PTSD,
	  ○ There is no recommendation for the use of CAM as first-line treatment [I]
	  ○ CAM may be considered as adjunctive treatment [C].

AASM SPC[14]
 	
2010
 	
USA
	• For pharmacological treatment of PTSD-associated nightmares,
	  ○ Prazosin is recommended [A]
	  ○ Clonidine and other drugs may be considered [C]
	  ○ Nefazodone [C] and venlafaxine [B] are not recommended
	  ○ There is no recommendation for clonazepam
	• For non-pharmacological option for nightmare disorder,
	  ○ CBT is recommended (i.e., image rehearsal therapy [A], lucid treatment therapy [C], exposure, relaxation and rescripting therapy [C], sleep dynamic therapy [C], self-exposure therapy [C], systematic desensitization [B])
	  ○ Progressive deep muscle relaxation [B], hypnosis [C], EMDR [C], and testimony method [C] are also recommended.

	○ There is no recommendation for individual psychotherapy.
WFSBP[15] 2008 Multi countries	• For pharmacological treatment for PTSD, ○ SSRIs (fluoxetine, paroxetine and sertraline), and SNRI (venlafaxine) are recommended as first-line treatment [1] ○ The efficacy of other drugs were noted with lower level of evidence • For non-pharmacological treatment for PTSD, ○ "Debriefing" is contraindicated ○ There are no concrete recommendations regarding CBT, exposure therapy, EMDR and repetitive transcranial magnetic stimulation.

ASD = acute stress disorder; BAP = The British Association for Psychopharmacology; CAGIG = Canadian Anxiety Guidelines Initiative Group; CBT = cognitive behavioral therapy; DBPC = double-blind placebo-controlled; EMDR = eye movement desensitization and reprocessing; MAOI = monoamine oxidase inhibitor; PTSD = post-traumatic stress disorder; rTMS = repetitive transcranial magnetic stimulation; SNRIs = serotonin norepinephrine reuptake inhibitors; SSRIs = selective serotonin reuptake inhibitors; VA/DoD = Veterans Health Administration, Department of Defense; WFSBP = World Federation of Society of Biological Psychiatry