PTSD: Treatment Opportunities

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RAMSAY MENTAL HEALTH
People caring for people
RAMSAY HEALTH CARE

THE UNIVERSITY OF MELBOURNE
Australia

DSM 5: PTSD – CRITERION A

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- exposure to: actual or threatened death, serious injury, or sexual violence, as follows: **(1 required)**

- **Via:**

1. directly experiencing
2. Witnessing in person the event occurring to others
3. Learning that it occurred to a family member or close friend – events violent or accidental
4. Repeated or extreme exposure to aversive details of traumatic events e.g. first responders; other occupational exposures

PTSD

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- How many Australians have been exposed to a potentially traumatic event?
- Females - 50%
- Males – 65%
- Examples of PTEs:

combat	other violent crimes
torture	severe accidents
rape victims	natural disasters

Mental Health Responses To Trauma

- Most people recover with no long term effects
- Some people report long term, extreme distress and social / occupational impairment
- Diagnoses:
  - Depression
  - Substance abuse
  - Anxiety, including panic, phobias, and post-traumatic stress disorder (PTSD)

PTSD (DSM-5)

- A: Objective experience of trauma
- B: Intrusive memories (images, smells, etc.) (1/5)
- C: Active attempts to avoid reminders (1/2)
- D: Negative alterations in cognitions and mood (2/7)
- E: Hyperarousal, tense, on edge, jumpy (2/6)
- F: Duration > 4 weeks
- G: Functional impairment and/or distress

COMMON PATTERNS OF RESPONSE FOLLOWING TRAUMA OR DISASTER (BONNANO)

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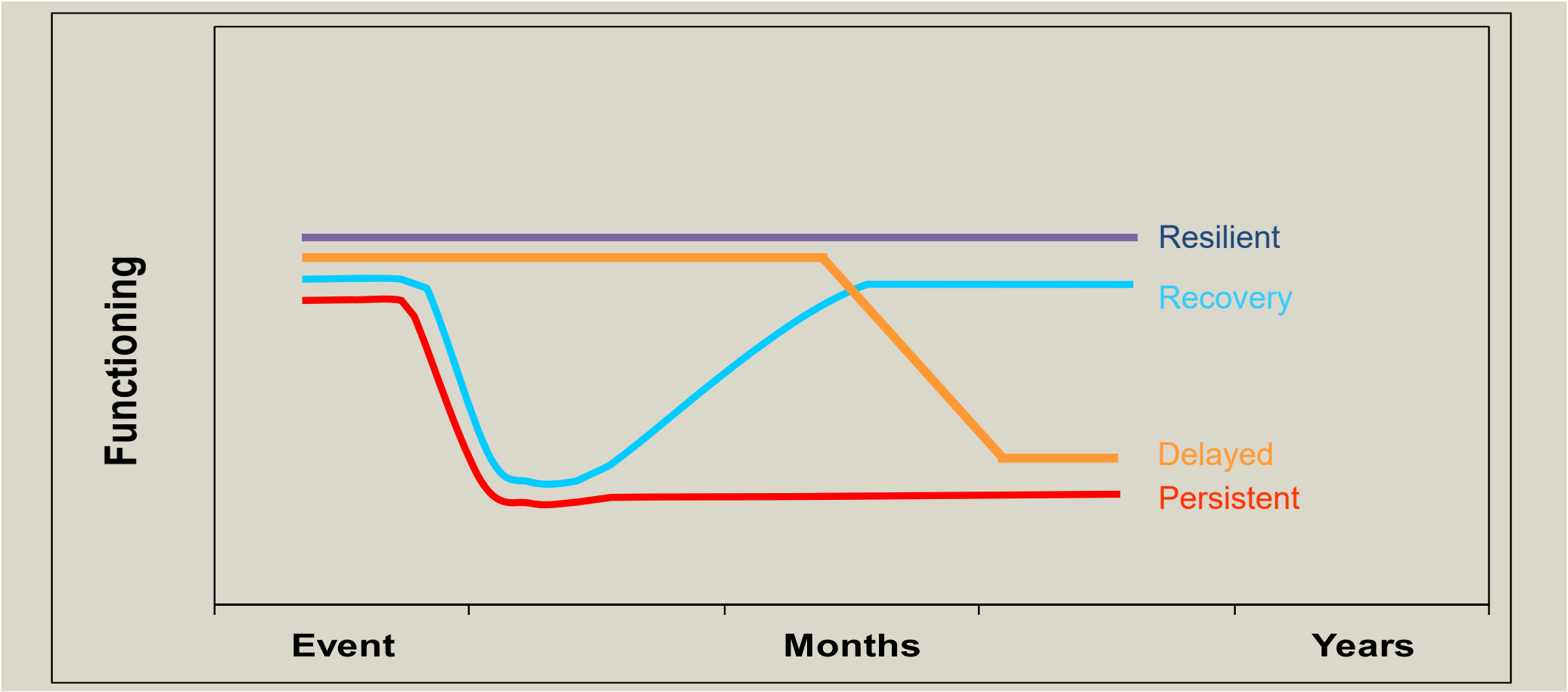


Epidemiology of PTSD

- Australian 12 Month Prevalence
  - 6.4% (Commonest Anxiety Disorder)

- Global Prevalence
  - 1.3-8.8% World Mental Health Survey using Worst Event Methodology

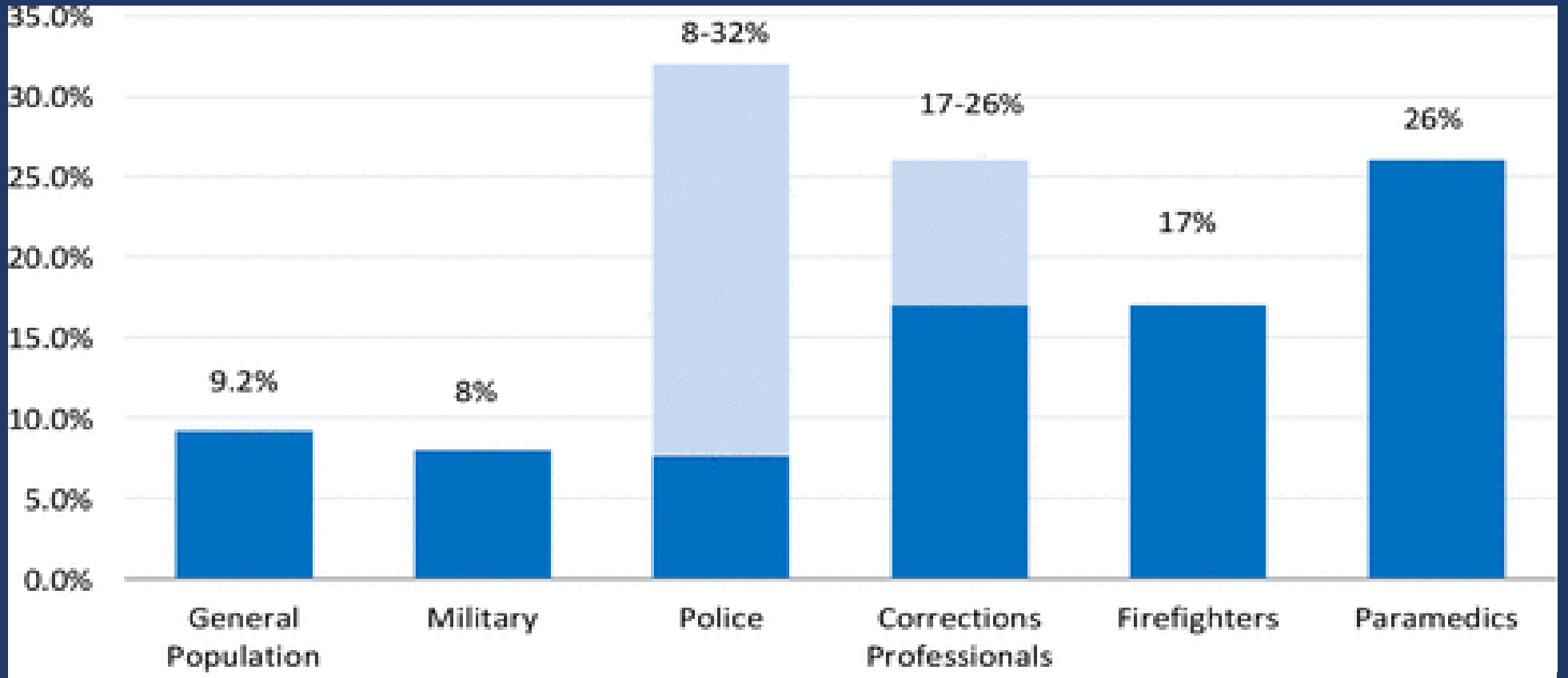
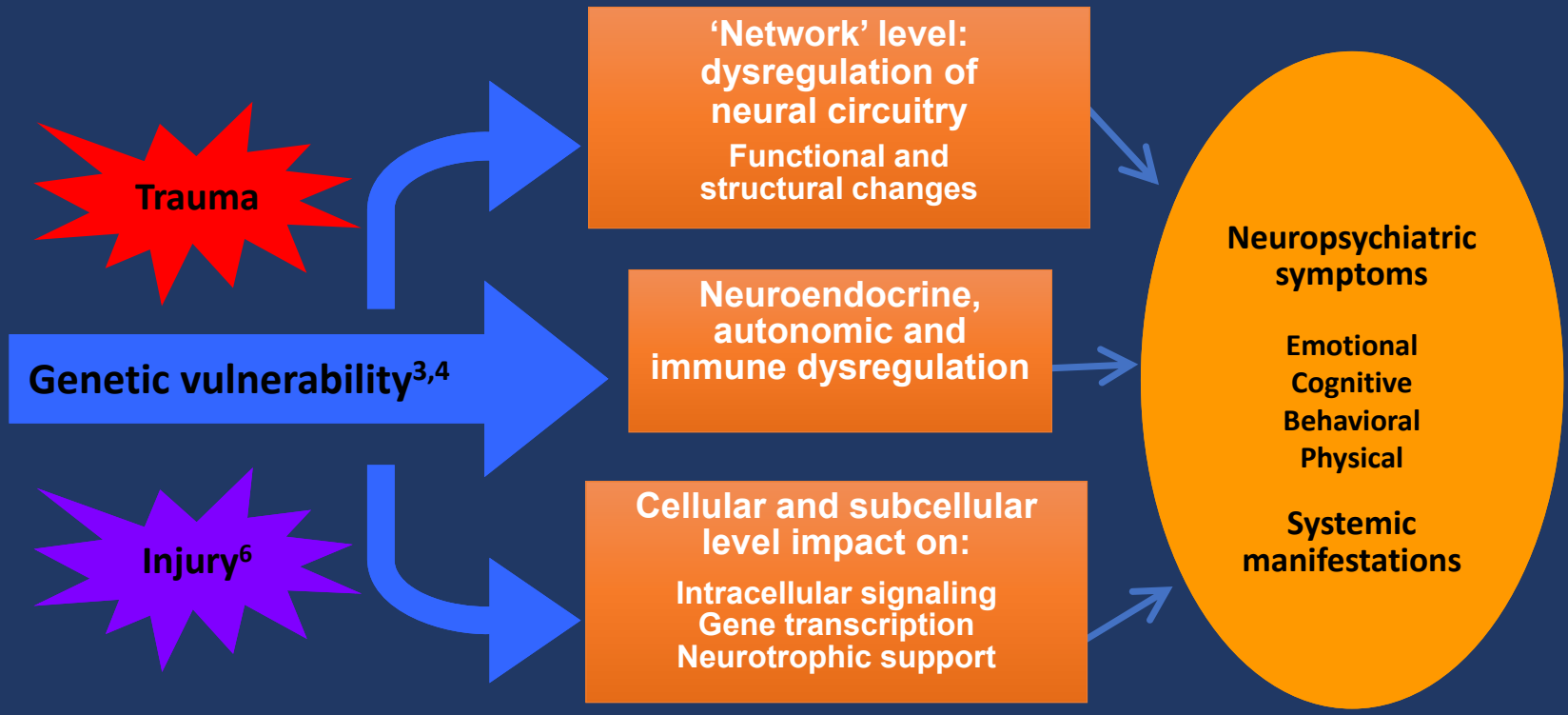


FIGURE 2 Lifetime PTSD Prevalence Rates: Specified Canadian Populations.
Sources: Van Ameringen, Mancini, Paterson et al. (2008); Boulos & Zamorski (2013); Marchand, Boyer, Martin et al. (2010); Asmundson & Stapleton (2008); Rosine (1992); Stadnyk (2004); Corneil, Beaton, Murphy et al. (1999); Regehr, Goldberg & Hughes (2002).

Micro to Macro Effects



Medication Classes Utilised in PTSD

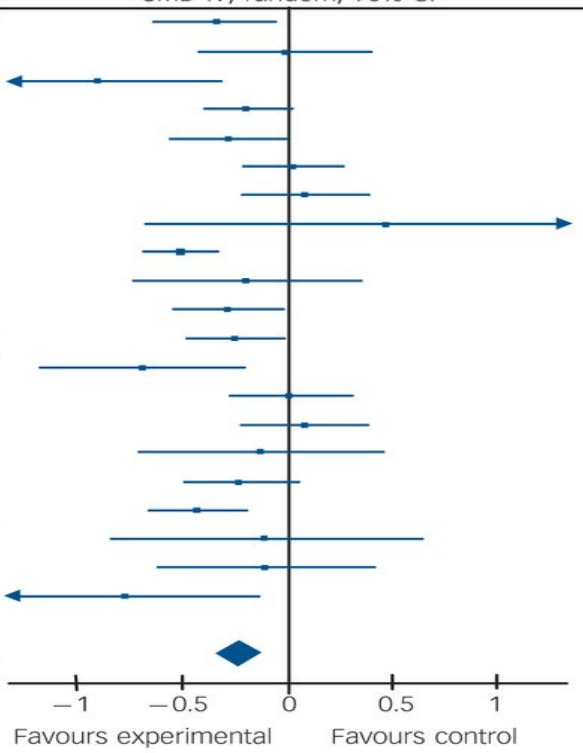
- Antidepressants
  - SSRIs
    - Fluoxetine
    - Paroxetine
    - Sertraline
    - Citalopram
    - Fluvoxamine
  - SNRIs
    - Venlafaxine
  - Atypical Antidepressants
    - Mirtazapine

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

	Experimental			Control				
Study or subgroup	Mean	s.d.	Total	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: $Z = 4.23$ ($P < 0.0001$)



Mathew Hoskins et al. BJP 2015;206:93-100

THE BRITISH JOURNAL OF PSYCHIATRY

Medication Classes Utilised in PTSD

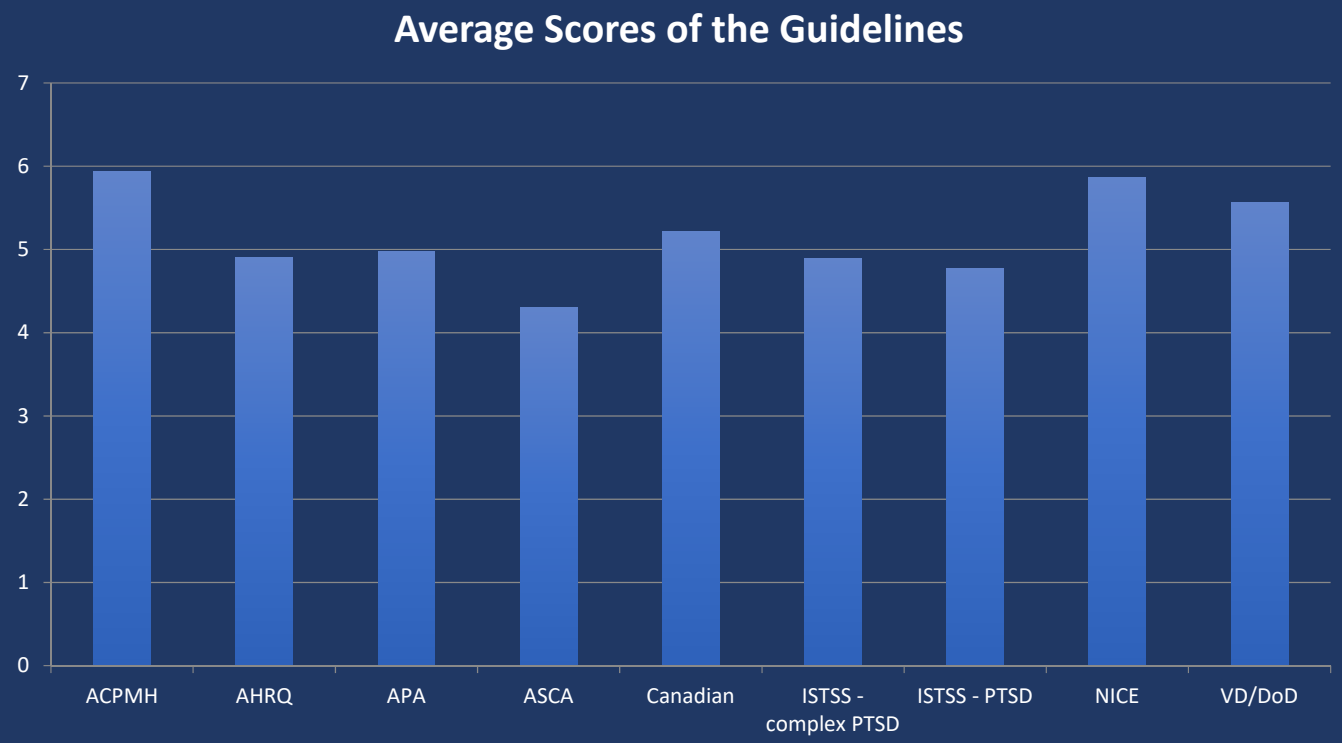
- Antipsychotics
  - Risperidone
  - Olanzapine
  - Quetiapine
- Benzodiazepenes
- Prazosin
- Topiramate

Evidence Based Use of medication in PTSD

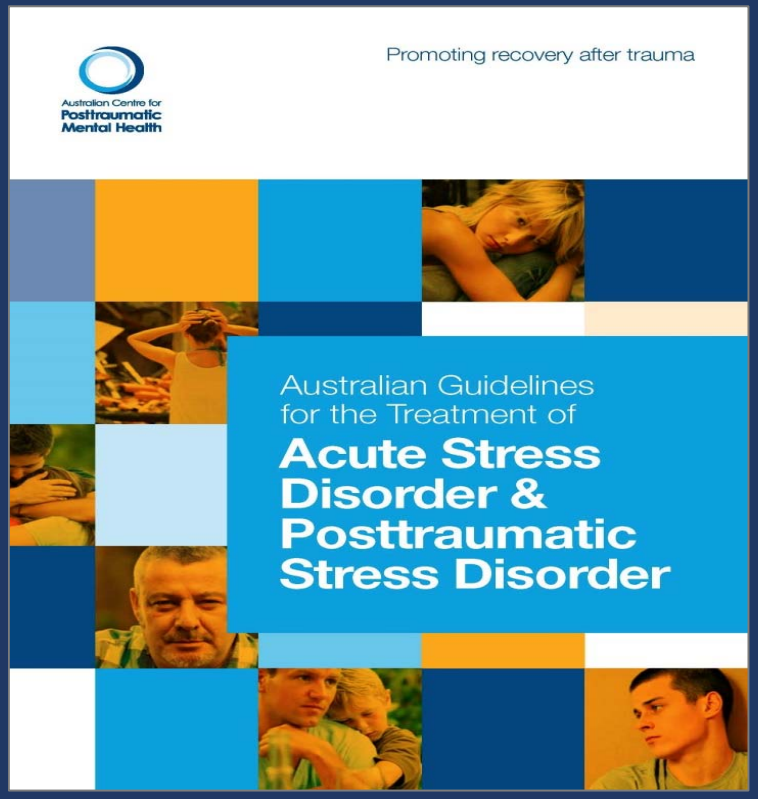
- Only SSRIs have the highest level evidence
  - Benefit is variable and modest in size
  - Only first line treatment in certain circumstances
- Other Antidepressants may be helpful
- Benzodiazepenes are for short term use wherever possible
- Atypical Antipsychotics may be useful but with a difficult risk benefit equation

Systematic Reviews & Guidelines:

- RANZCP AGREE II Survey 2013



Australian PTSD Guidelines - 2013



- Developed in consultation with experts and people affected by PTSD
- Supported by the Australian Government and approved by peak health research body - NHMRC
- Endorsed by professional associations – RACGP, RANZCP, APS

Available from www.acpmh.unimelb.edu.au

NHMRC Guideline Recommendations: Adults

- Trauma focussed CBT or EMDR is the treatment of choice for PTSD:
  - Trauma focused CBT included
    - In vivo and imaginal exposure
    - Cognitive therapy or cognitive processing therapy

- Medication should not be used as routine 1st line in preference to TF psychological treatment

- Where prescribed:
  - SSRIs
  - Other newer antidepressants, tricyclics, phenelzine

Outcomes of Trauma Focussed Therapy

Clinical Bottom Line

- • Posttraumatic stress disorder (PTSD) is a disabling psychiatric condition common among military personnel and veterans
- • A range of psychotherapies are available, but military-PTSD is complex and difficult to treat
- • The available evidence supports the use of structured trauma-focused or non–trauma-focused approaches
- • Although trauma-focused and non–trauma-focused interventions often improve symptoms, many patients continue to meet criteria for PTSD after treatment
- • There is an urgent need for innovative treatment strategies, whether trauma-focused or non–trauma-focused

Steenkamp et al JAMA 2015

Pharmacotherapy and prevention

- Covers the use of pharmacological agents post trauma to prevent development of symptoms
- Limited high level evidence
- ACPMH Guidelines (ACPMH,2013)
  - Should not be used for all those exposed as a preventative intervention

Pharmacotherapy and Prevention

- Pitman et al (Biol. Psychiatry 2002)
  - Propranolol (N= 18) V Placebo (23)
- Stein et al (J. Traumatic Stress 2007)
  - Propranolol (n=17) V Gabapentin(14) V Placebo (17)
  - No impact on severity of PTSD or depressive Symptoms
- Gelpin et al, (J. Clin. Psychiatry,1996)
  - Treatment with Clonazepam/Alprazolam (N= 10) V Placebo (N= 13)
  - No impact of treatment on anxiety or PTSD symptom scores
- Schelling et al (Biol. Psychiatry,2004)
  - Variable dose hydrocortisone V Placebo (N=91)
  - Significant reduction in chronic stress, but not PTSD symptoms in Steroid treated group ($p<.05$)

Conclusion

- PTSD is a common, complex and disabling disorder
- PTSD is particularly common in certain subgroups
- PTSD is a cause of high personal and economic burden
- Currently only Level 1 evidence for SSRIs
  - Effect size small-medium
- Most guidelines recommend psychotherapy as first line treatment but not always appropriate
- Marked unmet need