Antipsychotic Medications

Behavioural and psychological symptoms of dementia (BPSD) refer to the non-cognitive symptoms of disturbed perception, thought content, mood or behaviour that frequently occurs in patients with dementia.

**Approach to Managing BPSD**

1. Document the target symptoms
   - Describe the behaviour specifically
   - Use a tool like the Dementia Observation System (DOS)
2. Identify potential psychological and environmental triggers
3. Assess for medical causes (e.g. pain, infections, constipation, urinary retention, delirium)
4. Look for drug causes (e.g. anticholinergic effects)
5. Use non-pharmacological measures whenever possible
   - “Putting the P.I.E.C.E.S.™ Together” represents Physical, Intellectual, Emotional, Capabilities, Environment and Social components (see page 3-4)
6. Identify if symptoms require treatment
7. Reassess need for antipsychotics after 3 months as behaviours stabilize
8. Caution with combination and prn use of antipsychotics

**Antipsychotic Medications**

- **First Generation (Typical) Antipsychotics**
  - Mechanism of action: High affinity for dopamine (D₂) receptors
  - Differ in potency, not effectiveness: High-potency: haloperidol, fluphenazine; Mid-potency: perphenazine, loxapine; Low-potency: chlorpromazine
- **Second Generation (Atypical) Antipsychotics**
  - Mechanism of action: Moderate affinity for dopamine (D₂) receptors and high affinity for serotonin (5-HT₂A) receptors
  - Examples: olanzapine, risperidone, quetiapine, aripiprazole

**Use of antipsychotics may be indicated for aggression, agitation or psychosis if the target behaviour:**

- Is persistent or recurrent and can cause harm or significant distress to the patient or others
- Has not adequately responded to non-pharmacological intervention
- Is not due to reversible or treatable causes

**Antipsychotics are NOT indicated for:**

- Wandering, vocalizations, hoarding, inappropriate urination/defecation, repetition, eating inedibles

**Adverse effects**

- Predicted by affinity for other receptors in the brain
- Extrapyramidal symptoms (EPS) - blockade of dopamine receptors
  - Parkinsonism
  - Tardive dyskinesia
- Anticholinergic effects - blockade of muscarinic, receptors
- Sedation - blockade of histamine, receptors
- Hypotension - blockade of alpha₁-adrenergic receptors

**If drug treatment required:**

- Tailor to the target symptom(s)
- Consider potential harms
- Start low, go slow
- Reassess in 3-7 days for beneficial and adverse effects
- Use short term where possible and try tapering the dose or stopping after 3 months

**Antipsychotic Side Effects Comparison**

<table>
<thead>
<tr>
<th>Drug Brand Name (daily dose range)</th>
<th>Aripiprazole Ability (20-10 mg)</th>
<th>Haloperidol Haldol (0.25-2 mg)</th>
<th>Olanzapine Zypraxa (2.5-7.5 mg)</th>
<th>Quetiapine Seroquel (12.5-150 mg)</th>
<th>Risperidone Risperdal (0.25-2 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Movement Side Effects¹</td>
<td>[]</td>
<td>[■]</td>
<td>[■]</td>
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<tr>
<td>Central Nervous System</td>
<td>[■]</td>
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<tr>
<td>Sedation</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
</tr>
<tr>
<td>Confusion, delirium, cognitive worsening</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
</tr>
<tr>
<td>Worsening psychotic symptoms</td>
<td>0</td>
<td>0</td>
<td>[■]</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cardiovascular/Metabolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthostatic hypertension</td>
<td>[■?]</td>
<td>[■]</td>
<td>[■]</td>
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</tr>
<tr>
<td>Edema</td>
<td>[■?]</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
</tr>
<tr>
<td>Weight gain/glucose ↑</td>
<td>0</td>
<td>[■?]</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
</tr>
<tr>
<td>Triglyceride ↑</td>
<td>0</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
</tr>
<tr>
<td>Urinary incontinence, UTI</td>
<td>[■]</td>
<td>[■]</td>
<td>[■]</td>
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<td>[■]</td>
</tr>
</tbody>
</table>

= more boxes indicates greater risk. Colors are darker with increasing risk.
= evidence poor in dementia, but evidence in other conditions indicates some risk
= no clear evidence that the drug causes this side effect in a clinically important way, or very rarely

¹ Movement side effects = parkinsonism, akathisia (restlessness), dystonia, tardive dyskinesia
EVIDENCE REVIEW & RECOMMENDATIONS FOR LTC

WRHA LONG TERM CARE PROGRAM

Antipsychotic Medications

Evidence

- Review: Use and Safety of Antipsychotics (modified from Gareri 2014)
  ◦ Key points:
    1. Treatment with antipsychotic drugs must be started at low dosages, with gradual increases on a case-by-case basis.
    2. Titrating dosages might decrease the possible adverse events.
    3. The effectiveness and tolerability of treatment have to be verified at least every 2 months.
    4. Treatment has to be changed whenever there is no reduction in frequency and/or severity in target symptoms.
    5. Wherever a sufficient control of behavioral symptoms has been obtained, a decrease in antipsychotic dosage is indicated to find the lowest effective dose.
    6. If behavioral disorders are mild to moderate, manage behaviour non-pharmacologically.
    7. When delusions and hallucinations are the main symptoms and when elderly patients do not have extrapyramidal signs, start haloperidol (0.5-1.5 mg/d).
    8. When aggression and agitation, associated or not with delusions and hallucinations, an atypical antipsychotic drug with should be prescribed. Risperidone is first line, unless parkinsonian symptoms are present. Then other antipsychotics can be considered (e.g. olanzapine, quetiapine).
    9. Other drugs might have the potentiality of effectiveness in BPSD, but at present there are only preliminary studies.

- Cochrane Review: Withdrawal versus continuation of antipsychotics (Declercq 2013)
  ◦ Objectives: Evaluate successful withdrawal of antipsychotic agents; list different strategies for withdrawal; measure the effects of withdrawal on behaviour
  ◦ No significant difference between people withdrawn from and those continuing on antipsychotics at 3 months
  ◦ “…planned discontinuation programmes of antipsychotics should be incorporated into routine clinical care of older people with dementia, also because of the risk of adverse effects and the marked increased in mortality in this vulnerable group when using antipsychotics long term.” “…most behavioural complications of dementia are intermittent and do not persist for longer than three months.”

- Population-based Cohort: Mortality Risk According to Antipsychotic Drug (Huybrechts 2012)
  ◦ In a large cohort of elderly patients in nursing homes, antipsychotic drugs conferred a dose related risk of death: compared with risperidone, haloperidol users had an increased risk and quetiapine users a decreased risk (see forest plot)
  ◦ The effects were strongest shortly after the start of treatment and remained after adjustment for dose

- Systematic Review and Meta-Analysis: Efficacy & Adverse Effects (Maher 2011)
  ◦ Efficacy—Treatment of behavioural symptoms in dementia
    - The pooled estimate of the effect size was small but statistically significant for aripiprazole, olanzapine and risperidone. The pooled estimate of effect for quetiapine was similar but was not statistically different than zero.
    - The effect size for atypical antipsychotic medications is on average a small improvement in global symptoms
  ◦ Adverse Events - Elderly patients with dementia
    - Death: atypical antipsychotics had higher mortality (pooled OR 1.54; 95% CI 1.06-2.23; NNH = 87)
    - Cardiovascular symptoms were significantly more common with olanzapine and risperidone
    - Stroke: risperidone was associated with an increased risk of stroke (pooled OR 3.12; 95% CI 1.32-8.21; NNH = 53)

- CATIE-AD: Clinical Antipsychotic Trials of Intervention Effectiveness - Alzheimer’s Disease (Schneider 2006)
  ◦ Double-blind, placebo-controlled trial of outpatients with Alzheimer’s disease and psychosis, aggression, or agitation on atypical antipsychotics (risperidone 1 mg/day, quetiapine, ~50mg/day, olanzapine ~5mg/day)
  ◦ No significant differences with regard to time to discontinuation of treatment for any reason among the atypical antipsychotics and placebo
  ◦ The median time to discontinuation of treatment due to a lack of efficacy favoured olanzapine (22.1 weeks) and risperidone (26.7 weeks) compared to quetiapine (9.1 weeks) and placebo (9 weeks) (p=0.002)
  ◦ The time to discontinuation due to adverse effects or intolerability favoured placebo. 80% stopped therapy by 36 weeks. Olanzapine (24%), risperidone (18%) quetiapine (16%), placebo (5%) (p=0.009)
EVIDENCE REVIEW & RECOMMENDATIONS FOR LTC

WRHA LONG TERM CARE PROGRAM

Antipsychotic Medications

Evidence cont’d...

- **DART-AD**: The dementia antipsychotic withdrawal trail (Ballard 2008, Ballard 2009)
  - Randomized, blinded trial to continue neuroleptic treatment for 12 months or switch to placebo.
  -Withdrawal of neuroleptics had no detrimental effect on functional and cognitive status.
  - During the extended 54-months of follow-up, continued antipsychotic treatment had significantly higher mortality compared with those on placebo (HR 0.58; 95% CI 0.35 to 0.95). The difference in mortality was more pronounced after the first year.
  - “…still an important but limited place for atypical antipsychotics in the treatment of severe neuropsychiatric manifestations of AD, particularly aggression. However, the accumulating safety concerns, including the substantial increase in long-term mortality, emphasise the urgent need to put an end to unnecessary and prolonged prescribing.”

- **Meta-Analysis: Hip Fractures** (Oderda 2012)
  - First and second-generation antipsychotics are associated with an increased risk of hip fracture in older adults
  - The summary odds ratio for risk of hip fracture with antipsychotic use (OR 1.45; 95% CI 1.28 to 1.64) was consistent with those of previous meta-analyses, supporting a modest increased risk of 50% for falls and fractures.

<table>
<thead>
<tr>
<th>All Antipsychotics</th>
<th>Atypical Antipsychotics</th>
<th>Conventional Antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR = 1.443</td>
<td>OR = 1.299</td>
<td>OR = 1.683</td>
</tr>
<tr>
<td>95% CI 1.276 to 1.632</td>
<td>95% CI 1.135 to 1.486</td>
<td>95% CI 1.426 to 1.987</td>
</tr>
<tr>
<td>p= 0.014</td>
<td>p= 0.548</td>
<td>p= 0.185</td>
</tr>
</tbody>
</table>

- **Health Canada Warnings** (Valiyeva 2008)
  - Summary of results from 13 placebo-controlled randomized trials of risperidone, quetiapine and olanzapine showing increased absolute risk of all-cause mortality with risperidone (0.9%), quetiapine (2.3%) and olanzapine (2%) among elderly patients with dementia
  - Causes: heart related events (e.g. heart failure, sudden death) or infections (e.g. pneumonia)
  - All atypical antipsychotics are approved for the treatment of schizophrenia, but only risperidone is approved for short term symptomatic management of inappropriate behaviour due to aggression and/or psychosis in patients with severe dementia.
  - Advice: treatment with atypical antipsychotic medications of behavioural disorders in elderly patients is associated with increased risk of all-cause mortality.

Recommendations:

- Target symptoms should be identified, quantified, documented and regularly reassessed.
- Non-pharmacological interventions, such as P.I.E.C.E.S.™ are effective and should be tried first.
- The decision to use an antipsychotic should be made only when other interventions have failed.
- Antipsychotics may be beneficial for use in the treatment of dangerous, distressing, disturbing, or damaging target behaviours (e.g. severe agitation, aggression, psychosis).
- Antipsychotics show modest benefits when used in short term, but evidence of long-term benefits is scarce.
- Benefit has not been shown for wandering, vocalizations, hoarding, inappropriate urination/defecation, repetition, eating inedibles.
- The serious risks of antipsychotics include: death, stroke, hip fracture and falls.
- Monitoring for adverse effects of antipsychotics such as, sedation, extrapyramidal effects (EPS), anticholinergic effects and hypotension should occur frequently.
- An informed discussion should take place with the Resident/family about the use of antipsychotic medications.
- There is no evidence to support using more than one antipsychotic at a time.
- The benefits of antipsychotics become limited when treatment continues beyond three month.
- Gradual dose reduction should be considered at least every 3 months.
- There is little evidence to suggest that other medications such as: hypnotics (e.g. benzodiazepines, zopiclone) or anticonvulsants, are safer or more effective than antipsychotics. They are also associated with their own risks and adverse effects. The overall goal is to manage behaviour without medication whenever possible.
EVIDENCE REVIEW & RECOMMENDATIONS FOR LTC

WRHA LONG TERM CARE PROGRAM

Antipsychotic Medications

References:

- LTC Medical Director Advisory Committee. Practice Guideline—Antipsychotic Medications for Behavior in Dementia.
- Rx Files Trial Summary. CATIE-AD: The Effectiveness of Atypical Antipsychotic Drugs in Patients with Alzheimer’s Disease (AD). Sep 2011.
P.I.E.C.E.S.™

P.I.E.C.E.S. - A practical, effective approach to change and continuous improvement.

P.I.E.C.E.S. is a best practice learning and development initiative that provides an approach to understanding and enhancing care for individuals with complex physical and cognitive/mental health needs and behaviour changes. P.I.E.C.E.S. enables a comprehensive, interdisciplinary approach and promotes continuous improved shared care practices through human resource development and changes in practice. The Person and Family are the centre-point of the TEAM.

Delirium! Think 4 M’s
1. Medicine: prescription, OCD, substance misuse
2. Microbiol
3. Metabolic
4. Myocardial/Respiratory and other Medical disorders

Causes of Delirium: I Watch Death
Infections
W Withdrawal
A Acute Metabolic
T Toxins, drugs
C CNS Pathology
H Hypoxia
D Deficiences
E Endocrine
A Acute Vascular
T Trauma
H Heavy Metals

Psychoses/Behavioural challenges monitor, observe, record 7 Ds.
1. Dangerous - dangerousness/how threatening
2. Distressing - how distressing to self
3. Disturbing - disturbing quality/disturbing to others
4. Direct Action - whether the resident is acting on them
5. Jeopardizing Independence or social interactions
6. Distant vs Present - occurring in the past or present
7. Definite (fixed) - full or partial insight; are they fixed vs. insight

The Do’s & Don’ts for Psychosis/Behaviour:
- Do ensure the persons and your safety
- Do understand this is a response to a “real” perception of the individual
- Do focus on the effects on the person not the content (i.e. validate)
- Do distract
- Don’t confront the false beliefs

Remember the delusions may not emerge until a period of time has elapsed – it may take time to “organize” the delusion

Signs of Depression, SIG: E CAPS
- Sleep disturbed
- Interest decreased
- Guilt feelings
- Energy lower
- Concentration poor
- Appetite disturbed
- Psychomotor retardation or agitation
- Suicidal ideation

DOS – Dementia Observation System
1. Helps determine the % of time over 24-hr cycle that the person displayed a behaviour(s) of concern; helps team determine if behaviour(s) have responded to interventions and/or side effects to medications
2. Replaces opinion with measurable data by establishing the:
   - occurrence of specific behaviours of interest
   - frequency with which target behaviours occur
   - duration the target behaviours are displayed
   - frequency with which the target behaviours of greatest risk are displayed, in comparison with those behaviours that should be accommodated

Guidelines for Selection and Monitoring the Use, Risk, and Benefits of Psychotropics
- Why is the psychotropic being used or considered?
- How do I select the right medication?
- How do I monitor the response and side effects?

High Risk Elderly Where Competency May Be an Issue
6 Key Areas for Assessment:
1. Clinical
2. Capacity
3. Values & Preferences of Individual
4. Legal & least restrictive legal option, alternatives
5. Influences on our decision-making
6. Plan and reassessment; with specific indicators/triggers when to review

The P.I.E.C.E.S. 3-Question Template

“A proven strategy for the Person and Family’s Team in collaboration and shared solution-finding”

The P.I.E.C.E.S. holistic approach to understanding the meaning behind a person’s behaviour comes from considering the person’s: Physical, Emotional, and Intellectual health, supportive strategies to maximize Capabilities, the individual’s social and physical Environment, and his/her Social self (cultural, spiritual, Life Story). P.I.E.C.E.S. provides a shared understanding of the often multiple causes and associated risks so that care planning recognizes areas of need & builds on the person’s remaining strengths. The person and family are the centre-point of every TEAM.

The 3-question template:
- Guides the systematic, comprehensive TEAM approach that helps make the best use of everyone’s energy and resources.
- Easily integrates into day-to-day individual and TEAM assessment process.
- Shapes TEAM conversation, both in-the-moment and more formal dialogue; asking questions prevents jumping to solutions too quickly.
- Produces the TEAM’s shared understanding of, and contribution to the care plan.
- Encourages individual and TEAM reflective thinking.

TEAM collaboration and shared solution-finding requires:
- Committing to the P.I.E.C.E.S. approach that places the person and family at the centre of every TEAM.
- Being present in conversations, validating all observations and concerns, and acknowledging unique contributions of TEAM members.
- Understanding the factors that support better performance (e.g. information, resources, incentives, knowledge and skills).
- Focusing efforts on the gap between current & better practices; seeks solutions that build staff capacity rather than laying blame.

Q. 1 What has changed?
Q. 2 What are the RISKS and possible causes?
Q. 3 What is the action?

<table>
<thead>
<tr>
<th>Question</th>
<th>TEAM Assessment Framework, Guidelines, and Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q. 1: What has changed?</td>
<td>Avoid assumptions! Always ask, what has changed?</td>
</tr>
<tr>
<td></td>
<td>- Determine if the problem/behaviour represents a change.</td>
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<td>- Is the problem/behaviour new? If so, in what way and when did the change emerge?</td>
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<td></td>
<td>- Did the problem/behaviour already exist? If so, is it worse or different, and when did the change emerge?</td>
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<td>- Is the problem/behaviour long-standing and unchanged? If so, what else could have changed, for example, caregiver stress?</td>
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<tr>
<td></td>
<td>Remember to think atypical! Atypical presentations are very common in older persons.</td>
</tr>
<tr>
<td>Q. 2: What are the RISKS and possible causes?</td>
<td>1. Identify the RISKS and avoid assumptions!</td>
</tr>
<tr>
<td></td>
<td>- Is there a risk? And if so for whom? Person, other individuals, staff, family, visitors</td>
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<tr>
<td></td>
<td>- What is the risk? Remember the types of risks by using the acronym RISKs:</td>
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<tr>
<td></td>
<td>- R Roaming (wandering)</td>
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<td></td>
<td>- I Imminent physical; risk of harm - frailty (e.g. delirium), falls, fire, firearms</td>
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<td></td>
<td>- S Suicide Ideation</td>
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<td></td>
<td>- K Kinship Relationships (risk of harm by the older person or to the older person by others that includes avoidance of the person)</td>
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<td></td>
<td>- S Self-neglect, safe driving, and substance abuse</td>
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<td></td>
<td>- What is the degree of risk? How imminent is the risk? Is the risk increasing?</td>
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<tr>
<td></td>
<td>- Remember! For any intervention, consider both the potential risks and potential benefits. Be vigilant and carefully observe and assess the individual’s capacity to understand.</td>
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<tr>
<td></td>
<td>2. Remember, consider atypical presentation! Use P.I.E.C.E.S. to identify possible causes:</td>
</tr>
<tr>
<td></td>
<td>- Physical 5 D’s: Delirium, Disease, Drugs, Discomfort, Disability</td>
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<tr>
<td></td>
<td>- Intellectual 7 A’s: Amnesia, Aphasia, Apathy, Agnosia, Apraxia, Anosognosia, Altered Perception</td>
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<td>- Emotional 4 D’s: Disorder Adjustment, Disorders of Mood, Delusional, Disorders of Personality</td>
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<td>- Capabilities ADL’s, IADL’s</td>
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<td>- Environment Consider: over/under stimulation, relocation, change in routine, noise, lighting, colours</td>
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<td></td>
<td>- Social Consider: social network, life story, cultural heritage</td>
</tr>
<tr>
<td></td>
<td>3. Remember, all behaviour has meaning! Use “P.I.E.C.E.S.” to help you remember!</td>
</tr>
<tr>
<td></td>
<td>Intervention: What therapeutic approach, both nonpharmacological and pharmacological, may best address the person’s needs? What other investigations need to be undertaken? Use P.I.E.C.E.S.!</td>
</tr>
<tr>
<td></td>
<td>Interaction: Using what has changed and understanding of causes for interaction at bedside.</td>
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<tr>
<td></td>
<td>Information: Think P.I.E.C.E.S! What information should be shared with other team members, family, if the person is moved or requires transfer? How is the information shared? What are RISKS Factors?</td>
</tr>
<tr>
<td></td>
<td>2. Promote dialogue and shared TEAM solution-finding.</td>
</tr>
</tbody>
</table>