Redux Dementia: Behavioural and Psychological Symptoms in Neurocognitive Disorders

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Learning Objectives

- List the indications for initiating pharmacological treatment for behavioural and psychological symptoms of dementia (BPSD), and know some algorithms for treating BPSD
- Outline the process for withdrawing pharmacological treatment for behavioural and psychological symptoms of dementia (BPSD), particularly antipsychotics
- Describe the major side effects of the major psychotropic classes of medications used to treat BPSD, including "black box" warnings

Disclosure for Dr. Chan

- **Relationships with commercial interests: None**
- **Including:**
  - **Grants/Research Support**
  - **Speakers Bureau/Honoraria**
  - **Consulting Fees**
  - **Investments or Shares**
  - There will be discussion of off-label uses of psychotropic medications

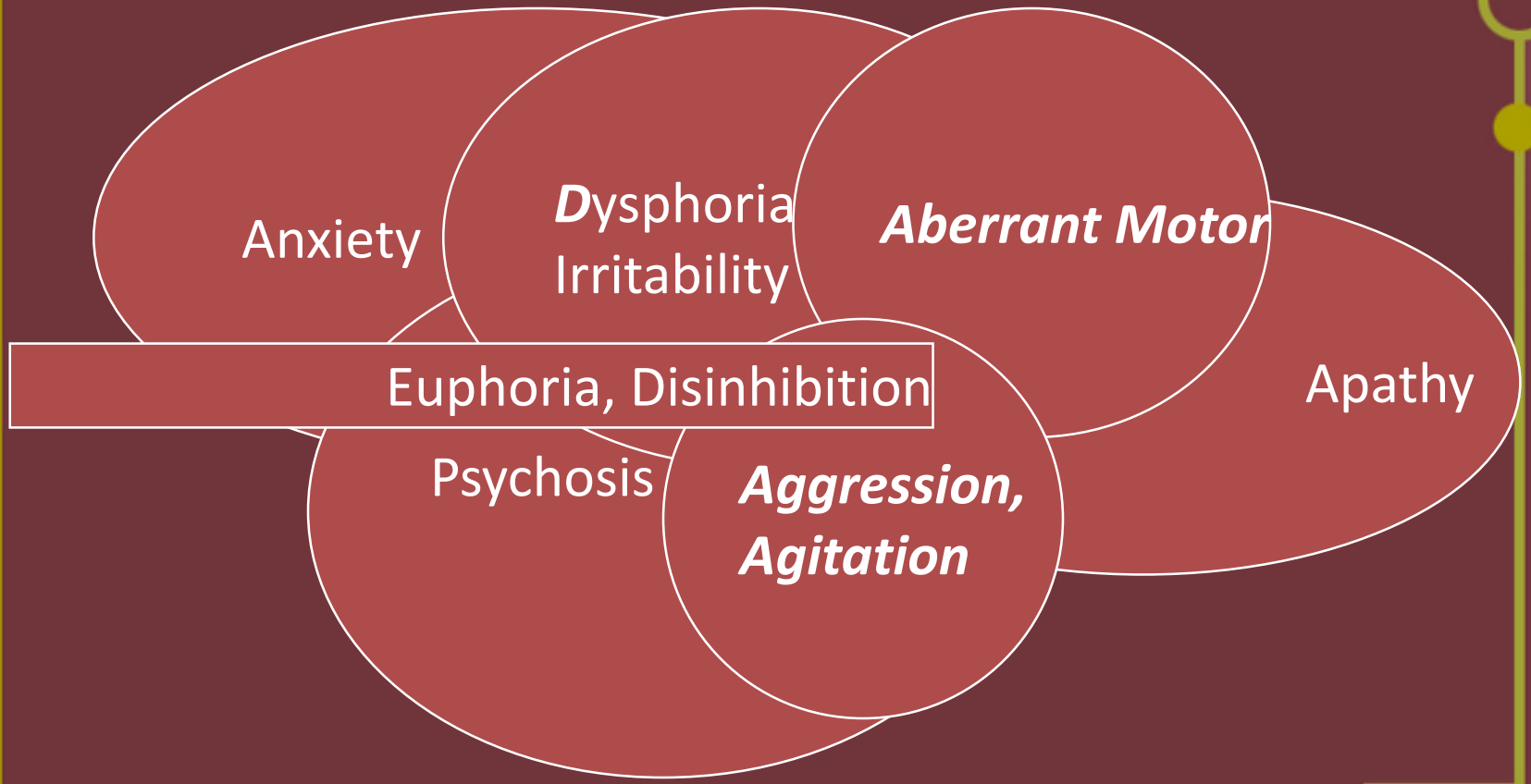
Mitigating Potential Bias

- Use of generic names for medications
- Review of various classes of pharmacological agents, and not focusing just a one class

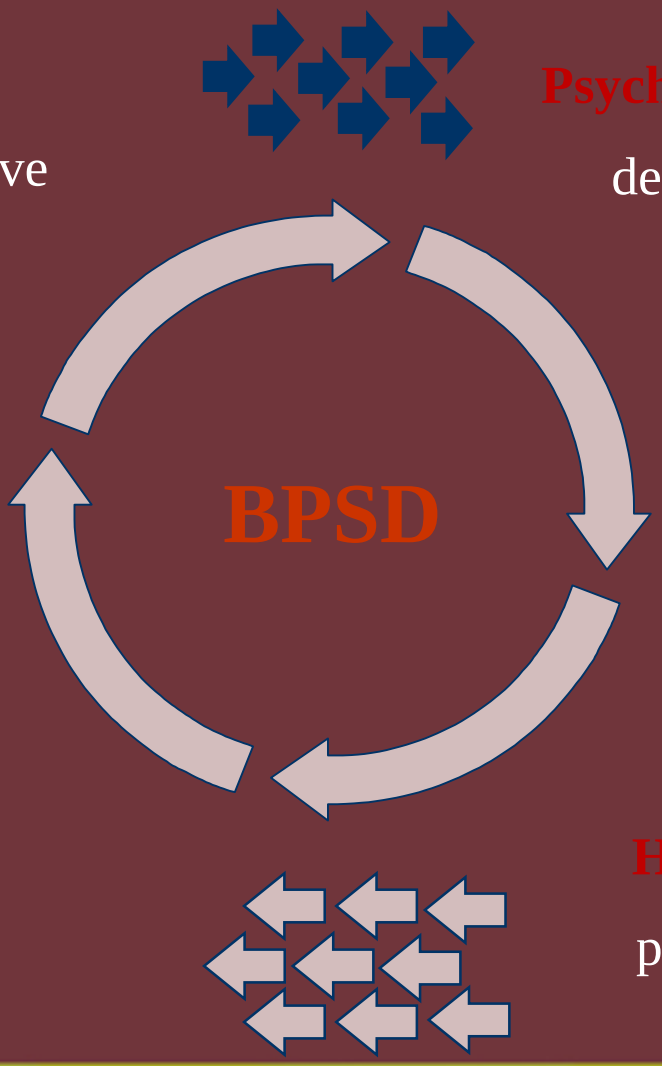
BPSD? NPS? BPSNCD??

- DSM 5:
  - “Major NeurocognitiveDisorder”=Dementia
  - “Minor Neurocognitive Disorder”=Mild Cognitive Impairment=MCI
- BPSD=NPS (Neuropsychiatric Symptoms)?
  - Multiple domains, may be concurrent and overlapping
  - Can occur at any stage of the disease

BPSD: Domains on NPI (Neuropsychiatric Inventory)



BPSD Clusters



Case #1

- 93 yo man, resides in extended care home. Advanced dementia, urinary incontinence. Generally seems pleasant to engage with some periods of calling out at times in the day. Poor historian. Strikes out during care, requiring multiple staff members to assist. Aggression led to staff injury so transported to hospital to rule out delirium…

Differential Diagnosis

- Delirium
  - Acute change, fluctuation. CAM to screen
- Major Depression
  - Difficult to diagnose in advanced dementia
- Pain (Flo et al. Drugs and Aging 2014)
  - Under-detected
  - Verbal vs. non-verbal cues

. . . 4 B's of discomfort in older adults with dementia. Harris , BMJ 2011

Bowels: when was the patient's last bowel movement

Bladder: when did they last urinate? Any urinary symptoms?

Beverage: are they hungry or thirsty? Have they been offered preferred beverages or food?

Bottom (to Top): Visual survey for obvious precipitants of distress and agitation

Treating Pain Husebo 2011, Husebo 2014

- Stepwise protocol for treatment of pain over 8 weeks in LTC residents with moderate-severe Dementia can:
  - Improve agitation
  - Improve mood
  - Improve apathy
  - Improve night-time behaviours
  - Improve appetite

  But NOT irritability or ADL's

Husebo's Stepwise Protocol

Stepwise protocol initiated if pain identified:

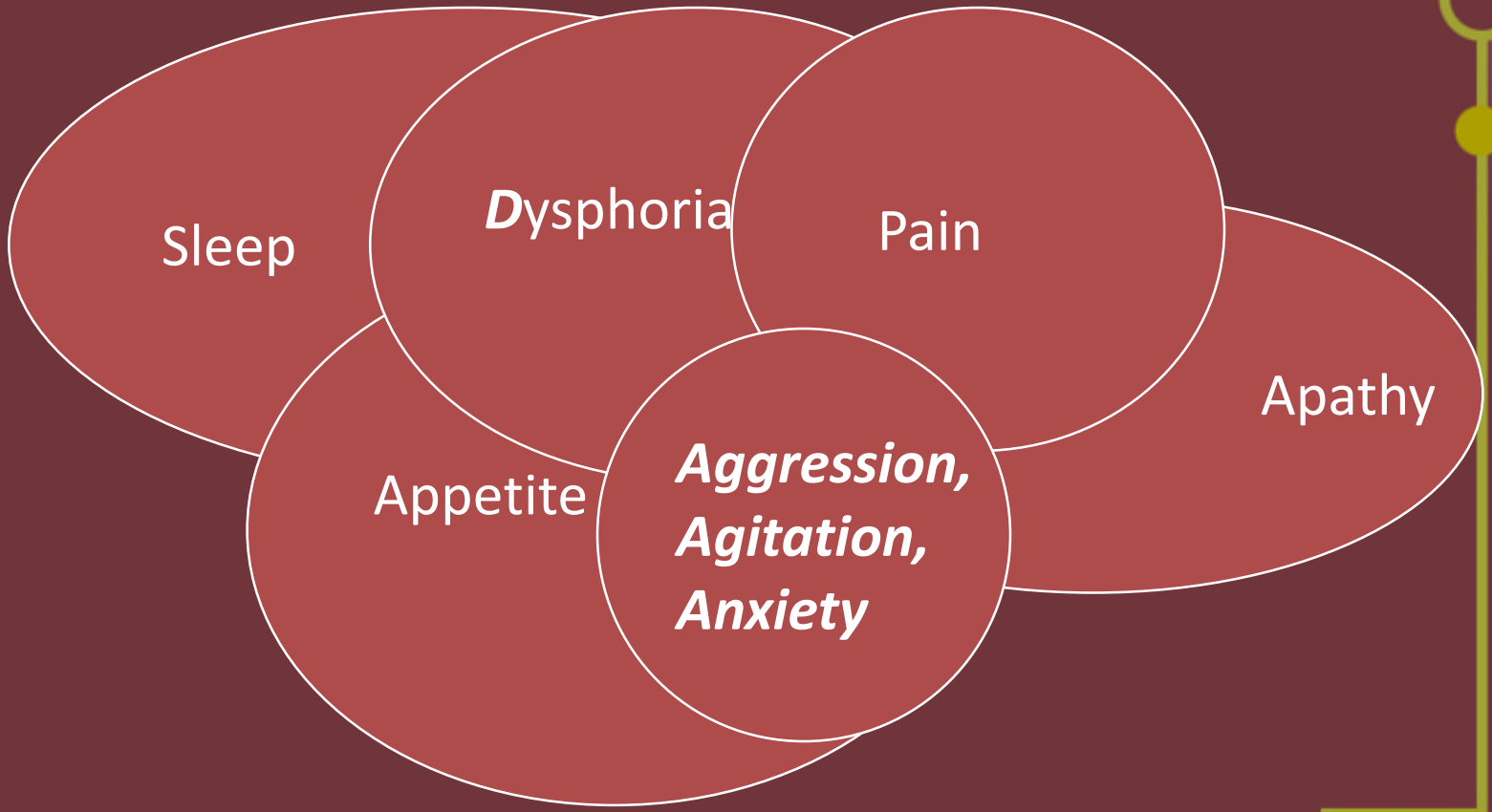
1. Acetaminophen
2. Oral morphine (up to 20mg/day)
3. Transdermal buprenorphine
4. Pregabalin

Alternative approach??

Sublingual Narcotic Passmore Int Psychogeri 2011

Sublingual Narcotic	Fentanyl	Sufentanil
Equivalent Dose	50-100 mcg	10 mcg
Dose for incident pain	10-50 mcg sl. Do not swallow for 5 min after a dose	5-25 mcg (max 50 mcg) sl. Do not swallow for 2 min after
Onset of action	5-15 minutes. Peaks at 20 minutes.	2-3 minutes
When to adminster	10 minutes prior	3-5 minutes prior
Duration	30-45 minutes	10-25 minutes
Monitoring	Watch resp rate q 5-10 minutes for 30 minutes	Watch resp rate q 5-10 minutes for 30 minutes

BPSD: Pain


Sleep
*D*ysphoria
Pain
Apathy
Appetite
Aggression, Agitation, Anxiety

Case #2-part 1

- 78 yo woman from residential intermediate care home, noticed to have acute change in behaviour and mobility over a month. Known history of dementia. Not on psychotropic medications usually, but getting Zopiclone lately . Shares a room. Refusing medications, calling out at times, sleeping poorly at night and so napping a lot in the day. Falling frequently. Maybe visually hallucinating. Now comes to hospital after a fall.

Management of BPSD

- Non-pharmacological
  - Needs Driven Model
- Pharmacological

BPSD and Response to Meds

Usually Not Respond to Medications

Simple Wandering

Inappropriate urination/defecation

Inappropriate dressing/undressing

Disruptive repetitive activities (perseveration) or vocalizations

Tugging at lapbelts

Hiding / hoarding

Can Be Responsive to Medications

Anxiety

Sadness, crying, sleep complaints and other depressive symptoms

Withdrawal and apathy

Elation, pressured speech and hyperactivity (manic-like)

Persistent and distressing delusions or hallucinations

Physical aggression or persistent verbal aggression

Sexually inappropriate behaviour

Sleep disturbance

Pharmacotherapy for BPSD

- Atypical Antipsychotics (AP's)
  - Risperidone, Olanzapine, Quetiapine
  - Clozapine, Ziprasidone, Aripriprazole
- Typical Antipsychotics
- Antidepressants
- Cholinesterase inhibitors (AchEI's)
- Memantine
- Anticonvulsants
- Benzodiazepines

Pharmacotherapy for BPSD

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- Antidepressants: SSRI's
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Antidepressants for agitation and psychosis in Dementia. Seitz et al. 2013, Cochrane Database; Barak 2011

- 9-10 RCT's
- Comparator to placebo or antipsychotic
- Citalopram, escitalopram, sertraline, trazadone
- Sig effect over placebo, comparable effect to antipsychotic

SSRI's Side effects

- Interaction with Warfarin, Digoxin, Statins, ß-Blockers and Calcium channel blockers via cytochrome P450 system
- Hyponatremia (SIADH) particularly in the elderly
- Risk of falls, fractures, and osteoporosis
- Risk of GI bleed doubled (Andrade, J. Clin. Psychiatry 2010), esp. with NSAID's, anticoagulants
- FDA warning (2011): ↑QT_c for Citalopram >40mg/d
- Health Canada (2012): For elderly, max dose 20 mg/d Citalopram and 10 mg/d Escitalopram.

Baseline Na level, Na within 4 weeks

Monitor carefully INR's if on warfarin, etc.

Consider baseline ECG

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- Cholinesterase inhibitors (ChEI's)
- Memantine
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- Benzodiazepines

BPSD Clusters: AchEI's, Memantine

Gauthier et al. Int. J. Psychogeriatrics, 2010

NPI

Includes 10 behavioral areas:

1. Delusions- Memantine
2. Hallucinations
3. Agitation/Aggression- Memantine
4. Depression-AchEI's
5. Anxiety-AchEI's
6. Elation/Euphoria
7. Apathy/Indifference-AchEI's
8. Disinhibition
9. Irritability-Memantine
10. Aberrant motor behavior

- May also include 2 neurovegetative areas:

11. Sleep and Nightime Behavior Disorders
12. Appetite and Eating Disorders

Monitoring with ChEI's and Memantine

- ECG at baseline highly suggested
- Can be safely combined with other psychotropics
- Monitor for unexplained falls, syncope
- Discontinue if bradycardic (memantine, ChEI's) or significant conduction abnormality (ChEI's)

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Antipsychotics are indicated when:

- there is a ***significant risk of harm*** to the patient or others **or**
- when agitation or aggressive symptoms are
  - ***persistent,***
  - ***recurrent, or***
  - ***severe enough***

  to cause significant suffering and distress, or significant interference with care

Salzman et al 2008; CCMHS 2006;GPAC 2008;Lyketsos et al 2006

Examples of Commonly Used Antipsychotic Dosages for the Elderly

Medication	Starting Dose (mg)	Dosing Frequency	Incremental Dose (mg)	Average Total Daily Dose (mg)
quetiapine	12.5	bid/tid/hs (if XR)	12.5-25	150
risperidone	0.25	od/bid	0.25	1
olanzapine	1.25	od (hs)/bid	1.2-2.5	5
loxapine	2.5	bid/tid	2.5-5	25
haloperidol	0.25	od/bid	0.25-0.5	2
aripiprazole	0.5	od	0.5-1	2-10

Avoid Risperidone, Olanzapine and Loxapine in Lewy Body Dementia (LBD) or Parkinson's Disease Dementia (PDD). Haloperidol contraindicated.

CCSMH

- Canadian Coalition for Senior's Mental Health (www.ccsmh.ca)
- CPG's published in 2006, update 2014
- "Assessment and Treatment of Mental Health Issues in Long-Term Care Homes"

Antipsychotics for BPSD

- We recommend that risperidone, olanzapine and aripiprazole be used for severe agitation, aggression and psychosis associated with dementia where there is risk of harm to the patient and/or others. The potential benefit of all antipsychotics must be weighed against the significant risks, such as cerebrovascular adverse events and mortality. (Grade 2A)

- There is insufficient evidence to recommend for or against the use of quetiapine in the management of severe agitation, aggression and psychosis associated with dementia. (Grade 2B)

Atypical Antipsychotics: Mortality Risk (Black Box Warning)

- Mortality risk
  - Odds Ratio= 1.7 times
    (FDA April 2005)
    - 17 studies: 5106 pts, 4.5% vs 2.6% placebo
  - Odds Ratio= 1.54 times
    (Schneider JAMA 2005;294:15)
    - 15 studies: 3353 pts, 3.5% vs 2.3% placebo

Bannerjee, S. The use of antipsychotic medication for people with dementia: Time for action. Report to UK Dept of Health, 2009

- “15 randomised placebo-controlled trials of atypical antipsychotics provides robust evidence for an increased risk of CVAEs, with a pooled relative risk of 2.57 (95% CI 1.41-4.66)”
- Base rate is less than 5%

Case #2-part 2a

- After initial management with Loxapine 15 mg/d and supplemented with Methotrimeprazine, she develops a gait disturbance and begins to lean to the right when upright.

Risks for EPS in Elderly on Antipsychotic Treatment

- Aging (pharmcodynamic drop off of D_2 receptors)
- Pharmacokinetic: slow metabolizers; aging
- Underlying Neurocognitive Condition
  - Lewy Body Dementia
  - Parkinson's Disease with or w/o Dementia
  - Parkinson's plus syndromes
  - Vascular Parkinsonism
  - Advanced AD
  - Wilson's Disease
  - Creutzfeld-Jacob Disease, HIV encephalopathy
- Non-antipsychotic Medications
  - SSRI's, Lithium
  - Metoclopramide (Maxeran)

Atypical AP's and side effects

- Risperidone, Olanzapine
  - EPS, Gait disturbance
  - Infection risk (UTI, URTI)
  - Peripheral edema, orthostasis (Risp)
  - Metabolic syndrome, wt gain uncommon
- Quetiapine
  - Orthostasis, sedation
  - Prolong QTc
  - Agitation, insomnia (norquetiapine)
- Aripiprazole
  - Insomnia, akathisia-like

Weighing Risk vs. Benefits of Atypicals

- NNT for benefit: 5 - 14 patients
- NNH for mortality: 100 patients
- 1 patient death for every 9 – 25 who benefit

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Anticonvulsants

- Anticonvulsants also have evidence for use in BPSD. However, studies of valproic acid, carbamazepine, oxcarbezpine and gabapentin have been shown conflicting results.
- Valproic acid is not usually recommended at this time due to negative trials and toxicity in elderly
- Gabapentin dosing reduced in those with renal impairment. Pregabalin?

Benzodiazepines

- not typically recommended in the elderly as they increase risk of falls, fractures and confusion
- For individuals who are bed-bound and resistive to nursing care, fast acting benzodiazepines, such as lorazepam
- Short-term use may sometimes be warranted, but long-half life benzodiazepines should be avoided (eg: diazepam)

BRITISH COLUMBIA

Best Practice Guideline for Accommodating and Managing Behavioural and Psychological Symptoms of Dementia in Residential Care

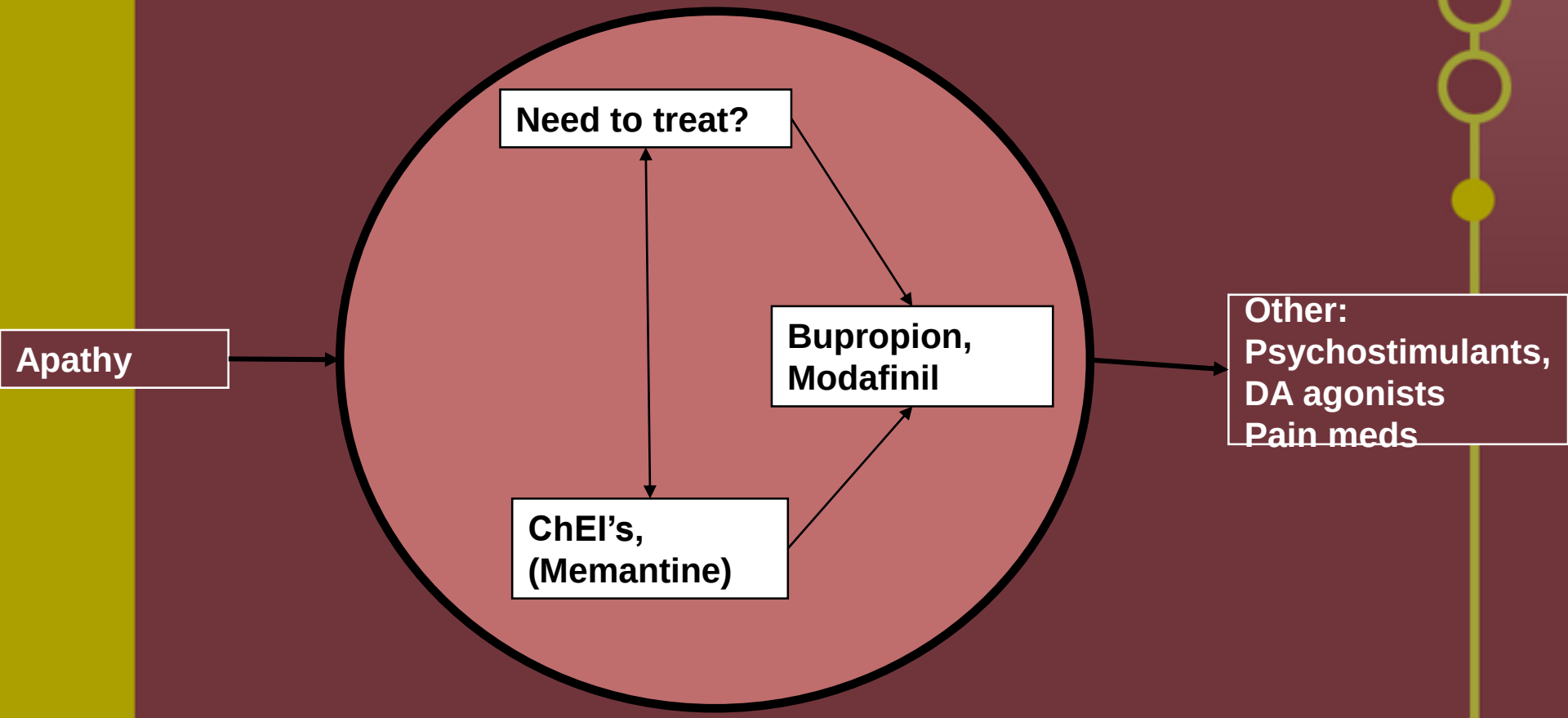
A Person-Centered Interdisciplinary Approach

October 25, 2012

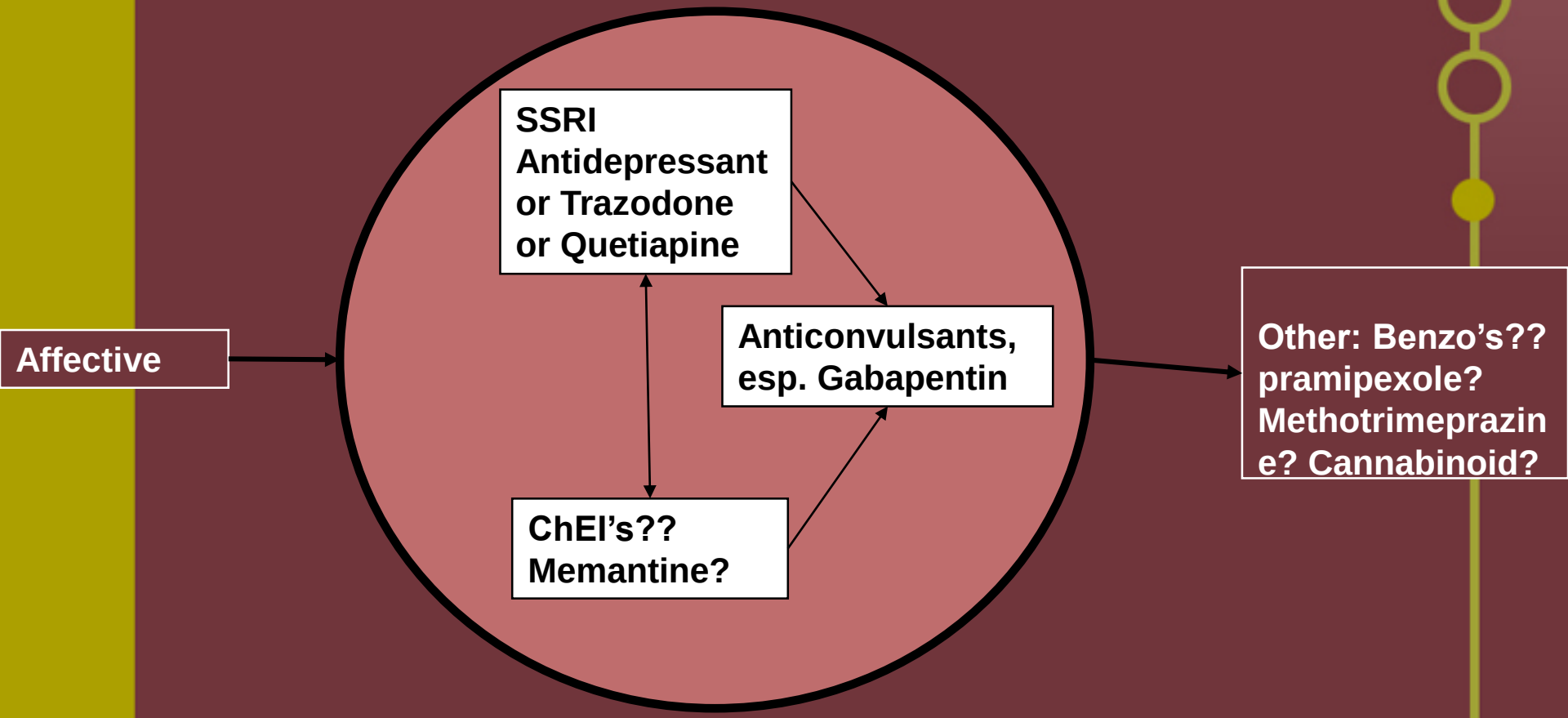
BPSD tools

- BC BPSD Project (www.bcbpsd.ca)
  - Interdisciplinary group including Drs. Elisabeth Drance and Carol Ward
  - Part 1: Interdisciplinary Decisional Support for BPSD
  - Part 2: Reassessment with Family Physician or Nurse Practitioner for BPSD

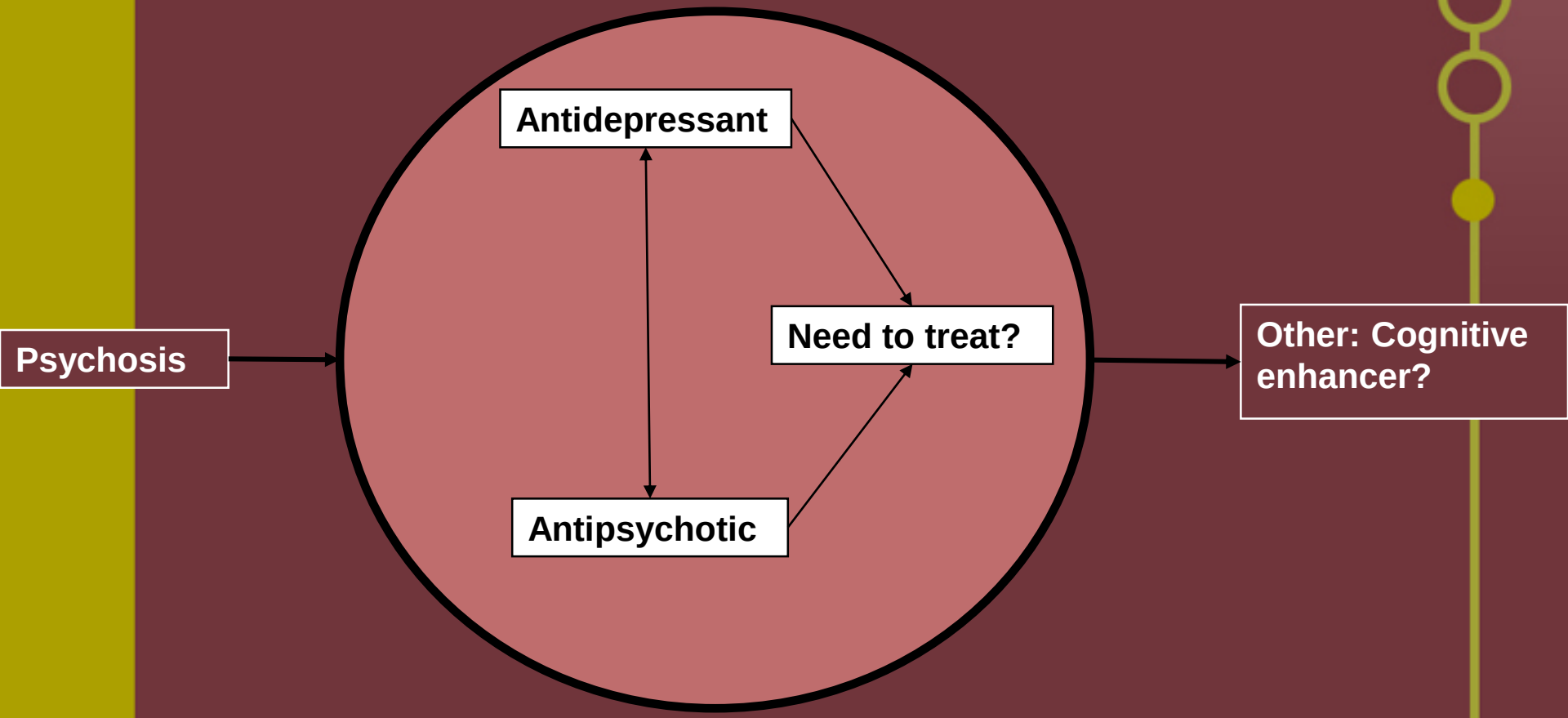
BPSD: Apathy


Apathy
Need to treat?
Bupropion, Modafinil
ChEI's, (Memantine)
Other: Psychostimulants, DA agonists Pain meds

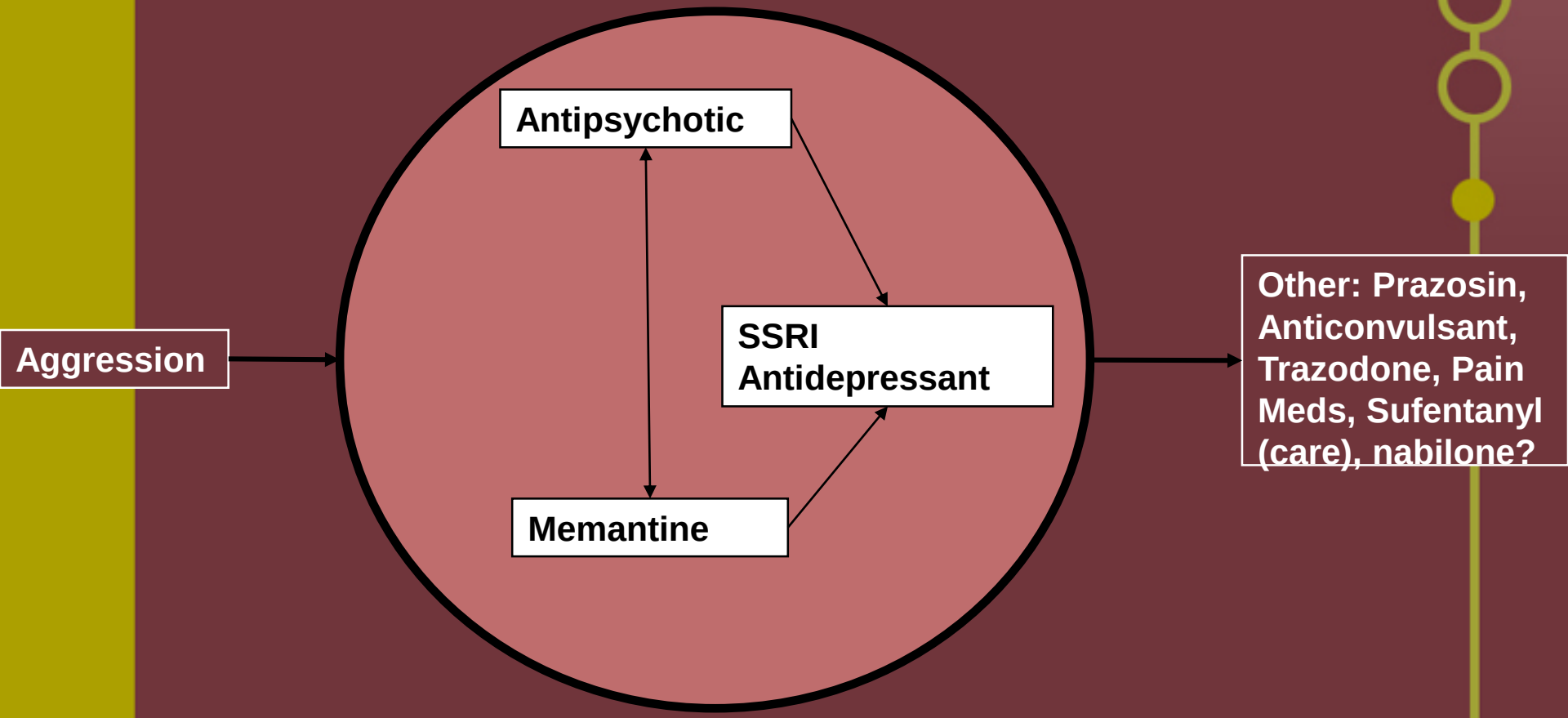
BPSD: Affective (Dysphoria, Irritability, Anxiety)



BPSD: Psychosis



BPSD: Physical Aggression



Take Home Points

- Consider stepwise approach to pain, if at all suspected, especially in advanced dementia
- SSRI's are possible alternatives to antipsychotics but have risks also
- Antipsychotics used for aggression and psychosis, but consent should be obtained by a substitute decision-maker
- Cognitive enhancers can be safely combined with other psychotropics

Web Resources

- BPSD tools: www.bpsdbc.ca
- BC Psychogeriatric Association. VCHA Algorithm for withdrawing antipsychotics
  - http://www.bcpga.bc.ca/2013/Atypical_Antipsychotics_Agents.pdf
- BPSD Best Practices Guidelines in BC (2012)
  - www.health.gov.bc.ca/library/publications/year/2012/bpsd-guideline.pdf
- Reference article: “Therapeutic Approaches in the Management of BPSD in the Elderly”. By: Drs Drouillard, Mithani, Chan. March 2013. BC Medical Journal.

  www.bcmj.org