USING ANTI-PSYCHOTICS IN GERIATRIC POPULATION

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BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA

-IMPACT

-FIVE DOMAINS:

01	02	03	04	05
COGNITIVE	MOTOR	VERBAL	EMOTIONAL	VEGETATIVE

BPSD

IMPLICATIONS

- Early institutionalization
- Lower quality of life, both of person and caregiver
- More severe cognitive impairment
- Increased mortality
- Prolonged in-hospital stay

Etiology/Cause

Interaction between an individual's biology, past and present

Areas of brain implicated

Neurotransmitters involved

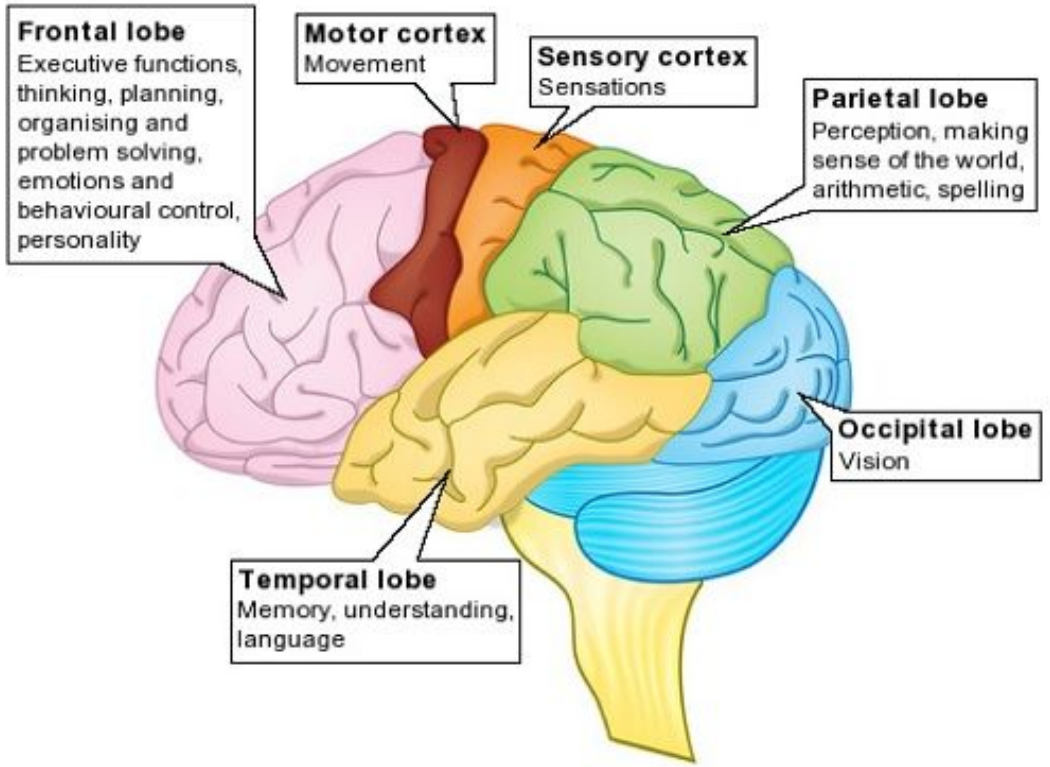


Figure 3. *Anatomy and functions associated with different brain regions. The temporal lobe houses the hippocampus, amongst other regions, and is where AD pathology is first seen. In VaD, the area affected by stroke or other vascular abnormalities will determine the cognitive symptoms observed.*

http://www.bsa.ualberta.ca/sites/default/files/____IPA_BPSD_Specialists_Guide_Online.pdf

Functional neuroimaging and BPSD in Alzheimer's disease

BPSD	Neuroimaging finding
Psychosis	Hypoperfusion in frontal and temporal lobes (Robert et al., 2005)
Depression	Hypoperfusion in frontal, temporal, and parietal lobes (Robert et al., 2005)
Aggression	Hypoperfusion in temporal cortex (Hirono et al., 2000; Lanctot et al., 2004)
Apathy	Hypoperfusion in frontosubcortical structures, especially anterior cingulate (Migneco et al., 2001; Benoit et al., 2002; Lanctot et al., 2007; Marshall et al., 2007)
Sleep loss	Hyperperfusion in right middle frontal gyrus (Ismail et al., 2009)
Appetite loss	Hypoperfusion in left anterior cingulate and left orbitofrontal cortices (Ismail et al., 2008)

Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD)

(1) paranoid and delusional ideation;

(2) hallucinations;

(3) activity disturbances;

(4) aggressiveness;

(5) diurnal rhythm disturbance

(6) affective disturbance; and

(7) anxiety and phobias

The New York Times

THE NEW OLD AGE

A Quiet Drug Problem Among the Elderly

Despite warnings from experts, older people are using more anti-anxiety and sleep medications, putting them at risk of serious side effects and even overdoses.

FDA Warning

Issued in 2005

Warning: Increased Mortality in Elderly Patients with Dementia-Related Psychosis • Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.

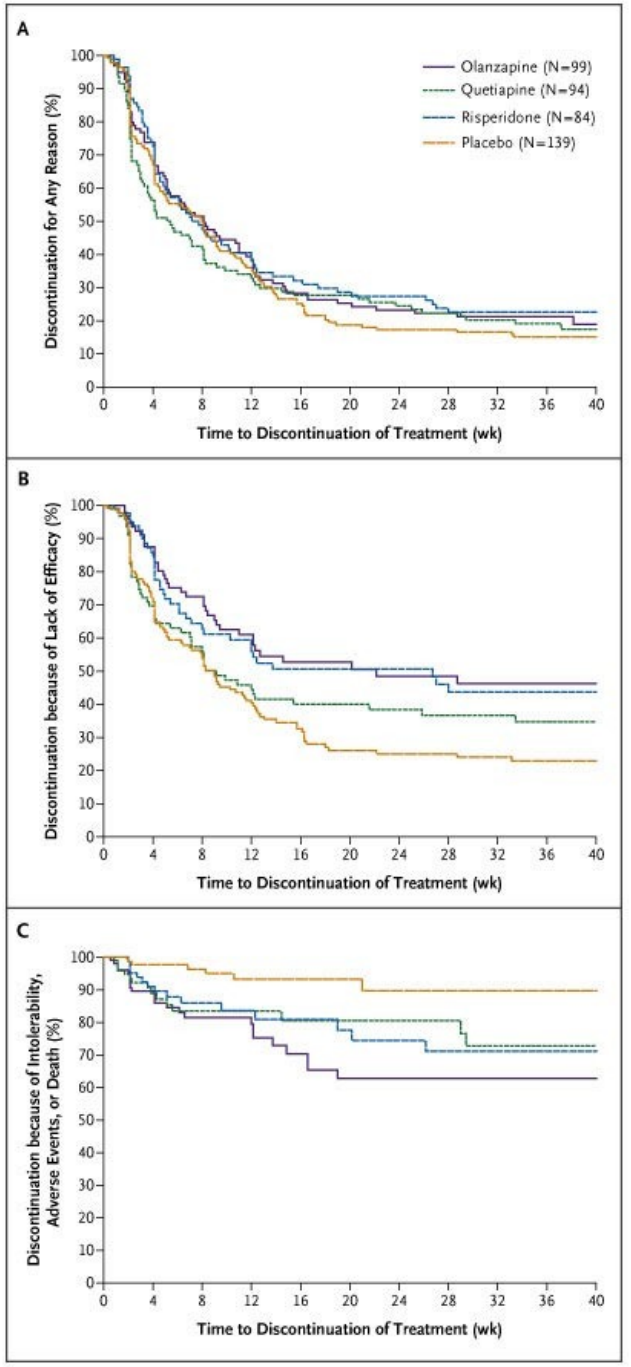
[Name of Antipsychotic] is not approved for the treatment of patients with dementia-related psychosis.

2008	• FDA issues an advisory and black box warning • "The treatment of behavioral disorders in elderly patients with dementia with ... antipsychotic medications is associated with increased mortality."
2011	• National Alzheimer's Project Act signed into law, establishes Advisory Council coordinated by ASPE
2011	• HHS Office of Inspector General issues report, "Medicare Atypical Antipsychotic Drug Claims for Elderly Nursing Home Residents" [oei-07-08-00150] • Found that 14% of elderly nursing home residents had Medicare claims for second generation antipsychotic drugs, and 88% of those were prescribed for dementia.
2012	• CMS launches National Partnership to Improve Dementia Care in Nursing Homes
2015	• Government Accountability Office issues report, "Antipsychotic Drug Use: HHS Has Initiatives to Reduce Use among Older Adults in Nursing Homes, but Should Expand Efforts to Other Settings" [GAO-15-211] • "Among Medicare Part D enrollees with dementia living outside of a nursing home [in 2012], about 14 percent were prescribed an antipsychotic," compared to about one third of older adults with dementia who had spent more than 100 days in a nursing home.

ARE THEY EFFECTIVE?

CATIE -AD STUDY

Compared Risperidone, olanzapine, and quetiapine for the treatment of BPSD in older adults with Alzheimer's disease



Double-blind, placebo-controlled trial

(Study funded by National Institute of Mental Health)

N=421 outpatients with Alzheimer disease and psychosis, aggression, or agitation

- Olanzapine (n=100)
- Quetiapine (n=94)
- Risperidone (n=85)
- Placebo (n=142)

Setting: 45 US sites

Enrollment: 2001-2004

Follow-up: Up to 36 weeks

Primary outcome: Time until discontinuation of treatment

Secondary outcome: Improvement on CGIC scale at week 12

Primary Outcome

Time to discontinuation of treatment for any reason				
Olanzapine	Quetiapine	Risperidone	Placebo	P value
8.1 weeks	5.3 weeks	7.4 weeks	8.0 weeks	0.52

Major Adverse Outcomes with Antipsychotics over 6-12 weeks

(Schneider et al 2005,Ballard et al 2009)

- Parkinsonism
- Sedation
- Gait disturbance
- Increased respiratory infections
- Edema
- Accelerated cognitive decline
- Stroke (>3 fold)
- Other thrombo-embolic events
- Mortality (1.5-1.7 fold)

Effect size	Agitation	Psychosis	Overall BPSD
Aripiprazole	Small	NS	Small
Olanzapine	Very small	NS	Very small
Quetiapine	NS	NS	NS
Risperidone	Small	Small	Very small
SGAs Overall	Small	Very small	**Very small**
Haloperidol	No diff from SGAs	Indeterminate	No diff from SGAs

Confidence in the findings based on quality of the research evidence

High confidence		Moderate		Low confidence		Insufficient data	

ADAPTED FROM: Maglione et al. Off-Label Use of Atypical Antipsychotics: An Update. Rockville (MD): AHRQ (US); 2011. PMID: 22132426. http://www.ncbi.nlm.nih.gov/books/NBK66081/

SIDE EFFECT PROFILE

Weight gain greatest with Olanzapine, Quetiapine

Postural Hypotension, sedation - Clozapine, Quetiapine

EPS, postural hypotension - Risperidone at higher doses

Ziprasidone - QTc prolongation

Factors that experts noted may influence their prescribing in individuals with dementia:

- Aripiprazole: Long half-life, potential for drug-drug interactions, partial agonist mechanism of action, greater rates of akathisia
- Olanzapine: Greater likelihood of anticholinergic effects, sedation, metabolic effects, and weight gain
- Risperidone: Greater likelihood of extrapyramidal symptoms and hyperprolactinemia
- Ziprasidone: Changes in absorption with food and greater likelihood of QTc prolongation

OTHER FACTORS IN MEDICATION SELECTION

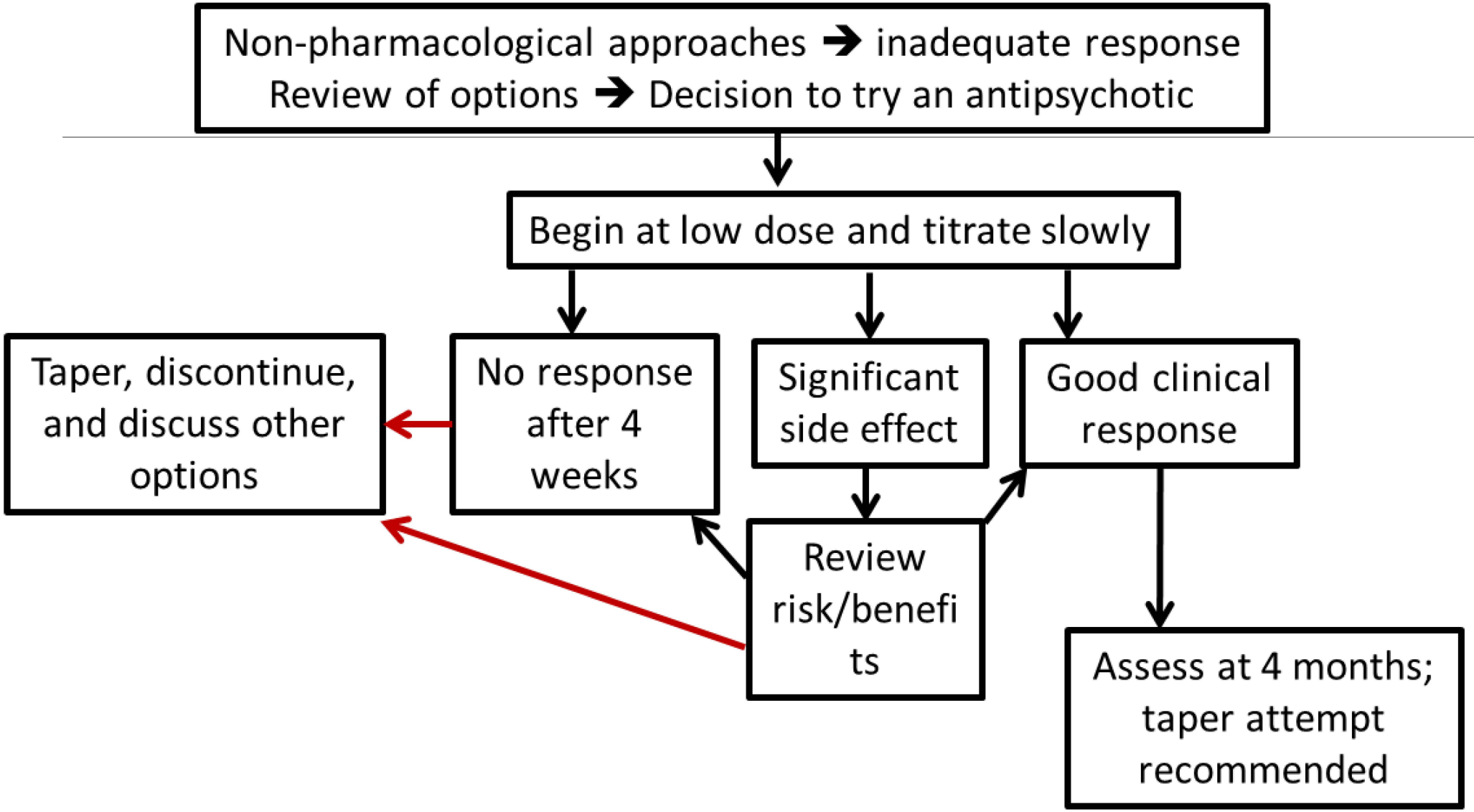
Does the patient have co-occurring physical conditions that would influence medication tolerability or potential for side effects?

Are there relevant pharmacokinetic considerations (e.g., drug interactions, active metabolites)?

What formulations of the medication are available that may assist with patient adherence?

Barriers to use of a specific medication (e.g., regulatory stipulations, cost considerations, formulary coverage, preauthorization requirements)?

Does the patient or family have a stated preference for a specific medication?


Non-pharmacological approaches → inadequate response
Review of options → Decision to try an antipsychotic
Begin at low dose and titrate slowly
Taper, discontinue, and discuss other options
No response after 4 weeks
Significant side effect
Good clinical response
Review risk/benefi ts
Assess at 4 months; taper attempt recommended

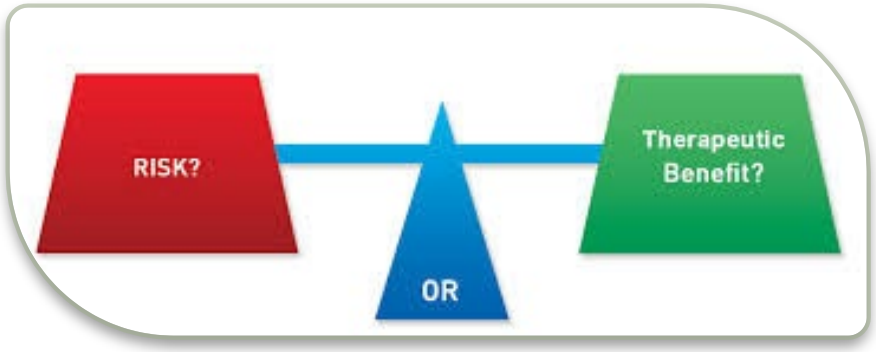
Dementia Antipsychotic Withdrawal Trial (DART-AD)

APA recommendation: Attempt to taper

Rationale:

- A substantial fraction of individuals can have antipsychotics tapered without recurrent symptoms, reducing potential harms of medication
- Predictors of success: Lower baseline severity, lower doses of antipsychotics needed for symptom control

Questions to ask before Rx



- Does the particular symptom or behavior warrant drug treatment, and why?
- Is this symptom or behavior likely to respond to pharmacotherapy? (DICE model)
- Which class of medication is most suitable for this symptom or behavior?
- What are the predictable and potential side-effects of a particular drug treatment?
- How long should the treatment be continued?

Limitations:

Behaviors unlikely to improve:

- Poor self care
- Refusal of care
- Memory problems
- Inattention
- Unfriendliness
- Repetitive verbalizations or questioning
- Shadowing
- Wandering, behaviors related to apraxia or agnosia (eg: urinating in trash can because it resembles a toilet bowl).

Questions?