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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

# PTSD: MEDICATION UPDATE

## DECEMBER 6, 2018


## DR. JESSICA WHITFIELD, MD, MPH


UW Medicine
UW SCHOOL OF MEDICINE

Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

# GENERAL DISCLOSURES

The University of Washington School of Medicine also gratefully acknowledges receipt of educational grant support for this activity from the Washington State Legislature through the Safety-Net Hospital Assessment, working to expand access to psychiatric services throughout Washington State.

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# SPEAKER DISCLOSURES

✓ I have no conflicts of interest to disclose.

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# OBJECTIVES

- Case discussion
- Brief overview PTSD diagnosis, treatment
- Review medication guidelines
- Review recent RCTs, reviews and meta-analyses

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# POST TRAUMATIC STRESS DISORDER

- A stress reaction characterized by 4 symptom clusters and difficulty functioning that persists after exposure to a dangerous event
- In US, 50% of adults experience a traumatic event in their lifetime
  - 10% - 15% go on to develop PTSD
- PTSD prevalence in US: 6.1 to 9.2 %
  - Veterans: 9.1-12.1%
  - Native Americans: 14.2 to 16.1%

*The Management of Post-Traumatic Stress Working Group . VA/DoD*

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# CASE

- A 26 year old female presents to your office to transfer care after her prior provider retired. She has a history of Major Depressive Disorder and Generalized Anxiety Disorder and no significant medical history. She describes worsening depression and anxiety symptoms in the last few months, with stressors as a break up in the last year, and her sister's boyfriend moving in to live with their family 6 mos ago. She notes feeling more irritable around her family, difficulty enjoying things, withdrawing, issues sleeping due to frequent vivid nightmares, difficult relaxing, difficulty being in public, and 'feeling jumpy a lot'. She is starting to have trouble going to work as a dog walker because of this. She has been on lorazepam 0.5mg BID for 3 months, but is not taking it consistently and not sure if it is helpful. She has never tried any other meds. She has also been in therapy for last year where she 'mostly vents'.

# WHAT DO YOU NOTICE?

- Symptoms of note:
  - Hyperarousal
  - ? re-experiencing (nightmares)
  - Irritability, mood changes
  - Sleeping issues
  - Social isolation
- Ask more:
  - Trauma history
  - Other PTSD sxs
    - Avoidance behavior, intrusion, re-experiencing, content of nightmares
  - Substance use
  - Safety (always)
  - Functioning

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# PTSD CRITERIA

**DSM-5 Diagnostic Criteria for PTSD**

**Criterion A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:**

1. Directly experiencing the traumatic event(s)
2. Witnessing, in person, the event(s) as it occurred to others
3. Learning that the traumatic event(s) occurred to a close family member or close friend

**Note:** In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.

4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains, police officers repeatedly exposed to details of child abuse)

**Note:** This does not apply to exposure through electronic media, television, movies or pictures unless this exposure is work-related.

**DSM-5 Diagnostic Criteria for PTSD**

**Criterion B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred.**

1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s)
2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s)
3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring (such reactions may occur on a continuum with the most extreme expression being a complete loss of awareness of present surroundings)
4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s)
5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s)

*The Management of Post-Traumatic Stress Working Group . VA/DoD*

**Criterion C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:**

1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s)
2. Avoidance or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s)

**Criterion D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred as evidenced by two or more of the following:**

1. Inability to recall an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs)
2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad.", "No one can be trusted.", "The world is completely dangerous.", "My whole nervous system is permanently ruined.")
3. Persistent distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others
4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, shame)
5. Markedly diminished interest or participation in significant activities
6. Feeling of detachment or estrangement from others
7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, loving feelings)

**Criterion E. Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:**

1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects
2. Reckless or self-destructive behavior
3. Hypervigilance
4. Exaggerated startle response
5. Problems with concentration
6. Sleep disturbance (e.g., difficulty falling or staying asleep, restless sleep)

# CASE REVIEW

- Thoughts regarding current/future treatment?
  - 26 yo with MDD and GAD in past
  - Trauma: interpersonal violence from recent relationship, meets criteria for PTSD
  - Lorazepam 0.5mg BID
  - Therapy

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# TREATMENT OVERVIEW

- Treatment of PTSD includes three broad categories of intervention:
  - psychotherapy
    - specific therapies (CBT, CPT)
  - pharmacological treatment
  - psychoeducation

# PHARMACOLOGIC TREATMENT

- FDA approval for PTSD: Paroxetine and sertraline
  - No medications developed specifically for PTSD
- Common off-label drugs: other antidepressants, second generation antipsychotics, benzodiazepines, adrenergic blockers (prazosin, propranolol)

*Shalev et al 2015*

# TREATMENT OVERVIEW

- Most patients with PTSD receive some form of pharmacologic treatment
  - antidepressants (89%), anxiolytic (61%), and antipsychotic agents (34%)

*Shalev et al 2015*

# OVERVIEW OF CURRENT PRACTICE GUIDELINES

- American Psychiatric Association (2004)
  - Update 2009
- Cochrane Meta-analysis (2006)
- VA/DoD (2010, 2017)
- NICE (UK; Dec 5 2018)

# APA (2004, 2009)

- 2004 recommendations with updates 2009:
  - **SSRIs and SNRIS** supported overall, address symptom clusters
    - Newer RCTs indicate less efficacy for combat-related PTSD
  - **Prazosin** promising for PTSD related nightmares
  - **Antipsychotics** promising for augmentation
  - **Anticonvulsants** less promising, mixed results
  - **Propranolol** mixed results
  - No comment on **benzodiazepines**
    - In 2004, maybe useful for anxiety, sleep; no mono therapy
      - Not recommended as mono-therapy
      - Dependence, increased incidence of PTSD with early use, worsening of PTSD symptoms after withdrawal

# COCHRANE META ANALYSIS (2006)

- 35 RCTs included in the analysis
  - 20 SSRI, 2 TCA, 2 mirtazapine, 4 MAOi, 7 others (alprazolam, olanzapine and risperidone, lamotrigine, venlafaxine, mirtazapine, nefazodone)
- Of the medication classes, evidence of treatment efficacy was most convincing for the SSRIs
  - More robust than TCAs, MAOi
  - No clear difference between SSRIs
  - Reduced severity of PTSD symptom clusters, comorbid depression and disability
  - Some evidence that combat related PTSD is more resistant to pharmacotherapy

# IN THE INTERIM …

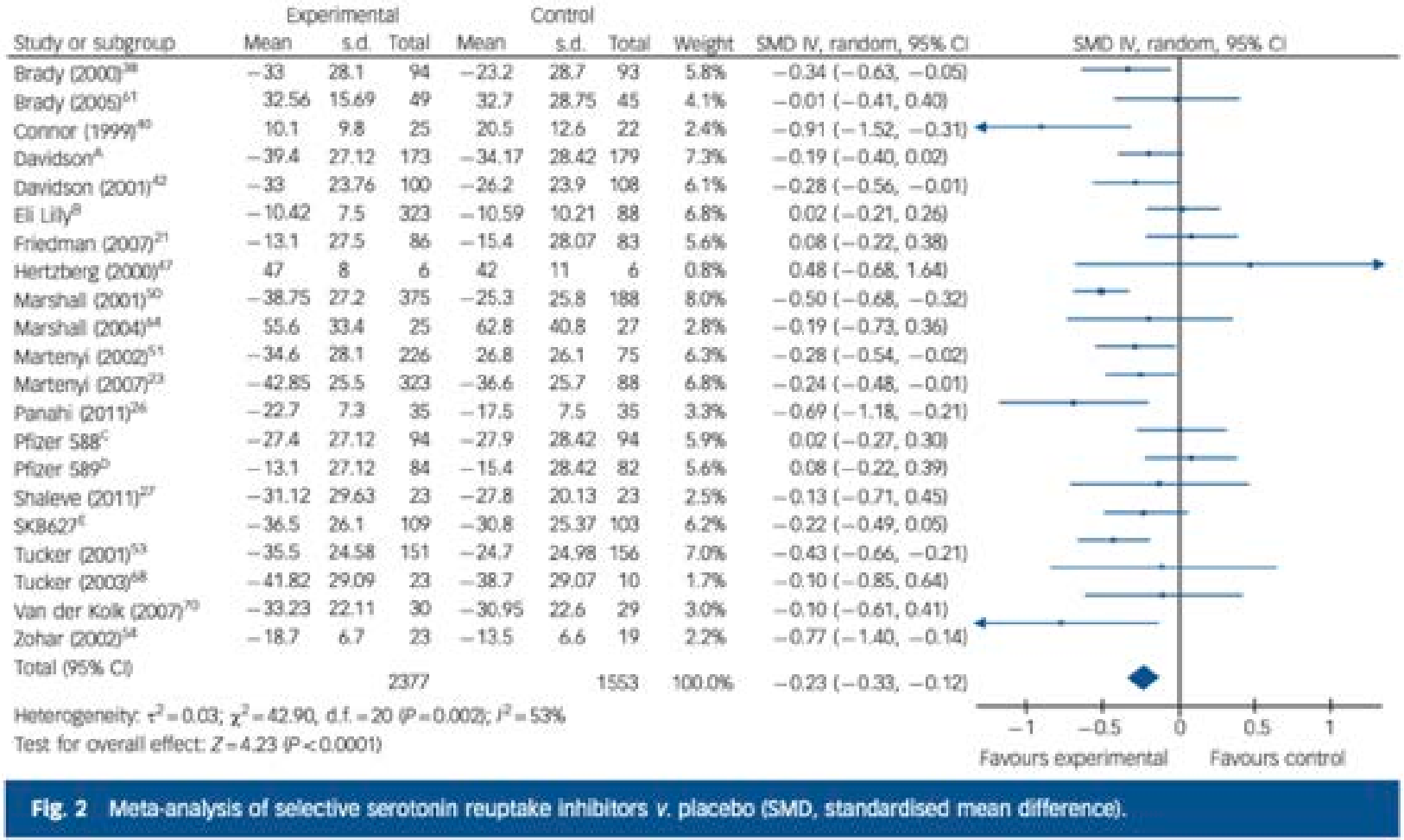
- Many more studies and RCTS
- Shifting understanding regarding:
  - benzodiazepines
  - prazosin
  - antipsychotics
  - propranolol
- Few updates to SSRI information

# META-ANALYSIS 2015

- Conclusions from 51 RCTs:
  - Evidence for three medications in the treatment of PTSD (**fluoxetine, paroxetine and venlafaxine)**
  - SSRIs found to perform better than placebo overall
    - Not enough data for other classes
  - No evidence for olanzapine, risperidone, escitalopram, citalopram, sertraline, topiramate, alprazolam, desipramine, imipramine, lamotrigine, nefazadone, tiagabine and valproic acid
  - Effect sizes for pharmacological treatments for PTSD are low and inferior to those reported for psychological treatments.
    - On par with effect sizes for depression

*Hoskins et al 2015*

# META-ANALYSIS 2015



| Study or subgroup | Experimental Mean | s.d. | Total | Control Mean | s.d. | Total | Weight | SMD IV, random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Brady (2000)[38] | −33 | 28.1 | 94 | −23.2 | 28.7 | 93 | 5.8% | −0.34 (−0.63, −0.05) |
| Brady (2005)[61] | 32.56 | 15.69 | 49 | 32.7 | 28.75 | 45 | 4.1% | −0.01 (−0.41, 0.40) |
| Connor (1999)[40] | 10.1 | 9.8 | 25 | 20.5 | 12.6 | 22 | 2.4% | −0.91 (−1.52, −0.31) |
| Davidson[A] | −39.4 | 27.12 | 173 | −34.17 | 28.42 | 179 | 7.3% | −0.19 (−0.40, 0.02) |
| Davidson (2001)[42] | −33 | 23.76 | 100 | −26.2 | 23.9 | 108 | 6.1% | −0.28 (−0.56, −0.01) |
| Eli Lilly[B] | −10.42 | 7.5 | 323 | −10.59 | 10.21 | 88 | 6.8% | 0.02 (−0.21, 0.26) |
| Friedman (2007)[21] | −13.1 | 27.5 | 86 | −15.4 | 28.07 | 83 | 5.6% | 0.08 (−0.22, 0.38) |
| Hertzberg (2000)[47] | 47 | 8 | 6 | 42 | 11 | 6 | 0.8% | 0.48 (−0.68, 1.64) |
| Marshall (2001)[50] | −38.75 | 27.2 | 375 | −25.3 | 25.8 | 188 | 8.0% | −0.50 (−0.68, −0.32) |
| Marshall (2004)[64] | 55.6 | 33.4 | 25 | 62.8 | 40.8 | 27 | 2.8% | −0.19 (−0.73, 0.36) |
| Martenyi (2002)[51] | −34.6 | 28.1 | 226 | 26.8 | 26.1 | 75 | 6.3% | −0.28 (−0.54, −0.02) |
| Martenyi (2007)[23] | −42.85 | 25.5 | 323 | −36.6 | 25.7 | 88 | 6.8% | −0.24 (−0.48, −0.01) |
| Panahi (2011)[26] | −22.7 | 7.3 | 35 | −17.5 | 7.5 | 35 | 3.3% | −0.69 (−1.18, −0.21) |
| Pfizer 588[C] | −27.4 | 27.12 | 94 | −27.9 | 28.42 | 94 | 5.9% | 0.02 (−0.27, 0.30) |
| Pfizer 589[D] | −13.1 | 27.12 | 84 | −15.4 | 28.42 | 82 | 5.6% | 0.08 (−0.22, 0.39) |
| Shaleve (2011)[27] | −31.12 | 29.63 | 23 | −27.8 | 20.13 | 23 | 2.5% | −0.13 (−0.71, 0.45) |
| SKB627[E] | −36.5 | 26.1 | 109 | −30.8 | 25.37 | 103 | 6.2% | −0.22 (−0.49, 0.05) |
| Tucker (2001)[53] | −35.5 | 24.58 | 151 | −24.7 | 24.98 | 156 | 7.0% | −0.43 (−0.66, −0.21) |
| Tucker (2003)[68] | −41.82 | 29.09 | 23 | −38.7 | 29.07 | 10 | 1.7% | −0.10 (−0.85, 0.64) |
| Van der Kolk (2007)[70] | −33.23 | 22.11 | 30 | −30.95 | 22.6 | 29 | 3.0% | −0.10 (−0.61, 0.41) |
| Zohar (2002)[54] | −18.7 | 6.7 | 23 | −13.5 | 6.6 | 19 | 2.2% | −0.77 (−1.40, −0.14) |
| Total (95% CI) | | | 2377 | | | 1553 | 100.0% | −0.23 (−0.33, −0.12) |

Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 42.90$, d.f. = 20 ($P = 0.002$); $I^2 = 53\%$

Test for overall effect: $Z = 4.23$ ($P < 0.0001$)

SMD IV, random, 95% CI

−1 −0.5 0 0.5 1

Favours experimental Favours control

**Fig. 2** Meta-analysis of selective serotonin reuptake inhibitors *v.* placebo (SMD, standardised mean difference).

*Hoskins et al 2015*

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# BENZODIAZEPINES

- Commonly used in the treatment of PTSD
- Review 2015:
  - 18 RCTs and observational studies, n = 5236
    - BZDs are ineffective for PTSD treatment and prevention
    - Associated with specific problems in patients with PTSD:
      - Risk of misuse/abuse, worse overall sx severity, significantly increased risk of developing PTSD with use after recent trauma, worse psychotherapy outcomes, aggression, depression, and substance use.
  - Conclusions: ***The results of this systematic review suggest that BZDs should be considered relatively contraindicated for patients with PTSD or recent trauma*.**

*Guina J et al 2015*

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# ANTIPSYCHOTICS

- Commonly prescribed for PTSD despite limited evidence
- VA Medical center prescriber review in 2013
    - PTSD was sole reason in 13% of long term antipsychotics (mostly quetiapine)
    - Efficacy or sedation

*Hermes et al 2013*

# ANTIPSYCHOTICS

- 2014 meta-analysis: 9 RCTs, n = 497 (olanzapine, risperidone)
- Monotherapy or augmentation
- Small decrease in CAPS score with antipsychotics (5.3 points)
- Higher drop out in antipsychotic group

| Study name | Std diff in means | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|---|
| Butterfield | 0.372 | 0.552 | 0.305 | -0.709 | 1.454 | 0.675 | 0.500 |
| Stein | -0.958 | 0.485 | 0.235 | -1.908 | -0.007 | -1.975 | 0.048 |
| Hamner03 | 0.075 | 0.329 | 0.108 | -0.570 | 0.720 | 0.227 | 0.820 |
| Reich | -0.438 | 0.446 | 0.199 | -1.313 | 0.436 | -0.982 | 0.326 |
| Bartzokis | -0.651 | 0.297 | 0.088 | -1.234 | -0.068 | -2.190 | 0.028 |
| Padala | -0.977 | 0.475 | 0.226 | -1.909 | -0.046 | -2.056 | 0.040 |
| Rothbaum | 0.024 | 0.449 | 0.202 | -0.857 | 0.905 | 0.052 | 0.958 |
| Krystal | -0.195 | 0.123 | 0.015 | -0.436 | 0.045 | -1.592 | 0.111 |
| Carey | -0.671 | 0.388 | 0.151 | -1.432 | 0.091 | -1.726 | 0.084 |
| | -0.289 | 0.093 | 0.009 | -0.471 | -0.106 | -3.103 | 0.002 |

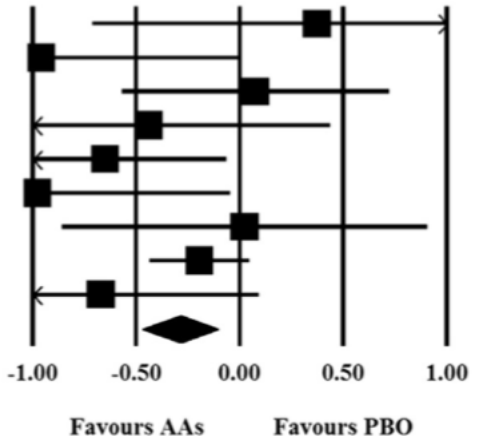


**Fig. 2.** Meta-analysis of the changes in the CAPS total score from baseline among studies.

*Han C et al 2014*

# ANTIPSYCHOTICS

- Aripriprazole:
  - 2017 review: monotherapy and adjunct therapy for PTSD
  - Significant improvements in CAPs score in all but 1 study analyzed (10 - 16 weeks; doses 2-15 mg daily).
  - Tolerated similar to general population

**TABLE 1.** Primary Outcome Results for the Use of Aripiprazole for the Treatment in PTSD

| | Author | Design | Population (N) | Follow-up, wk | Mean Dose (mg) | Primary Outcome | Baseline (SD) | Final (SD) | *P* |
|---|---|---|---|---|---|---|---|---|---|
| Monotherapy | Villarreal et al[16] | Open-label | Veteran (22) | 12 | 13.0 | CAPS | 74.9 (1.6) | 52.0 (5.4) | <0.001 |
| | Mello et al[17] | Open-label | Civilian (32) | 16 | 9.6 | CAPS | 82.7 (23.1) | 51.4 (31.4) | 0.0001 |
| | Youssef et al[18] | Open-label | Veteran (10) | 12 | 21.5 | CAPS | 78.1 (24.6) | 68.3 (27.3) | 0.04 |
| Adjunct therapy | Richardson et al[19] | Retrospective review | Veteran (27) | 12 | 12.4 | PCL-M | 56.1 (12.7) | 46.9 (13.5) | <0.0001 |
| | | | | | | BDI | 30.4 (7.9) | 20.7 (10.1) | <0.0001 |
| | Robert et al[20] | Open-label | Veteran (20) | 12 | 13.1 | CAPS | 78.2 (17.8) | 60.0 (23.5) | 0.002 |
| | Naylor et al[21] | Randomized controlled trial | Veteran (16) | 10 | 10.0 | CAPS | 90.6 (3.9) | 72.0 (41.4) | 0.52* |

*Compared with placebo.

*Britnell S et al 2017*

# ANTIPSYCHOTICS

- Quetiapine

| 2016 RCT | 2013 Open Label trial |
|---|---|
| • Monotherapy<br>• 12 weeks, n=80 veterans<br>• Primary outcome: CAPs | • Adjunct (stable SSRI)<br>• 8 weeks, n = 15 civilians<br>• Augment or mono therapy, 6-16 wks |
| • Avg dose 258mg (25mg to 800mg)<br>• Improvement in overall CAPs scores, reexperiencing and hyperarousal sub scores<br>• Adverse events and SE per expected | • Avg dose 216mg<br>• Improvement in overall CAPs scores, reexperiencing, avoidance and hyperarousal sub scores<br>• Adverse events and SE per expected |
| • Conclusion: quetiapine as a single agent is effective in treating military PTSD | • Conclusion: Patients with PTSD sxs on SSRI could benefit from quetiapine |

*Villareal et al 2016*

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# PRAZOSIN

- Multiple trials and reviews supported use for PTSD related nightmares
  - dose 2-6mg, 10-16mg for military patients
- NEJM RCT in 2018 (n= 304 veterans, 26 wks)
  - No significant differences btwn prazosin vs placebo for nightmare intensity/frequency or sleep quality
  - Sample: lower adrenergic activity, no veterans with psychosocial instability

*Green et al 2014, De Bardis D et al 2015, Simiski 2018, Raskind M et al 2018*

# PRAZOSIN

- Based on the results, prazosin was downgraded by American Academy of Sleep Medicine (AASM) and the VA
- No longer considered a first-line pharmacological intervention for PTSD nightmares by AASM and VA

*Simiski 2018, Raskind M et al 2018*

# BETA BLOCKERS

- $ß_{1,2}$-adrenoreceptor antagonist, crosses BBB
- Review 2016: No evidence reduction of PTSD sxs
- Cochrane meta-analysis 2013 for prevention of PTSD:
    - 3 RCTs (n=118) propranolol vs placebo (P value = 0.32)
    - No evidence for prevention
- 2018 Am J Psychiatry RCT (n=60, 6 wks)
    - Propranolol + therapy (pre-reactivation)
    - 11.5 point reduction in CAPS score

*Brunet et al. 2008, Steenen SA et al 2016, Lonergan MH et al 2013, Cochrane 2013, Giustino TF et al 2016*

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# VA GUIDELINES

- Practice guidelines updated in 2004, 2011 and 2017
- Strong evidence for: sertraline, paroxetine, fluoxetine, venlafaxine
- Strong evidence against: risperidone, benzodiazepines, antipsychotics for augmentation strategy, valproic acid
- Insufficient evidence: prazosin, mirtazapine

*Management of Post-Traumatic Stress Working Group 2017*

# VA GUIDELINES 2017

| | | | |
|---|---|---|---|
| | treatment of PTSD. | | |
| **c. Pharmacotherapy** | | | |
| 17 | We recommend sertraline, paroxetine, fluoxetine, or venlafaxine as monotherapy for PTSD for patients diagnosed with PTSD who choose not to engage in or are unable to access trauma-focused psychotherapy. | Strong For | Reviewed, New-replaced |
| 18 | We suggest nefazodone, imipramine, or phenelzine as monotherapy for the treatment of PTSD if recommended pharmacotherapy (see Recommendation 17), trauma-focused psychotherapy (see Recommendation 11), or non-trauma-focused psychotherapy (see Recommendation 12) are ineffective, unavailable, or not in accordance with patient preference and tolerance. (NOTE: Nefazodone and phenelzine have potentially serious toxicities and should be managed carefully.) | Weak For | Reviewed, New-replaced |
| 19 | We suggest against treatment of PTSD with quetiapine, olanzapine, and other atypical antipsychotics (except for risperidone, which is a Strong Against, see Recommendation 20), citalopram, amitriptyline, lamotrigine, or topiramate as monotherapy due to the lack of strong evidence for their efficacy and/or known adverse effect profiles and associated risks. | Weak Against | Reviewed, New-replaced |
| 20 | We recommend against treating PTSD with divalproex, tiagabine, guanfacine, risperidone, benzodiazepines, ketamine, hydrocortisone, or D-cycloserine, as monotherapy due to the lack of strong evidence for their efficacy and/or known adverse effect profiles and associated risks. | Strong Against | Reviewed, New-replaced |
| 21 | We recommend against treating PTSD with cannabis or cannabis derivatives due to the lack of evidence for their efficacy, known adverse effects, and associated risks. | Strong Against | Reviewed, New-added |

# VA GUIDELINES 2017

| # | Recommendation | Strength* | Category† |
|---|---|---|---|
| 22 | There is insufficient evidence to recommend for or against monotherapy or augmentation therapy for the treatment of PTSD with eszopiclone, escitalopram, bupropion, desipramine, doxepin, D-serine, duloxetine, desvenlafaxine, fluvoxamine, levomilnacipran, mirtazapine, nortriptyline, trazodone, vilazodone, vortioxetine, buspirone, hydroxyzine, cyproheptadine, zaleplon, and zolpidem. | N/A | Reviewed, New-replaced |
| **d. Augmentation Therapy** | | | |
| 23 | We suggest against the use of topiramate, baclofen, or pregabalin as augmentation treatment of PTSD due to insufficient data and/or known adverse effect profiles and associated risks. | Weak Against | Reviewed, New-replaced |
| 24 | We suggest against combining exposure therapy with D-cycloserine in the treatment of PTSD outside of the research setting. | Weak Against | Reviewed, New-added |
| 25 | We recommend against using atypical antipsychotics, benzodiazepines, and divalproex as augmentation therapy for the treatment of PTSD due to low quality evidence or the absence of studies and their association with known adverse effects. | Strong Against | Reviewed, New-replaced |
| 26 | There is insufficient evidence to recommend the combination of exposure therapy with hydrocortisone outside of the research setting. | N/A | Reviewed, New-added |
| 27 | There is insufficient evidence to recommend for or against the use of mirtazapine in combination with sertraline for the treatment of PTSD. | N/A | Reviewed, New-replaced |
| **e. Prazosin** | | | |
| 28a | For global symptoms of PTSD, we suggest against the use of prazosin as mono- or augmentation therapy. | Weak Against | Reviewed, New-replaced |
| 28b | For nightmares associated with PTSD, there is insufficient evidence to recommend for or against the use of prazosin as mono- or augmentation therapy. | N/A | Reviewed, New-replaced |
| **f. Combination Therapy** | | | |
| 29 | In partial- or non-responders to psychotherapy, there is insufficient evidence to recommend for or against augmentation with pharmacotherapy. | N/A | Reviewed, New-replaced |
| 30 | In partial- or non-responders to pharmacotherapy, there is insufficient evidence to recommend for or against augmentation with psychotherapy. | N/A | Reviewed, New-replaced |
| 31 | There is insufficient evidence to recommend for or against starting patients with PTSD on combination pharmacotherapy and psychotherapy. | N/A | Reviewed, New-added |

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# NICE GUIDELINES 2018

- YESTERDAY!
- Recommendations:
  - Consider venlafaxine or an SSRI if pt prefers pharmacotherapy
  - Consider antipsychotics such as risperidone second line only with severe hyperarousal or psychotic sxs
  - No benzodiazepines

*https://www.nice.org.uk/guidance/ng116*

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# A WORD ON CANNABIS

- 24 states list PTSD as indication for medical marijuana (WA included)
  - 2015: in these states, PTSD was primary indication for 38.5% of registered users
- Several studies have shown an increased risk of cannabis use disorders in adults with PTSD (veterans)
- 2 larger RCTs in next 3 years

*www.leafly.com, Yarnell S 2015*

# A WORD ON CANNABIS

- VA guidelines: “strong against” due to lack of evidence for efficacy, risks, adverse events

| Yarnell S 2015 Review | Shisiko I 2018 Review |
|---|---|
| • 46 studies (animal, case studies, commentaries, reviews, qualitative, no RCTs) | • 5 studies (1 RCT in Israel, 3 observational studies, and 1 retrospective chart review). |
| • Subjective sleep improvement short term, long term disruption | • 3 studies concluded there might be a benefit, 2 discouraged its use (worse PTSD outcomes) |

*Yarnell S 2015, Shisiko I et al 2018*

# TAKE HOME

- Therapy is important!
- SSRIs, venlafaxine have evidence for treating PTSD sxs and comorbid mood disorders
- No clear consensus on atypical antipsychotics or prazosin
- Benzodiazepines, mood stabilizers should be avoided

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# APA (2004)

- SSRIs: recommended as first-line medication for PTSD
  - Other antidepressants (TCA, MAOi) may also be beneficial
  - Relieves three symptom clusters (reexperiencing, avoidance, hyperarousal)
  - Not powered enough to show diff btwn SSRIs
- Benzodiazepines: maybe useful for anxiety, sleep
  - Not recommended as mono-therapy (dependence, increased incidence of PTSD with early use, worsening of PTSD symptoms after withdrawal).

# APA (2004)

- Antipsychotic medications (olanzapine, quetiapine, risperidone): may be helpful
- Anticonvulsant medications (divalproex, carbamazepine, topiramate, lamotrigine), α2-adrenergic agonists, and β-adrenergic blockers: may be helpful for specific symptom clusters