Anxiety Disorders II

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Diane McIntosh has received research support, spoken for, or sits on advisory boards for the following companies:

Lundbeck, Pfizer, Sanofi, Servier, Shire, Astra Zeneca, Valient, Otsuka, Eli Lilly, Bristol Myers Squibb, Janssen-Ortho, Sunovion
Treatment Guidelines
### Levels of evidence:

<table>
<thead>
<tr>
<th>Level</th>
<th>Evidence Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Meta-analysis or at least 2 randomized controlled trials (RCTs) that included a placebo condition</td>
</tr>
<tr>
<td>2</td>
<td>At least 1 RCT with placebo or active comparison condition</td>
</tr>
<tr>
<td>3</td>
<td>Uncontrolled trial with at least 10 subjects</td>
</tr>
<tr>
<td>4</td>
<td>Anecdotal reports or expert opinion</td>
</tr>
</tbody>
</table>

Levels of evidence do not assume positive or negative or equivocal results, they merely represent the quality and nature of the studies that have been conducted. Level 1 and Level 2 evidence refer to treatment studies in which randomized comparisons are available. Recommendations involving epidemiological or risk factors primarily arise from observational studies, hence the highest level of evidence for these is usually Level 3. Recommendations, such as principles of care, reflect consensus opinion based on evidence from various data sources, and therefore are primarily Level 4 evidence.
# Treatment recommendation summary

<table>
<thead>
<tr>
<th>Category</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line</td>
<td>Level 1 or Level 2 evidence plus clinical support for efficacy and safety</td>
</tr>
<tr>
<td>Second-line</td>
<td>Level 3 evidence or higher plus clinical support for efficacy and safety</td>
</tr>
<tr>
<td>Third-line</td>
<td>Level 4 evidence or higher plus clinical support for efficacy and safety</td>
</tr>
<tr>
<td>Not recommended</td>
<td>Level 1 or Level 2 evidence for lack of efficacy</td>
</tr>
</tbody>
</table>
### Medications with Health Canada–approved indications for anxiety and related disorders

<table>
<thead>
<tr>
<th>ANTIDEPRESSANTS</th>
<th>Anxiety disorders</th>
<th>PD</th>
<th>SAD</th>
<th>OCD</th>
<th>GAD</th>
<th>PTSD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SSRIs</strong></td>
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<tr>
<td>Escitalopram (Cipralex®)</td>
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<td>X</td>
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<tr>
<td>Fluoxetine (Prozac®)</td>
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<tr>
<td>Fluvoxamine (Luvox®)</td>
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<td>X</td>
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<tr>
<td>Paroxetine (Paxil®)</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Paroxetine CR (Paxil® CR)</td>
<td>X</td>
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<td>X</td>
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<tr>
<td>Sertraline (Zoloft®)</td>
<td>X</td>
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<td><strong>TCAs</strong></td>
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<tr>
<td>Clomipramine</td>
<td>X</td>
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<tr>
<td><strong>Other antidepressants</strong></td>
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<tr>
<td>Venlafaxine XR (Effexor® XR)</td>
<td></td>
<td>X</td>
<td>X</td>
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<tr>
<td>Duloxetine (Cymbalta®)</td>
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<td>X</td>
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<tr>
<td><strong>AZAPIRONES</strong></td>
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<tr>
<td>Buspirone (BuSpar®, Buspirex®)</td>
<td></td>
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<td>X</td>
<td></td>
</tr>
<tr>
<td><strong>BENZODIAZEPINES</strong></td>
<td></td>
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<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

Data from respective Canadian product monographs [84]. *Multiple generic and brand name products, consult product monographs: alprazolam, bromazepam, chlordiazepoxide, clorazepate, diazepam, lorazepam, and oxazepam are indicated for anxiety disorders; alprazolam is also indicated for panic disorder. CR = controlled release; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; XR = extended release.
### Components of cognitive behavioral interventions

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
</table>
| **Exposure**                  | • Encourage patients to face fears  
• Patients learn corrective information through experience  
• Extinction of fear occurs through repeated exposure  
• Successful coping enhances self-efficacy |
| **Safety response inhibition**| • Patients restrict their usual anxiety-reducing behaviors (e.g., escape, need for reassurance)  
• Decreases negative reinforcement  
• Coping with anxiety without using anxiety-reducing behavior enhances self-efficacy |
| **Cognitive strategies**       | • Cognitive restructuring, behavioral experiments, and related strategies target patients’ exaggerated perception of danger (e.g., fear of negative evaluation in SAD)  
• Provides corrective information regarding the level of threat  
• Can also target self-efficacy beliefs |
| **Arousal management**         | • Relaxation and breathing control skills can help patient control increased anxiety levels |
| **Surrender of safety signals**| • Patient relinquishes safety signals (e.g., presence of a companion, knowledge of the location of the nearest toilet)  
• Patients learn adaptive self-efficacy beliefs |
## Strength of evidence of treatments for anxiety and related disorders in children and adolescents

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Antidepressants</th>
<th>Benzodiazepines and other treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCD</td>
<td>Fluoxetine, Clomipramine (Level 1)</td>
<td>Antipsychotics</td>
</tr>
<tr>
<td></td>
<td>Citalopram, sertraline (Level 2)</td>
<td>Adjunctive aripiprazole (Level 3)</td>
</tr>
<tr>
<td></td>
<td>Fluvoxamine, paroxetine (Level 2)</td>
<td>Other</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Riluzole (Level 4)</td>
</tr>
<tr>
<td>PD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAD</td>
<td>Fluoxetine (Level 1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluvoxamine, paroxetine (Level 2)</td>
<td>Alprazolam (Level 4)</td>
</tr>
<tr>
<td></td>
<td>Venlafaxine XR (Level 2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Escitalopram, sertraline (Level 3)</td>
<td></td>
</tr>
<tr>
<td>SAD</td>
<td>Fluoxetine, fluvoxamine (Level 2)</td>
<td>Alprazolam (Level 2, -ve)</td>
</tr>
<tr>
<td>GAD</td>
<td>Fluoxetine, Fluvoxamine (Level 2)</td>
<td>Anxiolytics</td>
</tr>
<tr>
<td></td>
<td>Sertraline (Level 2)</td>
<td>Clonazepam (Level 2, -ve)</td>
</tr>
<tr>
<td>School-</td>
<td>Citalopram (Level 4)</td>
<td>Anxiolytics</td>
</tr>
<tr>
<td>refusal</td>
<td></td>
<td></td>
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<td></td>
<td>Adjunctive imipramine (Level 2)</td>
<td>Alprazolam (Level 2, -ve)</td>
</tr>
<tr>
<td>PTSD</td>
<td>Sertraline (Level 2, -ve)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adjunctive sertraline (Level 2, -ve)</td>
<td></td>
</tr>
</tbody>
</table>
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

*Journal of Psychopharmacology* 2014, Vol. 28(5) 403–439

Abstract
This revision of the 2005 British Association for Psychopharmacology guidelines for the evidence-based pharmacological treatment of anxiety disorders provides an update on key steps in diagnosis and clinical management, including recognition, acute treatment, longer-term treatment, combination treatment, and further approaches for patients who have not responded to first-line interventions. A consensus meeting involving international experts in anxiety disorders reviewed the main subject areas and considered the strength of supporting evidence and its clinical implications. The guidelines are based on available evidence, were constructed after extensive feedback from participants, and are presented as recommendations to aid clinical decision-making in primary, secondary and tertiary medical care. They may also serve as a source of information for patients, their careers, and medicines management and formulary committees.
Table 1. Levels of evidence and strength of recommendations.

**Categories of evidence relevant to treatment**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I [M]</td>
<td>Evidence from meta-analysis of randomized double-blind placebo-controlled trials</td>
</tr>
<tr>
<td>I [PCT]</td>
<td>Evidence from at least one randomized double-blind placebo-controlled trial</td>
</tr>
<tr>
<td>II</td>
<td>Evidence from at least one randomized double-blind comparator-controlled trial (without placebo)</td>
</tr>
<tr>
<td>III</td>
<td>Evidence from non-experimental descriptive studies</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence from expert committee reports or opinions and/or clinical experience of respected authorities</td>
</tr>
</tbody>
</table>

**Categories of evidence relevant to observational findings and associations**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence from large representative population samples</td>
</tr>
<tr>
<td>II</td>
<td>Evidence from small, well designed but not necessarily representative samples</td>
</tr>
<tr>
<td>III</td>
<td>Evidence from non-representative surveys, case reports</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence from expert committee reports or opinions and/or clinical experience of respected authorities</td>
</tr>
</tbody>
</table>

**Strength of recommendations**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Directly based on category I evidence (either I [M] or I [PCT])</td>
</tr>
<tr>
<td>B</td>
<td>Directly based on category II evidence or an extrapolated recommendation from category I evidence</td>
</tr>
<tr>
<td>C</td>
<td>Directly based on category III evidence or an extrapolated recommendation from category I or II evidence</td>
</tr>
<tr>
<td>D</td>
<td>Directly based on category IV evidence or an extrapolated recommendation from other categories</td>
</tr>
<tr>
<td>S</td>
<td>Standard of clinical care</td>
</tr>
</tbody>
</table>

Useful guidelines provide extensive recommendations, including diagnosis, treatment (pharmacology and psychotherapy) and a good review of special populations.
Generalized Anxiety Disorder
GAD: DSM-5 Diagnostic Criteria (Unchanged)

- Excessive, pervasive, difficult-to-control, more days than not, anxiety/worry about a variety of situations ≥ 6 months

- **At least 3 of:** (one in children)
  - Restless/edgy feeling
  - Fatigue
  - Sleep disturbance
  - Problems concentrating
  - Irritability
  - Muscle tension

- Anxiety or physical symptoms cause **clinically significant distress or functional impairment**

Epidemiology of GAD

- Mean age of onset: late, although often life long worriers
- Only one-half of patients ever seek treatment (usually more than 10 years after onset of symptoms)
- Of those seeking treatment up to 50% are not diagnosed (masked by somatic symptoms +/- comorbidity)
- 2:1 women:men
- > 90% comorbidity
Making the Diagnosis- GAD

- Do your family members or others close to you consider you to be a worry wart?
- How long have you been a worrier?
- Do you worry about “every little thing”, so much so that you feel your worry is out of control?
- When you try to get to sleep, do you find your brain won’t “turn off”?
- Do you worry about worry?
- Are you afraid to stop worrying?
## Recommendations for pharmacotherapy for GAD

<table>
<thead>
<tr>
<th>Level</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line</strong></td>
<td>Agomelatine, duloxetine, escitalopram, paroxetine, paroxetine CR, pregabalin, sertraline, venlafaxine XR</td>
</tr>
<tr>
<td><strong>Second-line</strong></td>
<td>Alprazolam*, bromazepam*, bupropion XL*, buspirone, diazepam*, hydroxyzine, imipramine, lorazepam*, quetiapine XR*, vortioxetine</td>
</tr>
<tr>
<td><strong>Third-line</strong></td>
<td>Citalopram, divalproex chrono, fluoxetine, mirtazapine, trazodone</td>
</tr>
<tr>
<td><strong>Adjunctive therapy</strong></td>
<td>Second-line: pregabalin</td>
</tr>
<tr>
<td></td>
<td>Third-line: aripiprazole, olanzapine, quetiapine, quetiapine XR, risperidone</td>
</tr>
<tr>
<td></td>
<td>Not recommended: ziprasidone</td>
</tr>
<tr>
<td><strong>Not recommended</strong></td>
<td>Beta blockers (propranolol), pexacerfont, tiagabine</td>
</tr>
</tbody>
</table>

CR = controlled release; XL = extended release; XR=extended release. *Note: These have distinct mechanisms, efficacy and safety profiles. Within these second-line agents, benzodiazepines would be considered first in most cases, except where there is a risk of substance abuse, while bupropion XL would likely be reserved for later. Quetiapine XR remains a good choice in terms of efficacy, but given the metabolic concerns associated with atypical antipsychotic, it should be reserved for patients who cannot be provided antidepressants or benzodiazepines. Please refer to text for further rationale for the recommendations.

GAD Acute Treatment

● Choose an evidence-based acute treatment [A]
  ○ pharmacological: most SSRIs (citalopram, escitalopram, paroxetine, sertraline), duloxetine, venlafaxine, pregabalin, agomelatine, quetiapine, some benzodiazepines (alprazolam, diazepam, lorazepam), imipramine, buspirone, hydroxyzine and trazodone [A]
  ○ psychological: cognitive-behaviour therapy, applied relaxation [A]

● Consider an SSRI for first-line pharmacological treatment [A]

● SNRIs and pregabalin may be considered as alternative initial treatments if SSRIs are judged to be unsuitable [A]

● Remember that higher daily doses of pregabalin may be associated with greater response rates [A]

● Advise the patient that treatment periods of up to 12 weeks may be needed to assess efficacy [S] but recognize that an absence of clinical benefit within four weeks warns that a response to unchanged treatment is unlikely [A]

GAD Longer-term treatment

● Continue drug treatment for up to 18 more months in patients who have responded to treatment [A]

● Use a treatment approach that is known to be efficacious in preventing relapse [S]

● Recommend CBT over other forms of psychological treatment as it may reduce relapse rates better than other psychological treatments [C]

● Monitor effectiveness and acceptability regularly over the course of treatment [S]

● When stopping treatment, reduce the dose gradually over an extended period to avoid discontinuation and rebound symptoms [A]: in the absence of evidence a minimum of three months is recommended for this taper period [D]

Combination of drugs and psychological treatment

● Routinely combining drug and psychological approaches is not recommended for initial treatment [A]
GAD When initial treatments fail

- Consider raising the dosage of pregabalin if the current dosage is well tolerated [A]
- Consider switching to another evidence-based treatment [D]
- Consider combining evidence-based treatments only when there are no contraindications [S]
- Consider pregabalin augmentation after a non-response to initial SSRI or SNRI treatment [A]
- Consider use of benzodiazepines after a non-response to SSRI, SNRI, pregabalin and buspirone treatment [S]
- Consider combining drug treatment and cognitive behaviour therapy [D]
- Consider referral to regional or national specialist services in treatment refractory patients [S]
Question

Regarding social anxiety disorder (SAD), which of the following is not correct?

1. Using a public bathroom is impossible for some people with SAD.
2. Benzodiazepines have evidence for safety and efficacy in the treatment of SAD.
3. A diagnosis of SAD includes avoidance of social situations, or enduring them with distress.
4. Like specific phobia, medications are not generally effective for the treatment of social phobia.
Social Anxiety Disorder: DSM-5 Diagnostic Criteria

• Marked fear of performance or social interaction situations

• Excessive fear of scrutiny or negative evaluation

• Fear of acting in a way (or showing anxiety symptoms) that will be humiliating or embarrassing

• Results in avoidance or endurance with distress

Social Anxiety Disorder

- Lifetime prevalence 13%¹
- Most common anxiety disorder¹
- Third most common psychiatric disorder¹
- High comorbidity²

SAD: Early Onset

- Typically in adolescence (age 11-15 years)$^{1-3}$
- Onset possible in early childhood$^2$
- Earlier onset = more chronic debilitating course$^3$
- Low probability of remission without intervention$^{4,5}$
- Mean episode duration before diagnosis is 20 years$^6$

Making the Diagnosis- SAD

• Are you nervous being around people you don’t know well?
• Are you uncomfortable being the centre of attention?
• To what extent does your discomfort effect your life?
• Do you feel you’ve lost out as a result of your discomfort?
**Recommendations for pharmacotherapy for SAD**

<table>
<thead>
<tr>
<th>First-line</th>
<th>Escitalopram, fluvoxamine, fluvoxamine CR, paroxetine, paroxetine CR, pregabalin, sertraline, venlafaxine XR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second-line</strong></td>
<td>Alprazolam, bromazepam, citalopram, clonazepam, gabapentin, phenelzine</td>
</tr>
<tr>
<td><strong>Third-line</strong></td>
<td>Atomoxetine, bupropion SR, clomipramine, divalproex, duloxetine, fluoxetine, mirtazapine, moclobemide, olanzapine, selegiline, tiagabine, topiramate</td>
</tr>
</tbody>
</table>
| **Adjunctive therapy** | **Third-line:** aripiprazole, buspirone, paroxetine, risperidone  
**Not recommended:** clonazepam, pindolol |
| **Not recommended** | Atenolol*, buspirone, imipramine, levetiracetam, propranolol*, quetiapine |

CR = controlled release; SR = sustained release; XR = extended release.*Beta-blockers have been successfully used in clinical practice for performance situations such as public speaking. Note: although there is limited evidence for citalopram in SAD, it is likely as effective as the other SSRIs, in contrast there are negative trials of fluoxetine in SAD suggesting it may be less effective than other SSRIs.
SAD Acute treatment

- **pharmacological**: most SSRIs (escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline), venlafaxine, phenelzine, moclobemide, some benzodiazepines (bromazepam, clonazepam) and anticonvulsants (gabapentin, pregabalin), and olanzapine

- **psychological**: cognitive-behaviour therapy

- Avoid prescribing atenolol or buspirone [A]
- Consider an SSRI for first-line pharmacological treatment [A]
- Routine prescription of higher doses of SSRIs is not recommended [A], but individual patients may benefit from higher doses [D]
- Advise the patient that treatment periods of up to 12 weeks may be needed to assess efficacy [A]
SAD Longer-term treatment

- Use an approach that is known to be efficacious in preventing relapse [S]
- Continue drug treatment for at least six months in patients who have responded to treatment [A]
- Consider cognitive therapy with exposure as this may reduce relapse rates better than drug treatment [A]
- Consider cognitive therapy after response to drug treatment, in patients with a high risk of relapse [D]
- Monitor effectiveness and acceptability regularly over the course of treatment [S]

Combination of drugs and psychological treatment

- Routinely combining drug and psychological approaches is not recommended for initial treatment in the absence of consistent evidence for enhanced efficacy over each treatment when given alone [A]
Panic Disorder
Panic Attack “Specifier”

A discrete period of fear or discomfort, in which at least four of the following symptoms developed abruptly and reached a peak within 10 minutes

<table>
<thead>
<tr>
<th>Physical</th>
<th>Psychological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Racing or pounding heart</td>
<td>Feeling unreal (derealization) or detached</td>
</tr>
<tr>
<td>Sweating</td>
<td>(depersonalization)</td>
</tr>
<tr>
<td>Trembling or shaking</td>
<td>Fear of dying</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>Fear of going crazy or losing control</td>
</tr>
<tr>
<td>Feeling of choking</td>
<td></td>
</tr>
<tr>
<td>Chest pain or discomfort</td>
<td></td>
</tr>
<tr>
<td>Nausea or abdominal distress</td>
<td></td>
</tr>
<tr>
<td>Dizzy, unsteady or faint</td>
<td></td>
</tr>
<tr>
<td>Paresthesias (numbness or tingling sensation)</td>
<td></td>
</tr>
<tr>
<td>Chills or hot flushes</td>
<td></td>
</tr>
</tbody>
</table>

Panic Attacks ≠ Panic Disorder

Anyone can have a panic attack (30% without psychiatric disorder)

May occur in other mental disorders besides PD:
- Substance Induced Anxiety Disorder
- Anxiety Disorder due to General Medical Condition
- Major Depression/Bipolar Depression/Mixed
- Social Anxiety Disorder/OCD/Phobias/PTSD
- Borderline Personality Disorder
- Schizophrenia
- Medical disorders

DSM IV-TR, American Psychiatric Association, 2000
Panic Disorder: DSM-5 Diagnostic Criteria

- Recurrent unexpected panic attacks
- May occur abruptly from a relaxed state, or from an anxious state
- One or both of the following for at least 1 month:
  - Persistent concern about having another panic attack or worrying about the consequences of an attack (e.g., having a heart attack)
  - Significant maladaptive behaviour related to the attacks (agoraphobic avoidance)
- Not due to a substance or medical condition
- Not better accounted for by another mental disorder

DSM IV-TR, American Psychiatric Association, 2000
PD Comorbidity Issues

• 1/3 to 1/2 of individuals diagnosed with panic disorder also have agoraphobia

• Highly co-morbid with other anxiety disorders

• Among individuals diagnosed with panic disorder the prevalence of Major Depression is 50-60%

• For individuals with both panic disorder and depression:
  • The onset of depression precedes the onset of panic disorder in one-third of this population
  • The onset of depression coincides with or follows the onset of panic disorder in the remaining two-thirds

1 American Psychiatric Association, treatment Practice Guidelines (www.psych.org)
Making the Diagnosis- Panic

• Do you ever have episodes of anxiety that come on so suddenly you go from no anxiety to extremely high anxiety in a matter of minutes?
• Do these events always follow an upsetting or stressful situation or do they sometimes occur out of the blue?
• As a result of these episodes, have you changed your normal routines or activities?
## Recommendations for pharmacotherapy for panic disorder

<table>
<thead>
<tr>
<th>Category</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line</strong></td>
<td>Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, paroxetine CR, sertraline, venlafaxine XR</td>
</tr>
<tr>
<td><strong>Second-line</strong></td>
<td>Alprazolam, clomipramine, clonazepam, diazepam, imipramine, lorazepam, mirtazapine, reboxetine</td>
</tr>
<tr>
<td><strong>Third-line</strong></td>
<td>Bupropion SR, divalproex, duloxetine, gabapentin, levetiracetam, milnacipran, moclobemide, olanzapine, phenelzine, quetiapine, risperidone, tranylcy promine</td>
</tr>
<tr>
<td><strong>Adjunctive therapy</strong></td>
<td><strong>Second-line</strong>: alprazolam ODT, clonazepam <strong>Third-line</strong>: aripiprazole, divalproex, olanzapine, pindolol, risperidone</td>
</tr>
<tr>
<td><strong>Not recommended</strong></td>
<td>Buspirone, propranolol, tiagabine, trazodone</td>
</tr>
</tbody>
</table>

CR = controlled release; ODT = orally disintegrating tablets; SR = sustained release; XR = extended release.

Panic Disorder: Acute treatment

○ **pharmacological**: all SSRIs, some TCAs (clomipramine, desipramine, imipramine, lofepramine), venlafaxine, reboxetine, some benzodiazepines (alprazolam, clonazepam, diazepam, lorazepam), some anticonvulsants (gabapentin, sodium valproate) [A]

○ **psychological**: cognitive–behaviour therapy [A]

- Avoid prescribing propranolol, buspirone and bupropion [A]
- Consider an SSRI for first-line pharmacological treatment [S]
- Consider increasing the dose if there is insufficient response, but remember that the evidence for a dose-response relationship with SSRIs and venlafaxine is inconsistent [A]
- Initial side effects can be minimized by slowly increasing the dose or by adding a benzodiazepine for a few weeks [D]
- Advise the patient that treatment periods of up to 12 weeks may be needed to assess efficacy [A]
Panic Disorder Longer-term treatment

- Continue drug treatment for at least six months in patients who have responded to treatment [A]
- Use an approach that is known to be efficacious in preventing relapse [S]
- Monitor effectiveness and acceptability regularly over the course of treatment [S]
- When stopping treatment, reduce the dose gradually over an extended period to avoid discontinuation and rebound symptoms [A]
- In the absence of evidence a minimum of three months is recommended for this taper period [D]
Panic Disorder Combination of drugs and psychological treatment

- Consider combining cognitive therapy with antidepressants as this has greater efficacy and may reduce relapse rates better than drug treatment alone [A]
- Consider combining cognitive therapy with benzodiazepines (being mindful of potential long-term problems) as this probably has greater efficacy than drug treatment alone [A]

When initial treatments fail

- Consider raising the dosage if the current dosage is well tolerated [A]
- Consider switching to another evidence-based treatment [D]
- Consider combining evidence-based treatments only when there are no contraindications [S]
- Consider combining evidence-based pharmacological and psychological treatments [A]
- Consider referral to regional or national specialist services in treatment refractory patients [S]

Question

Which of the following is true of OCD?

1. Compulsive behaviours are a necessary part of the DSM diagnosis, but obsessions are not.
2. Obsessive thoughts occur repeatedly, but they are not generally unusual or strange thoughts.
3. Compulsions may be performed to prevent a negative outcome.
4. People with OCD rarely recognize their compulsive behaviour is excessive and/or inappropriate, because it is necessary to reduce their anxiety.
5. Most patients with OCD don’t have good insight.
Obsessive Compulsive Disorder
Figure 1

Normal conditions

Frontal neocortex
OFC  ACC

Thalamus

Striatum

From cortical regions

OCD

Frontal neocortex
OFC  ACC

Thalamus

Striatum

From cortical regions

Hypothetical dysfunctional corticostriatal circuitry in OCD. In normal conditions (top), the excitatory corticostriatal projections modulate striatal activity through a balance between excitation and inhibition. Medium spiny neurons (MSNs) are maintained under tonic inhibition by a network of parvalbumin (PV)-positive interneurons (and possibly other interneuron’s not shown here), with the PV interneurons tightly interconnected through gap-junctions. In pathological OCD conditions (bottom), both cortical and striatal regions are hyperactive, possibly due to a decrease in the number and/or function of striatal PV interneurons that could lead to enhancement of MSN excitation by corticostriatal inputs and eventually to an increased activity throughout the affected corticostriatal loops.

Current Opinion in Neurobiology 2015, 30:59–65
OCD DSM-5

Obsessions
- Recurrent and persistent thoughts, urges, images
- Inappropriate, intrusive, unwanted, cause marked anxiety or distress
- Not simply excessive worry
- Attempts are made to ignore, suppress, or neutralize by a thought or action

Compulsions
- Repetitive behaviours or mental acts driven to perform
- Behaviors designed to reduce distress or some dreaded event
OCD: Natural history

- Early onset, chronic, waxing and waning course.
- 2 year follow up after treatment (n = 65) (Rasmussen and Eisen 1991)
  - 50% partial remission
  - 48% of these relapsed
  - 12% complete remission
- 47 year follow up (n = 144) (Skoog and Skoog 1999)
  - Complete recovery 20%
  - Recovery with continued subclinical symptoms 28%
  - Continued OCD but clear improvement 35%
  - No improvement 17%
Making the Diagnosis- OCD

• Do you have thoughts that repulse you or cause you great distress; thoughts you can’t seem to get out of your head?
• Are these thoughts frightening; do they involve harming yourself or others?
• Do you have any rituals or activities you must follow? What happens if you don’t do the activity?
• Do you have any mental games or repetitive thoughts that you must continue to think about?
Question

Which is not an effective medication strategy for treatment-resistant OCD?

1. The addition of clonazepam to the antidepressant
2. IV clomipramine
3. A trial of an MAOI
4. A switch from a SSRI to an SNRI or mirtazapine
5. Add an atypical antipsychotics as adjunctive treatment
# Recommendations for pharmacotherapy for OCD

<table>
<thead>
<tr>
<th>First-line</th>
<th>Escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Second-line</td>
<td>Citalopram, clomipramine, mirtazapine, venlafaxine XR</td>
</tr>
<tr>
<td>Third-line</td>
<td>IV citalopram, IV clomipramine, duloxetine, phenelzine, tramadol, tranylcypromine</td>
</tr>
<tr>
<td>Adjunctive therapy&lt;br&gt;First-line</td>
<td>aripiprazole, risperidone</td>
</tr>
<tr>
<td>Second-line</td>
<td>memantine, quetiapine, topiramate</td>
</tr>
<tr>
<td>Third-line</td>
<td>amisulpride, celecoxib, citalopram, granisetron, haloperidol, IV ketamine, mirtazapine, N-acetylcysteine, olanzapine, ondansetron, pindolol, pregabalin, riluzole, ziprasidone</td>
</tr>
<tr>
<td>Not recommended</td>
<td>buspirone, clonazepam, lithium, morphine</td>
</tr>
<tr>
<td>Not recommended</td>
<td>Clonazepam, clonidine, desipramine</td>
</tr>
</tbody>
</table>
OCD Acute treatment

- **pharmacological**: clomipramine and all SSRIs [A]
  - **psychological**: exposure therapy, cognitive-behaviour therapy, cognitive therapy [A]

- Drug and psychological approaches have broadly similar efficacy in acute treatment
- Consider an SSRI for first-line pharmacological treatment [D]
- Consider increasing the daily dosage of SSRIs if there is insufficient response at lower dosage [A]
- Advise the patient that initial treatment periods beyond 12 weeks may be needed to assess efficacy [A]
OCD Longer-term treatment

● Use an approach that is known to be efficacious in preventing relapse [S]
● Continue drug treatment for at least 12 months in patients who have responded to treatment [A]
● Monitor effectiveness and acceptability regularly over the course of treatment [S]

Combination of drugs with psychological treatments

● Consider combining an SSRI or clomipramine with an evidence-based psychological treatment when efficacy needs to be maximized [D]
OCD When initial treatments fail

- Consider raising the dosage if the current dosage is well tolerated [A]
- Consider switching to another evidence-based treatment [D]
- Consider combining evidence-based treatments only when there are no contraindications [S]
- Consider combining evidence-based pharmacological and psychological treatments [A]
- Consider augmentation of an SSRI or clomipramine with an antipsychotic drug [A]
- Consider augmentation of an SSRI or clomipramine with a 5-HT3 antagonist [A]
- Consider augmentation of an SSRI with topiramate [A] or lamotrigine [A]
- Consider augmentation of an SSRI with morphine [A]
- Consider augmentation of an SSRI with riluzole [C]
- Consider referral to regional or national specialist obsessive-compulsive disorder services in treatment refractory patients [S]
Treatment Resistant OCD: Review

- 9 RCTs including haloperidol, risperidone, quetiapine, olanzapine for 4 – 16 weeks
- \( N = 278 \)
- Responders overall
  - Antipsychotic augmentation 32%
  - Placebo augmentation 11%
  - NNT 4.5 (95% CI 3.2 to 7.7)

Psychological treatment of OCD: Exposure and response prevention

• **Functional assessment**
  - Obsessional ideas, thoughts, impulses
  - External triggers
  - Rituals and avoidances
  - Anticipated harmful consequences of not performing ritual

• **Exposure and response prevention**
  - 16 sessions, twice weekly, 20 to 120 minutes, over 8 weeks
  - Observed exposure in session
  - Homework for self-exposure
  - Actual vs imaginal exposure
Psychological treatments versus treatment-as-usual (TAU) for OCD

• Meta-analyses compared cognitive and/or behavioural treatments versus TAU control groups.

• Patients receiving any variant of CBT exhibited significantly fewer symptoms post-treatment than those receiving TAU (SMD -1.24, 95% CI -1.61 to -0.87, I² test for heterogeneity 33.4%).

• Different types of cognitive and/or behavioural treatments showed similar differences in effect when compared with TAU.

• The overall treatment effect appeared to be influenced by differences in baseline severity.

Gava I, Cochrane Database of Systematic Reviews 2007, Issue 2.
All psychological treatments versus TAU in OCD

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Psychol treatments</th>
<th>Treatment as usual</th>
<th>Std. Mean Difference IV,Random,95% CI</th>
<th>Weight</th>
<th>Std. Mean Difference IV,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cordioli 2003</td>
<td>22 15.1 (7.8)</td>
<td>23 23.2 (5.5)</td>
<td>-</td>
<td>16.1 %</td>
<td>-1.18 [-1.82, -0.55]</td>
</tr>
<tr>
<td>Freeston 1997</td>
<td>12 12.2 (9.6)</td>
<td>14 22 (6)</td>
<td>-</td>
<td>11.7 %</td>
<td>-1.21 [-2.06, -0.36]</td>
</tr>
<tr>
<td>Jones 1998</td>
<td>10 4.14 (7.45)</td>
<td>9 17.7 (5.27)</td>
<td>-</td>
<td>7.7 %</td>
<td>-1.99 [-3.13, -0.84]</td>
</tr>
<tr>
<td>McLean 2001a</td>
<td>19 16.89 (5.64)</td>
<td>13 21.85 (5.67)</td>
<td>-</td>
<td>13.8 %</td>
<td>-0.86 [-1.60, -0.12]</td>
</tr>
<tr>
<td>McLean 2001b</td>
<td>16 12.56 (7.3)</td>
<td>20 22.8 (5.42)</td>
<td>-</td>
<td>13.3 %</td>
<td>-1.58 [-2.35, -0.82]</td>
</tr>
<tr>
<td>O'Connor 1997</td>
<td>6 13.3 (8.6)</td>
<td>5 17.5 (4)</td>
<td>-</td>
<td>7.0 %</td>
<td>-0.55 [-1.77, 0.67]</td>
</tr>
<tr>
<td>Van Balkom 1998a</td>
<td>13 21.5 (10.4)</td>
<td>7 26.4 (6.8)</td>
<td>-</td>
<td>10.3 %</td>
<td>-0.50 [-1.44, 0.43]</td>
</tr>
<tr>
<td>Van Balkom 1998b</td>
<td>16 18.6 (8.5)</td>
<td>7 26.4 (6.8)</td>
<td>-</td>
<td>10.3 %</td>
<td>-0.93 [-1.87, 0.00]</td>
</tr>
<tr>
<td>Vogel 2004a</td>
<td>10 13.6 (6.6)</td>
<td>6 25.2 (3.5)</td>
<td>-</td>
<td>6.6 %</td>
<td>-1.93 [-3.20, -0.66]</td>
</tr>
<tr>
<td>Vogel 2004b</td>
<td>7 10.1 (4.6)</td>
<td>6 25.2 (3.5)</td>
<td>-</td>
<td>3.3 %</td>
<td>-3.40 [-5.30, -1.49]</td>
</tr>
</tbody>
</table>

Total (95% CI) 131 110 100.0 % -1.24 [-1.61, -0.87]

Heterogeneity: Tau² = 0.11; Chi² = 13.51, df = 9 (P = 0.14); P = 33%
Test for overall effect: Z = 6.62 (P < 0.00001)

Psychological treatments versus treatment as usual for obsessive compulsive disorder (OCD), Gava I et al. Cochrane Review, 2009, DOI: 10.1002/14651858.CD005333.pub2,
## CBT versus TAU in OCD

**Review:** Psychological treatments versus treatment as usual for obsessive compulsive disorder (OCD)
**Comparison:** Cognitive behaviour therapy versus Treatment as usual
**Outcome:** Obsessive compulsive symptoms

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Psychol treatments</th>
<th>Treatment as usual</th>
<th>Mean Difference IV,Fixed,95% CI</th>
<th>Weight</th>
<th>Mean Difference IV,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cordioli 2003</td>
<td>22</td>
<td>23</td>
<td>-8.10 [-12.06, -4.14]</td>
<td>30.5%</td>
<td></td>
</tr>
<tr>
<td>Freeston 1997</td>
<td>12</td>
<td>14</td>
<td>-9.80 [-16.08, -3.52]</td>
<td>12.1%</td>
<td></td>
</tr>
<tr>
<td>McLean 2001a</td>
<td>19</td>
<td>13</td>
<td>-4.96 [-8.95, -0.97]</td>
<td>30.0%</td>
<td></td>
</tr>
<tr>
<td>O'Connor 1997</td>
<td>6</td>
<td>5</td>
<td>-4.20 [-11.92, 3.52]</td>
<td>8.0%</td>
<td></td>
</tr>
<tr>
<td>Vogel 2004a</td>
<td>10</td>
<td>6</td>
<td>-11.60 [-16.56, -6.64]</td>
<td>19.4%</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI)**

Heterogeneity: Chi^2 = 5.45, df = 4 (P = 0.24); I^2 = 27%
Test for overall effect: Z = 6.94 (P < 0.00001)
Test for subgroup differences: Not applicable

---

Psychological treatments versus treatment as usual for obsessive compulsive disorder (OCD), Gava I et al. Cochrane Review, 2009, DOI: 10.1002/14651858.CD005333.pub2
Cognitive/Behavioural treatments versus TAU

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment Mean(SD)</th>
<th>Control Mean(SD)</th>
<th>Std. Mean Difference IV,Fixed,95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones 1998</td>
<td>4.14 (5.45)</td>
<td>1.7 (3.27)</td>
<td>-1.99 [-3.13, -0.84]</td>
<td>47.4%</td>
</tr>
<tr>
<td>Van Balkom 1998a</td>
<td>21.5 (0.4)</td>
<td>2.4 (0.6)</td>
<td>-3.50 [-4.44, 0.43]</td>
<td>53.6%</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>23</strong></td>
<td><strong>16</strong></td>
<td><strong>-1.21 [-2.66, 0.25]</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Review: Psychological treatments versus treatment as usual for obsessive compulsive disorder (OCD)

Outcome: 1. Obsessive compulsive symptoms

No difference individual Vs group; 6 to 14 sessions vs 14+ sessions  Gava et all 2009
FIGURE 2. Yale-Brown Obsessive Compulsive Scale (Y-BOCS) Scores of Patients With Obsessive-Compulsive Disorder in a 12-Week Randomized, Placebo-Controlled Trial Comparing the Effects of Treatment With Exposure and Ritual Prevention, Clomipramine, and Their Combination.

N = 122

*Linear mixed-effects model analyses.*

Foa E et al Am J Psychiatry 162:1, January 2005
Clinical Practice: OCD

- Trial of at least 2 separate SSRI/SNRIs in full dose
- Augmentation with atypical antipsychotic
- Trial of clomipramine in full dose
- Trial of expert CBT using ERP (exposure with response prevention) for 16+ sessions
- Increase intensity of CBT, include in-patient stay
- Augment with anticonvulsants or use MAOI
- Assess suitability for psychosurgery/DBS
Post traumatic Stress Disorder
PTSD DSM-IV Criteria

- Witnessed, or was confronted with an event or events that involved **actual or threatened death or serious injury**, or a threat to the physical integrity of self or others

- The person’s response involved **intense fear, helplessness, or horror**.
DSM-5 Changes

• Outlines specific situations that might lead to PTSD
  • Direct experience
  • Witness something happening to another
  • Learning trauma happened to someone close to you
  • Repeated, extreme exposure to details of trauma (first responders)
  • Does not include exposure over internet, TV, movies unless work related

• Some changes in the criteria
  • Negative alterations in cognitions and mood associated with traumatic event
  • Dissociative symptom specifier: Depersonalization, derealization
  • PTSD Criteria for children 6 and under
Acute stress and PTSD

Definition of trauma in both disorders:
• Response involves intense fear, helplessness or horror.
• Intrusive memories, negative mood, dissociative symptoms, avoidance and arousal symptoms
• Clinically significant distress and impairment
• Acute: Duration is 3 days to 1 month after trauma

70% of population experience at least one traumatic event meeting criterion A1.
Trauma Exposure and Lifetime Prevalence of PTSD in NCS (n=5877, aged 15-54, DSM-III-R)

Kessler et al, Arch Gen Psychiatry 1995
Prevalence of Trauma and PTSD

Violent assault carries the highest risk of developing PTSD

Kessler et al, Arch Gen Psychiatry 1995
PTSD Risk Factors

• **Pre-trauma**
  - Female, personal and family psychiatric history, low SES or educational level, previous trauma and child abuse, cultural factors

• **Peri-trauma**
  - Personal, protracted, violent/ risk of death, sexual/ degrading, dissociation

• **Post-trauma**
  - Lack of social support, shame / guilt / self-doubt, ongoing life stressors, lack of appropriate early treatment or access to services, recovery-related secondary stressors like stigma/ re-traumatization

Yehuda et al, Biol Psychiatry 1998
Brewin et al, J Consult Clin Psychol 2000
Figure 1
Fear structure and conditioned fear-cued associations after the 9/11 World Trade Center attacks.
Making the Diagnosis- PTSD

• Have you experienced, at any time during your life, physical, sexual or emotional abuse?
• Have you had any distressing events occur during your life that you don’t seem to be able to get over?
• Do you feel like you are reliving the event frequently, through vivid memories or dreams?
• Do you tend to avoid situations or places that remind you of the event?
• Are you jumpy or irritable, or is your sleep poor, particularly if you are reminded of the event?
PTSD Pearls

• PTSD is an abnormal response to a traumatic event- most common response to trauma is acute distress and recovery
• Many have previous/multiple trauma
• Personal, protracted, violent or sexual trauma is most likely to cause PTSD
• PTSD is not the only MH outcome associated with trauma
• Trauma is subjective
Evidence-Based Treatment of Post-Traumatic Stress Disorder

JoAnn Difede, Megan Olden, and Judith Cukor
Department of Psychiatry, Weill Cornell Medical College, New York, New York 10065


Despite multiple studies documenting the lack of efficacy of a variety of agents used to treat PTSD, patterns of prescription persist. In light of the ongoing controversy regarding the evidence base for pharmacotherapy, and in the absence of strong evidence that medications offer a cure for PTSD, perhaps the most useful conceptualization of medication is as a means to offer symptom relief and improve daily functioning and quality of life.
Pharmacotherapy for PTSD

- 35 short-term (14 weeks or less) RCTs (N = 4597).
  - 17 trials Medication >> PBO (WMD -5.76, 95% CI -8.16 to -3.36, N = 2507)
  - 13 trials responder status superior with medication Vs PBO (RR 1.49, 95% CI 1.28 to 1.73, NNT = 4.85, 95% CI 3.85 to 6.25, N = 1272).
- Medication response 59.1% Vs PBO response 38.5%
- SSRIs best evidence of treatment efficacy
- Medication > PBO for severity of PTSD symptom clusters, comorbid depression and disability
- 3 maintenance trials suggested long term medication may be required.

Stein DJ Cochrane Database of Systematic Reviews 2006, Issue 1.
## Recommendations for pharmacotherapy for core symptoms of PTSD

<table>
<thead>
<tr>
<th>First-line</th>
<th>Fluoxetine, paroxetine, sertraline, venlafaxine XR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second-line</strong></td>
<td>Fluvoxamine, mirtazapine, phenelzine</td>
</tr>
<tr>
<td><strong>Third-line</strong></td>
<td>Amitriptyline, aripiprazole, bupropion SR, buspirone, carbamazepine, desipramine, duloxetine, escitalopram, imipramine, lamotrigine, memantine, moclobemide, quetiapine, reboxetine, risperidone, tianeptine, topiramate, trazodone</td>
</tr>
</tbody>
</table>

### Adjunctive therapy

<table>
<thead>
<tr>
<th>Second-line:</th>
<th>eszopiclone, olanzapine, risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Third-line:</td>
<td>aripiprazole, clonidine, gabapentin, levetiracetam, pregabaline, quetiapine, reboxetine, tiagabine</td>
</tr>
</tbody>
</table>

**Not recommended:** bupropion SR, guanfacine, topiramate, zolpidem

| **Not recommended** | Alprazolam, citalopram, clonazepam, desipramine, divalproex, olanzapine, tiagabine |

SR = sustained release; XR = extended release. 
PTSD Prevention of post-traumatic symptoms

● After major trauma, discuss the potential for preventing the emergence of post-traumatic symptoms, and providing there are no contra-indications, consider preventive treatment with propranolol or sertraline [A] or trauma-focused CBT [A]
● Do not recommend routine single-session or multiple session ‘debriefing’ [A]

PTSD Acute treatment of chronic post-traumatic stress disorder

○ pharmacological: paroxetine, sertraline, venlafaxine [A]
○ psychological: trauma-focused individual CBT or EMDR [A]
● Consider an SSRI for first-line pharmacological treatment[A]
● Advise the patient that treatment periods of up to 12 weeks may be needed to assess efficacy [A].
PTSD Longer-term treatment

- Use an approach that is known to be efficacious in preventing relapse [S]
- Continue drug treatment for at least 12 months in patients who have responded to treatment [A]
- Monitor effectiveness and acceptability regularly over the course of treatment [S]

PTSD Combination of drugs with psychological treatment

- Routinely combining drug and psychological approaches is not recommended for initial treatment in the absence of consistent evidence for enhanced efficacy over each treatment when given alone [A]: but paroxetine may enhance the effectiveness of exposure therapy [A]
PTSD When initial treatments fail

- Consider raising the dosage if the current dosage is well tolerated [D]
- Consider switching to another evidence-based treatment [D]
- Consider combining evidence-based treatments only when there are no contraindications [S]
- Consider combining evidence-based pharmacological and psychological treatments [A]
- Consider augmentation of antidepressants with olanzapine [A] risperidone [A] or prazosin [A]
- Consider referral to regional or national specialist services in treatment refractory patients [S]
Psychotherapy PTSD: CBT based

- **Exposure therapy**
  - Repeated intentional recall of traumatic memories
  - In vivo exposure to situations, objects
  - Relaxation, controlled breathing, information

- **Anxiety management therapies**
  - Stress inoculation training

- **Cognitive therapies**
  - Identification of trauma related exaggerated or inaccurate beliefs leading to challenging the thoughts

- **Eye movement desensitization and reprocessing**
  - Exposure to trauma related thoughts and feelings accompanied by oscillating eye movements, tapping etc
AUTHOR'S CONCLUSIONS:

• 1. Psychological treatment can reduce traumatic stress symptoms in individuals with PTSD.
• 2. Trauma focused CBT and EMDR have the best evidence for efficacy at present and should be made available to PTSD sufferers.

Stress management and group TFCBT were also useful and non-trauma-focused therapy did not work (psychodynamic, hypnosis, mindfulness)
Combined pharmacotherapy and psychological therapies for PTSD (Review)

4 trials were eligible for inclusion (N = 24)

• 100% SSRI plus prolonged exposure or CBT
• 2 trials combination vs pharmacological treatment
• 2 trials combination vs psychological treatment.

• No differences between combined interventions vs psychological therapy (mean difference 2.44, 95% CI -2.87, 7.35 one study, n = 65) or pharmacotherapy (mean difference -4.70, 95% CI -10.84 to 1.44; one study, n = 25).

• No significant differences between combination and single intervention groups in the other two studies. There were very little data reported for other outcomes, and in no case were significant differences reported.

Hetrick SE et al, Cochrane Database of Systematic Reviews 2010, Issue 7
Question

The following are true about acute trauma debriefing:

1. Benzodiazepines are helpful before debrief sessions.
2. A single-session debriefing is preferable to multiple sessions of psychotherapy after an acute trauma.
3. A wait and see approach is preferable to psychological interventions after an acute traumatic event
4. Medications should not be used to help cope with acute trauma
5. Distraction is not preferable to a supportive discussion with a caring healthcare professional after a severe emotional trauma
### Psychological debriefing in trauma

Review: Psychological debriefing for preventing post traumatic stress disorder (PTSD)
Comparison: 1 Debriefing versus Control
Outcome: 1 PTSD diagnosis - ITT data

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Debriefing n/N</th>
<th>Control n/N</th>
<th>Peto Odds Ratio Peto,Fixed,95% CI</th>
<th>Weight</th>
<th>Peto Odds Ratio Peto,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Up to 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conlon 1999</td>
<td>2/18</td>
<td>4/22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>18</strong></td>
<td><strong>22</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events: 2 (Debriefing), 4 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.62 (P = 0.54)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 3-6 months</td>
<td></td>
<td></td>
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<tr>
<td>Conlon 1999</td>
<td>0/18</td>
<td>3/22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rose 1999</td>
<td>18/54</td>
<td>17/51</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Bisson 1997</td>
<td>32/77</td>
<td>17/56</td>
<td></td>
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</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>149</strong></td>
<td><strong>129</strong></td>
<td></td>
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<tr>
<td>Total events: 50 (Debriefing), 37 (Control)</td>
<td></td>
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<tr>
<td>Heterogeneity: Chi² = 3.36, df = 2 (P = 0.14); I² =49%</td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 0.61 (P = 0.54)</td>
<td></td>
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<tr>
<td>3 6-12 months</td>
<td></td>
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</tr>
<tr>
<td>Rose 1999</td>
<td>10/54</td>
<td>10/51</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>54</strong></td>
<td><strong>51</strong></td>
<td></td>
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<tr>
<td>Total events: 10 (Debriefing), 10 (Control)</td>
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<tr>
<td>Heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 0.14 (P = 0.89)</td>
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<tr>
<td>4 12 months or more</td>
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<tr>
<td>Bisson 1997</td>
<td>26/77</td>
<td>14/56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>77</strong></td>
<td><strong>56</strong></td>
<td></td>
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<tr>
<td>Total events: 36 (Debriefing), 14 (Control)</td>
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<tr>
<td>Heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 2.55 (P = 0.011)</td>
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<tr>
<td>Test for subgroup differences: Chi² = 4.70, df = 3 (P = 0.20); I² =38%</td>
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</table>

**Analysis 1.1.** Comparison 1 Debriefing versus Control, Outcome 1 PTSD diagnosis - ITT data.
Psychological debriefing in trauma

Authors’ conclusions:
…no evidence that single session….debriefing is a useful treatment for the prevention of PTSD after traumatic incidents.
- Compulsory debriefing of victims of trauma should cease.
- A more appropriate response could involve a ’screen and treat’ model

Rose SC et al 2009 Cochrane reviews
Stress De-Briefing

Victims should not indiscriminately attend debriefing programs

• Interferes with avoidance that is part of the natural processing of a traumatic event
• May act as a form of re-exposure without sufficient time for habituation (as seen in therapy)
• May lead victim to bypass usual supports
• Risk of story telling in a hyper-adrenergic state

McNally, Briant 2003; Rose, Bisson 2003; VanEmmerick et al 2002
What About benzodiazepines and anxiety?
Benzodiazepines

Advantages
• Alleviate anxiety symptoms
• Rapid onset
• Cheap

Disadvantages
• Not recommended for long-term use?
• Can exacerbate depression?
• Can cause psychomotor/cognitive impairment
• May develop tolerance?
• Potential for abuse

ROLE OF BENZODIAZEPINES IN THE TREATMENT
OF ANXIETY DISORDERS IN 2014
Stéphanie de Mesmaeker, Nicolas Zdanowicz, Christine Reynaert & Denis Jacques
Université Catholique de Louvain, Psychosomatics Unit, Mont-Godinne University Hospital, 5530 Yvoir, Belgium

SUMMARY

Background: This article aims at determining the place of benzodiazepines in the current treatment of anxiety disorders in opposition to antidepressants, neuroleptics and anticonvulsants. Belgium and France are the only two European countries which prescribe the most benzodiazepines despite the dissuasion of the international guidelines (NICE) issued in the nineties concerning the high risk of dependance of these molecules. What about the respect of these guidelines and the use of benzodiazepines in general practice in 2014?

Methods: Review of the literature with the following key words «anxiety disorder, benzodiazepines, anxiolytic, treatment» in the international database of PubMed, Medline, PsycINFO, PsycARTICLES and consulting of various reference books.

Results: No class of molecules could measure up to benzodiazepines until now, neither from the point of view of efficiency, nor from the point of view of cost-efficiency. This is why the guidelines (NICE) discourage the few available alternatives in the general practice. International figures from Belgium and France show a continuous increase in the use of benzodiazepines in the treatment of anxiety disorders, even after the nineties. Given the fact that benzodiazepines differ from one another at the level of their action profile (graphical representation in “stars”) and are therefore able to relieve several symptoms simultaneously, these molecules still respond nowadays to many expectations of the clinical practitioners.

Conclusions: The divergence between the guidelines and the practice confirm the irreplaceability of benzodiazepines at the present time. Nevertheless, the expectation of new molecules with fewer side effects should be investigated in further research.
Results:
According to the systematic review, no consistent evidence emerged supporting the advantage of using TCA over BDZ in treating generalized anxiety disorder (GAD), complex phobias and mixed anxiety-depressive disorders. Indeed, BDZ showed fewer treatment withdrawals and adverse events than AD. In panic disorder with and without agoraphobia our meta-analysis found BDZ treatments more effective in reducing the number of panic attacks than TCA (risk ratio, RR = 1.13; 95% CI = 1.01–1.27). Furthermore, BDZ medications were significantly better tolerated than TCA drugs, causing less discontinuation (RR = 0.40; 95% CI = 0.20–0.57) and side effects (RR = 0.41; 95% CI = 0.34–0.50). As to newer AD, BDZ trials resulted in comparable or greater improvements and fewer adverse events in patients suffering from GAD or panic disorder. Conclusions: The change in the prescribing pattern favoring newer AD over BDZ in the treatment of anxiety disorders has occurred without supporting evidence. Indeed, the role and usefulness of BDZ need to be reappraised.
What About Benzodiazepines and anxiety?

• **A bandage**
  useful and compassionate in those experiencing severe anxiety, requiring sedative effects, or for akathisia during antipsychotic crossover.

• **Safe**: Overdoses are almost never fatal unless occurring in combination with other sedative agents such as alcohol or opiates.¹

• **Low addiction potential**: BZDs as a primary substance of abuse in people admitted for addiction treatment make up less than 1% of all admissions.²


Starting the pharmacological treatment

• Start low, go slow, aim for remission
• Anxiety disorders may require higher doses and longer time to response/ remission
• Anxiety patients tend to be highly sensitive to side effects; tendency to somatize
• Psychoeducation imperative-
  • A brain illness
  • Chronic condition
  • The first 3-4 weeks are greatest challenge
Information Sources

www.anxietycanada.ca

www.adaa.org

www.anxietybc.com

www.anxietytreatment.ca

www.ocfoundation.org

www.anxietydisordersontario.ca

www.adam.mb.ca

www.ataq.org (L'Association / Troubles Anxieux du Québec)

www.socialphobia.ca

www.martinantony.com
Good Luck!!!