**Highlights**

1. **Psychotropics**
   - Hypersexuality
   - Anticholinergic

2. Guidelines/Reviews
   - CCCTD
   - Pt/Caregiver
   - RxFiles

3. Other Reviews
   - Cognitive Impairment

4. Pt/Caregiver Resources
   - First Link Program

5. RxFiles Related
   - Anticholinergic Drug List
   - Antipsychotic Chart
   - BSDP Tx Chart
   - CATIE-AD Trial Summary
   - Hypersexuality Tx Chart
   - Psychotropics Newsletter

6. Background Issues
   - Behavioural and psychological symptoms of dementia (BPSD) create a significant caregiver challenge. Key symptoms include aggression, agitation, psychosis and mood disorders.

<table>
<thead>
<tr>
<th>Table 1: Common BSDP Neuropsychiatric Symptoms</th>
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<tbody>
<tr>
<td><strong>Symptoms</strong></td>
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<tr>
<td>- agitation*</td>
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<tr>
<td>- apathy</td>
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<tr>
<td>- aggression, verbal/physical</td>
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<tr>
<td>- calling out, screaming</td>
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<tr>
<td>- hostility</td>
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<tr>
<td>- sexual disinhibition</td>
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| *Symptoms with some evidence for benefit of antipsychotics |

<table>
<thead>
<tr>
<th>Table 2: Common BSDP Psychosocial Factors</th>
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<tbody>
<tr>
<td><strong>Psychosocial</strong></td>
</tr>
<tr>
<td>Distress</td>
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<tr>
<td>Fear of danger</td>
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<tr>
<td>Misinterpretation</td>
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<tr>
<th>Table 3: Risks of Various Psychotropic Meds</th>
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<tbody>
<tr>
<td><strong>Risks</strong></td>
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<tr>
<td>- Benzodiazepines: falls, fractures, confusion</td>
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<tr>
<td>- Carbenzamazine: falls, many DIs &amp; side effects</td>
</tr>
<tr>
<td>- Antidepressants: ↓sodium, falls, osteoporosis</td>
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<tr>
<td>- Opioids: delirium; constipation, fractures, ?CV</td>
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</table>

**What do we know about the benefits and risks of psychotropic meds in BPSD?**

- Evidence for psychotropic use is limited and all classes have limited efficacy and serious adverse event (SAE) concerns. (See Table 3)

**Where do Antipsychotics (APs) Fit?**

| **AP effectiveness** in BSDP is modest & their role is limited due to SAEs. |
| **SAEs** with APs include stroke (OR: 1.3-3.2), seizures, EPS effects, ↓ falls, drowsiness, cognitive decline, pneumonia & death. |

- ADL: reduced mortality by ~25% in 2 years in long-term follow-up to the DART-AD RCT. [n=165, age ~85; Alzheimer’s patients] for >3 months & SPS; 2 arms: stop AP & switch to placebo vs AP use x12months; no significant difference in survival at 12 months; survival at 2yrs: 71% vs 46%; NNT=4 (2yrs; survival over 2-4.5yrs: 54% vs 38%, NNT=8; CI: 5-42)

**Stopping long-term antipsychotics** reduced mortality by ~25% at 2 years in long-term follow-up to the DART-AD RCT. [n=165, age ~85; Alzheimer’s patients] for >3 months & SPS; 2 arms: stop AP & switch to placebo vs AP use x12months; no significant difference in survival at 12 months; survival at 2yrs: 71% vs 46%; NNT=4 (2yrs; survival over 2-4.5yrs: 54% vs 38%, NNT=8; CI: 5-42)

- **BPSD outcomes**: no statistical difference except verbal fluency better in patients who stopped at 6 mos. There may have been individual differences (e.g. in the more severe).

- **Remember**, if antipsychotic use is restricted, alternative drugs could be just as harmful!

Avoid the use of psychotropic meds for BPSD if at all possible. When needed, assess for tolerability in ≤3-7 days & reassess for possible taper and/or discontinuation every 3 months.
**Table 4: Select Non-drug Treatment Tips**

- **Allow behaviours** that are not dangerous
  - Ok to wander within limits; delusions can be ok
  - Institute a patient centered or relaxed schedule that allows flexibility for the preferential routines of each patient:
    - e.g. medication times, meals, bathing, sleep times, activities
  - Assess daytime naps: limit/avoid in most, but may be ok to allow aggressive patient to sleep while others are awake
  - Make time for regular exercise to reduce restlessness; refer to daytime programs if available
  - Encourage daily activities to minimize sun-downing (e.g. playing cards, gardening)
- **Make a positive environment** that avoids triggering factors:
  - aromatherapy
  - play music suitable to the individual
  - reduce noise or number of persons in room
  - remove keys from view if no longer driving
  - distract person with snack or activity
  - if wandering, ensure house/room etc. is safe, put buzzers on doors, provide light, 
  - fall risk
  - provide clock & calendar if confused regarding time & date
  - if inappropriate sexual behaviour, consider room placement changes to minimize interactions of concern
- **Minimize unnecessary & problem drugs.** Tools to review include the Beer’s list 29,30,31,32, or the START / STOPP Criteria. 29,30,31,32
- **Difficulty swallowing** can cause severe agitation. If drug necessary, look for better formulations (e.g. dissolvable tablets)
  - As disease advances to the end of life, face becomes more important than care, rather than curative/preventative
  - Review meds with consideration for stopping statins, vitamins, herbs, bisphosphonates
  - Review BP & blood sugar goals; too low can lead to falls
  - Only do lab work when necessary
  - Providing access to false teeth, hearing aids & glasses may reduce agitation in some patients, the opposite may be true if patient is sound sensitive, or if these aids are considered bothersome by the patient (esp. hearing aid)

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**Sleep Insomnia & Dementia**

- **Sleep patterns naturally change as you get older.** Older adults:
  - Sleep fewer hours & take longer to fall asleep
  - Sleep less deeply & wake up more often during the night
  - Have more trouble adjusting to changes in sleeping conditions, such as a new bed
  - Have changes in their sleep cycle → Older adults spend less time in the most restful stage of sleep
  - Sleep disturbance in Alzheimer’s Disease (AD) is very common; nocturnal sleep disturbance in AD patients is often accompanied by increased daytime napping, frequently in direct association with the extent of dementia
  - An after dinner walk may help in promoting nighttime sleep
  - In the later stages of AD, patients may spend ~40% of their time in bed awake and a significant proportion of day-time hours asleep. This ↑day-time sleep consists almost exclusively of stage 1 & 2 sleep; it does not replace or compensate for the night-time loss of slow-wave sleep (SWS) or REM sleep
  - Cholinesterase inhibitors can cause insomnia (and nightmares) 3
  - The presentations of abnormal nocturnal behavior in AD often exceed the limits of what might otherwise be termed insomnia in a nondemented geriatric population 7
  - Behavioural intervention should be tried before pharmacological interventions whenever possible
  - Limit drug tx to short term/intermittent use whenever possible

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**Agents sometimes used for insomnia, and their limitations**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Limitations</th>
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<tbody>
<tr>
<td><strong>Melatonin</strong></td>
<td><img src="https://via.placeholder.com/150" alt="Image" /> <a href="https://www.something.com">Link</a></td>
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<tr>
<td><strong>Trazodone</strong></td>
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<tr>
<td><strong>Zopiclone</strong></td>
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<tr>
<td><strong>Zolpidem</strong></td>
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<tr>
<td><strong>Quetiapine</strong></td>
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<tr>
<td><strong>Methotrimeprazine</strong></td>
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Reference List of Drugs with Anticholinergic Effects – February 2012 1, 2, 3, 4
WHENEVER POSSIBLE, AVOID DRUGS WITH HIGH ANTICHOLINERGIC ACTIVITY IN THE ELDERLY

**Antidepressants**
- amitriptyline
- clomipramine
- desipramine
- doxepin
- imipramine
- nortriptyline
- SSRIs
  - citalopram
  - escitalopram
  - fluoxetine
  - fluvoxamine
  - paroxetine
  - sertraline
- trimipramine

**Antipsychotics**
- aripiprazole
- chlorpromazine
- clozapine
- fluphenazine
- haloperidol
- loxapine
- methotrimeprazine
- olanzapine
- paliperidone
- perphenazine
- pimozide
- pipotiazine
- quetiapine
- risperidone
- thioproperazine
- thiothixene
- trifluoperazine
- zuclopenthixol

**Antimuscarinics**
- darifenac
- flavoxate
- oxybutynin
- tolterodine
- trospium

**Antispasmodics**
- dicyclomine
- glycopyrrolate
- hyoscine butylbromide

**Antiseizure Drugs**
- carbamazepine
- divalproex
- oxcarbazepine
- valproic acid

**Antibiotics**
- ampicillin
- cefoxitin
- clindamycin
- gentamicin
- piperacillin
- vancomycin

**Antihistamines/Antipruritics**
- brompheniramine
- chlorpheniramine
- cyproheptadine
- dimenhydrinate
- diphenhydramine
- hydroxyzine
- pyrilamine
- trimeprazine

**Cardiovascular Agents**
- atenolol
- captopril
- chlorthalidone
- digoxin
- diuretics
- diospyramide
- furosemide
- hydralazine
- isosorbide
- metoprolol
- nifedipine
- quinidine
- triamterene

**Gastrointestinal Agents**
- belladonna
- chlorzoxazone/clidinium
- cimetidine
- dicyclomine
- diphenoxylate/atropine
- famotidine
- loperamide
- metoclopramide
- nizatidine
- prochlorperazine
- ranitidine

**Muscle Relaxants**
- baclofen
- cyclobenzaprine
- methocarbamol
- orphenadrine
- tizanidine

**Immunosuppressants**
- azathioprine
- cyclosporine

**Respiratory Meds**
- fluticasone/salmeterol
- theophylline

**Antihistamines/Antipruritics**
- brompheniramine
- chlorpheniramine
- cyproheptadine
- dimeshydrinate
- diphenhydramine
- hydroxyzine
- pyrilamine
- trimeprazine

**Preferred Alternatives**
- bisacodyl
- PPIs
- domperidone
- ranitidine

**Miscellaneous**
- colchicine
- dipyridamole
- ketotifen ophthalmic
- lithium

**Moderate/High anticholinergic activity**
- X: Denotes agents with anticholinergic activity that may be better tolerated than others. Whenever possible, anticholinergic drugs should be avoided, & the preferred agents used.
- = Unable to confirm anticholinergic activity
- = EDS (exception drug status) in Saskatchewan
- = non-formulary in Saskatchewan
- = prior approval NHB
- = not covered by NHB

**Preferred Alternatives**
- acetaminophen, NSAIDS (eg. ibuprofen, naproxen)

**Respiratory Meds**
- fluticasone/salmeterol
- theophylline
MANAGEMENT OF BEHAVIOURAL & PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)

**Background:** very common - 50% in dementia; a major cause of distress to pts/families/caregivers; harm to self & others; huge cost (e.g. institutionalization).

**Diagnosis:** (Evaluate behaviour → ABC's Antecedents (causes; Physical, Psychological, Emotional, Cultural, Environmental, genetic), Behaviours & Consequences,
→ Assess history, unique factors like Down's Sx; physical exam, cognitive tests, mental status exam; & nurse observations; collaborative family info essential!

**Lab Tests:** Recommend CBC, electrolytes, calcium, B12, glucose & TSH; Optional: BUN & Scr, ferritin, magnesium, LFTs, arterial blood gases, ECG, CT/MRI if suggestion of structural lesion. ng wrong use of the past tense or cases in which significant risk. Specify problem behaviour (e.g. "agitation" is less useful than "screaming!", "hitting when bathed"). Identify what brings it on & what makes it go away. Identify whom the behaviour is bothering (pt, caregiver/staff or other pts). Human interactions (e.g. activity, mood, emotionality & depression, depression assoc.

**Sexually Inappropriate Behaviour**

Consider Trazodone, Moclobemide, TCA's, SSRIs; trial at an adequate dose (May worsen apathy in some patients; irritability, agitation, emotionality & depression, depression assoc.

** ANXIETY**

- use non-pharmacological intervention - minimize provocation - consider antidepressant therapy if anxiety is secondary to depression or very chronic in nature

**ANTIANXIETY Medication**

- consider short term as needed
  - lorazepam 0.5-2mg/day
  - oxazepam 5-30mg/day
  - clonazepam 0.125-0.25mg/day

(Caution long-acting!)

**Benzodiazepines—caution!**

SE: sedation, ataxia, altered sleep architecture, motor & cognitive impairment & propensity to cause withdrawal Sx when D/C. Paradoxical excitation, disinhibition & falls may occur. An intermediate acting such as temazepam/oxazepam/lorazepam can be best used for short term, if possible sleep/ anxiety states or before planned anxiety provoking situations (eg, bathing, dental work)

**Trazodone**: 12-50mg/day considered option by some 50-100mg po hs

Buspirone: 5-10mg/day; ↓ sedation, ↓ DI's, ↓ withdrawal & ↓ impairment of motor fx; option – chronic anxiety but delayed onset ~3wk

**APATHY**

Tx with external activity & environmental measures. Possible drug options (not without concerns): methylphenidate, dopamine agonists or cholinesterase inhibitors.

**Cholinesterase Inhibitors (ChEIs)**

-moderate cognitive, functional & behavioural benefit; may help apathy, hallucinations & delusions & post-hoc analyses; unlikely to help agitation & aggression - not better than placebo for agitation. Howard 07; may help Lewy Body dementia

Consider cholinesterase inhibitors in Alzheimer's (donepezil, galantamine, rivastigmine) & SE: nausea/vomiting, fatigue, anorexia, ↓ heart rate, urinary incontinence

Memantine** NMDA receptor antagonist, may help agitation, aggression, disinhibition, sleep disturbances, delusions & psychosis.

**Anticonvulsants**

- carbamazepine 100-600mg/day; 400mg/day in BPSD, SE: sedation, ataxia, falls, rash, headache, leukopenia & ↑ liver tests & DI's. Good for impulsivity or for brain injury.

- topiramate 25-300mg/day; cognitive difficulties; may improve cognitive function, agitation, depression & psychosis.

- other agents gabapentin, lamotrigine, levetiracetam benefit unknown – concerns re: worsening existing behaviour gabapentin-worsening agitation if Lewy Body dementia

**BETA BLOCKER**

-propranolol 10-80mg/day; possible ↓ agitation but does not improve Sx; ↓ heart rate & hypotension Caution: asthma, PVD & possibly depression Hx.

**MAJOR DEPRESSION**

↓ mood, apathy, amotivation

Moderate to severe → **ANTIDEPRESSANT Tx**

- use non-pharmacological intervention - minimize provocation - consider antidepressant therapy if anxiety is secondary to depression or very chronic in nature

**SSRIs**: venlafaxine, mirtazapine, duloxetine, moclobemide, bupropion. See also RxFiles Charts book pg 104-5.

In general → may be good for depression, depression assoc. agitation, emotionality & irritability. (May worsen apathy in some patients)

Allow >6 week for adequate trial at an adequate dose

**SSRIs:**

- **nausea, vomiting, restlessness, falls, insomnia, ↓ weight, agitation**
- **methylphenidate, hypomania & bleeding**

**Citalopram**: 10-20mg/d, escitalopram 10-20mg/d, sertraline 25-100mg/d,

**Venlafaxine**: 75-225mg XR od; [Similar SE as SSRI, but high GI SE & may ↑ BP]; XR cap: can sprinkle on food.

**Bupropion**: 150-200mg bid or 50-150mg XR od to activate pt with withdrawal or psychomotor retardation

**TCAs**: Avoid anticholinergics → less nortriptyline 10-75mg hs & desipramine 25-150mg/d;

**SE:** hypotension, blurred vision, urinary hesitancy, cardiac conduction changes

**Mirtazapine**: consider if anorexia/anxiety/sleep problem; RD rapid dose increase if diffiiculty swelling; ≤7.5-45mg/d

**Moclobemide**: role in anxiety & mood dx but may ↑ stimulation; 100mg od-300mg bid

**Trazodone**: low doses used for sedation & some anxiolytic effect;

- monitor for hypotension, serotonin syndrome & rare priapism in d

Consider ECT in management of treatment resistant or severe depression

**SEXUALLY INAPPROPRIATE BEHAVIOUR**

- assess for medical reason & any drug causes (e.g. testosterone, dopamine agonists).

Remove disinhibiting drugs including benzo's & alcohol.

**Behavioural interventions** (e.g. distraction, auditory prompt, non-punitive, antipsychotics, cholinesterase inhibitors). See also RxFiles Hypersensitivity Chart.

**Sleep Disturbance**

- assess for medical reason & Sumatriptan, melatonin, prolactin, melatonin; Options: behavioural, trazodone 50-100mg, zopiclone 5mg, ramelteon 3mg, 0.25mg, Limit to 3-4wk

**Pain**

- consider trial of acetaminophen ≤3.2g/day (e.g. 650mg po QID or long-acting 1300mg BID sulindac) to reduce agitation & pain

**CAPSYL** (Caution long-acting!)

- opiates if necessary in select individuals

**Cholinesterase Inhibitors (ChEIs)**

- modest cognitive, functional & behavioural benefit; may help apathy, hallucinations & delusions & post-hoc analyses; unlikely to help agitation & aggression - not better than placebo for agitation. Howard 07; may help Lewy Body dementia

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BP: blood pressure; CH: cardiovascular disease; D: disorder; f: function; HR: heart rate; Hx: history; N: nausea/vomiting; Pending PVD: peripheral vascular disease; SE: side effect; Sx: symptom

Tx: treatment; W: Exception Drug Status Sask. X: non-formulary in Sask. ⊗: not covered by NHIB; ▼: covered by NHIB; ♦: prior approval NHIB

Prepared by: Brent Jensen BSP