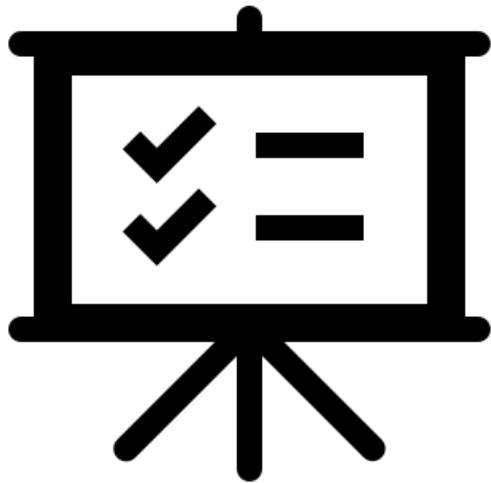


Pharmacological management of behavioral & psychological symptoms of dementia, part 1

this content is up-to-date as of
May 3, 2021

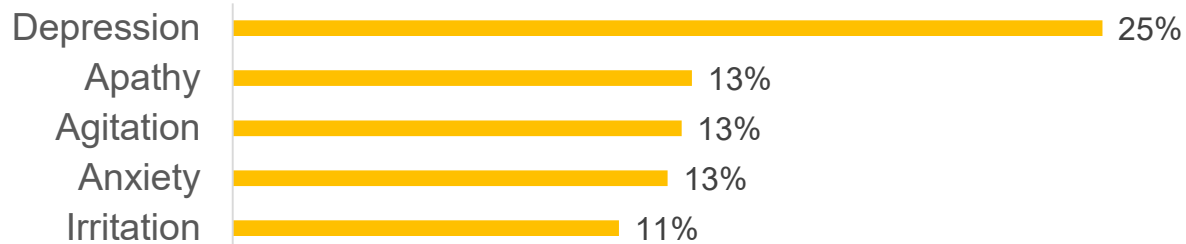


Learning objectives



- Develop an algorithm for managing BPSD
- List the risks and benefits of using antipsychotics for agitation or psychosis in dementia

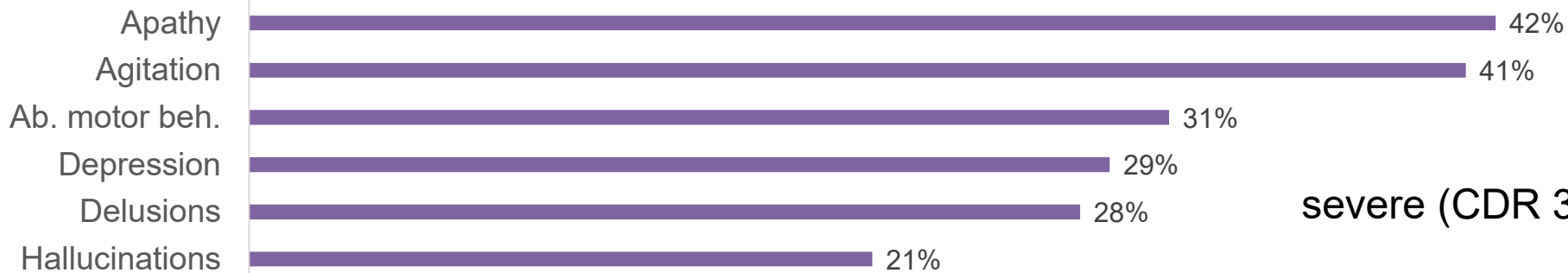
Most common BPSD



mild (CDR 0.5 or 1)



moderate (CDR 2)



severe (CDR 3)

Overview of management

- treat underlying medical causes
- discontinue offending medications & substances
- support & educate caregivers & other family members
- develop a psychological, behavioral & environmental management plan
- avoid adding new medications, unless there is risk of harm to patient or others
- if a medication is added, regularly monitor outcomes & attempt discontinuation
- ensure that patients & caregivers are in a safe environment

When to turn to medications for BPSD

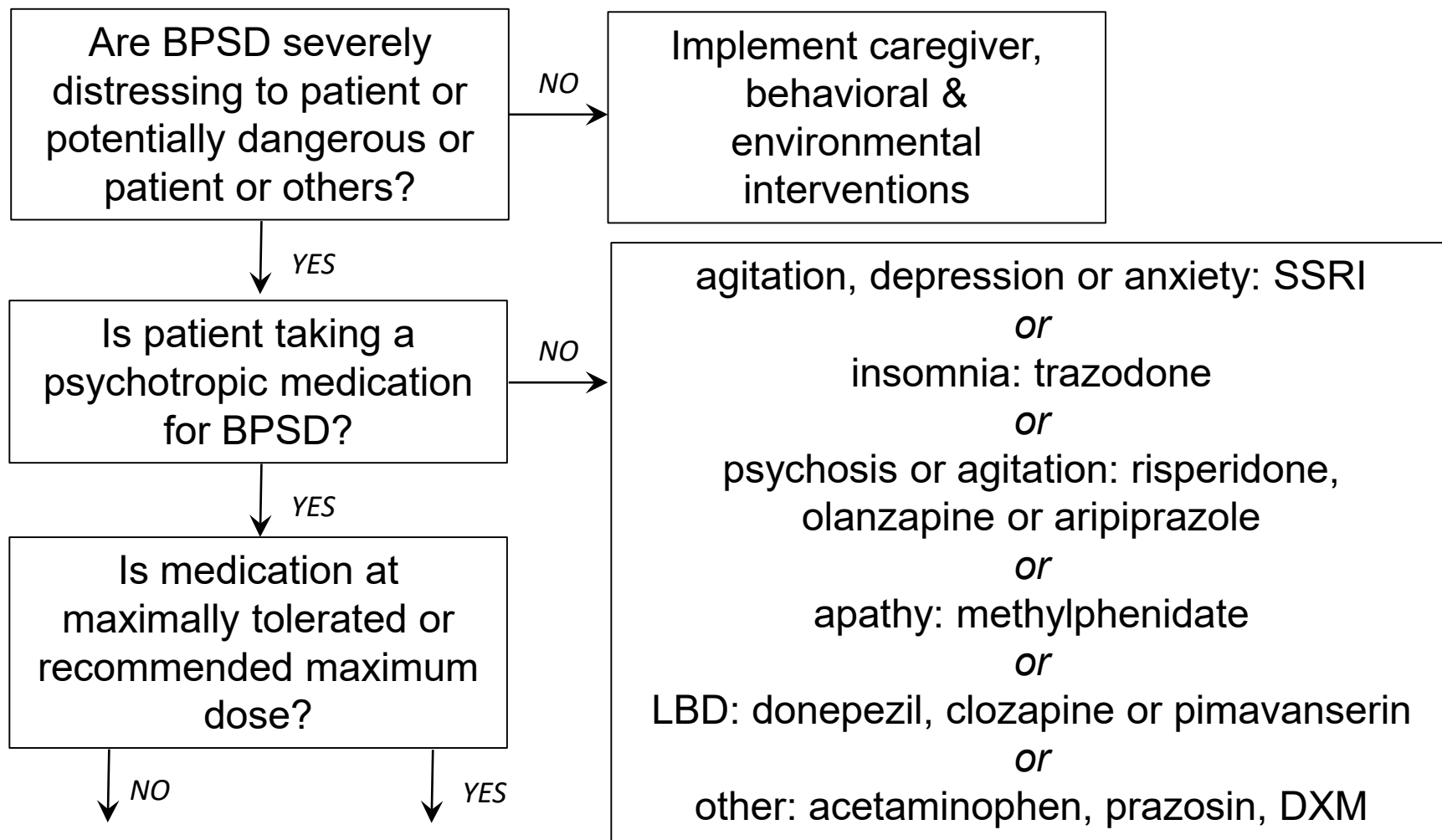
Nonemergency antipsychotic medication should only be used for the treatment of agitation or psychosis in patients with dementia when symptoms are severe, are dangerous, and/or cause significant distress to the patient (*emphasis added*)

Before treatment, the potential risks and benefits from antipsychotic medication should be assessed by the clinician and discussed with the patient, surrogate decision maker, or other family member

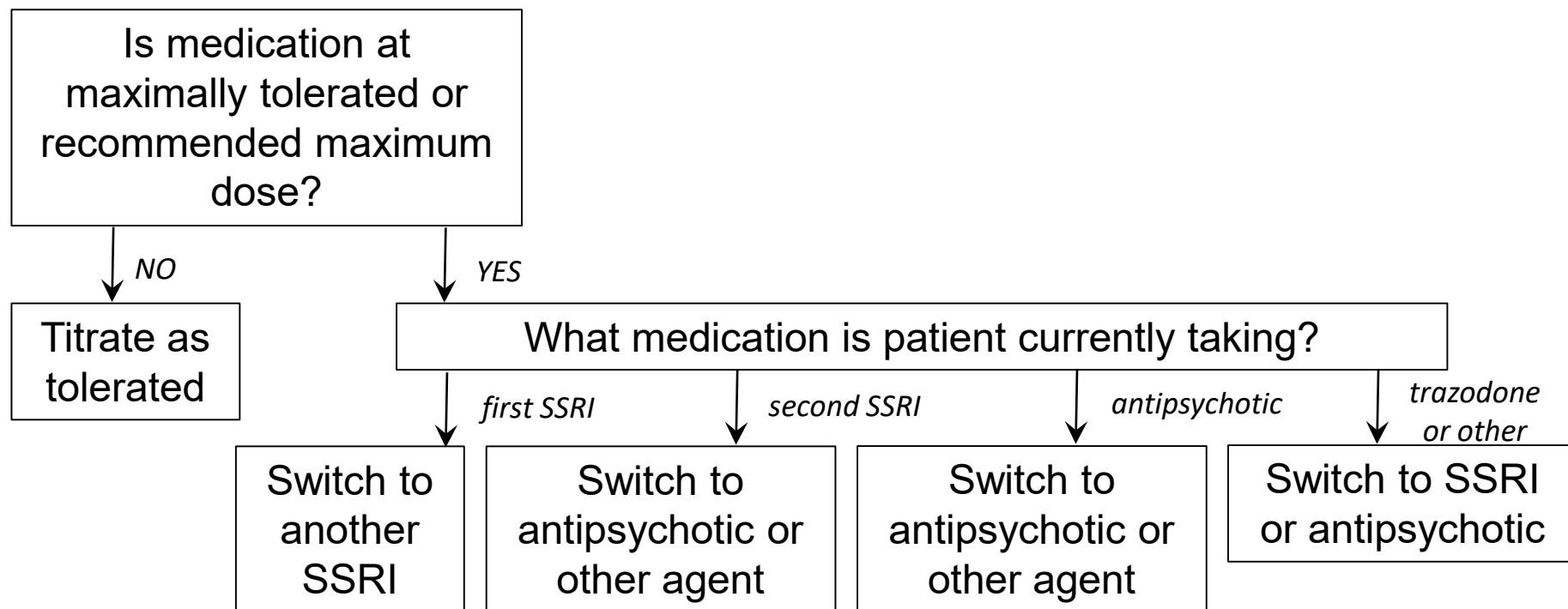
Caveats to using medications for BPSD

- patients with dementia may already have significant polypharmacy (which could be contributing to cognitive impairment or BPSD)
- clinical trials have shown only modest efficacy for medications in treating BPSD
- there are significant risks associated with the use of medications for BPSD, esp. mortality with antipsychotics
- no medications approved for use in BPSD (except risperidone in Europe)

Treatment algorithm* (1)



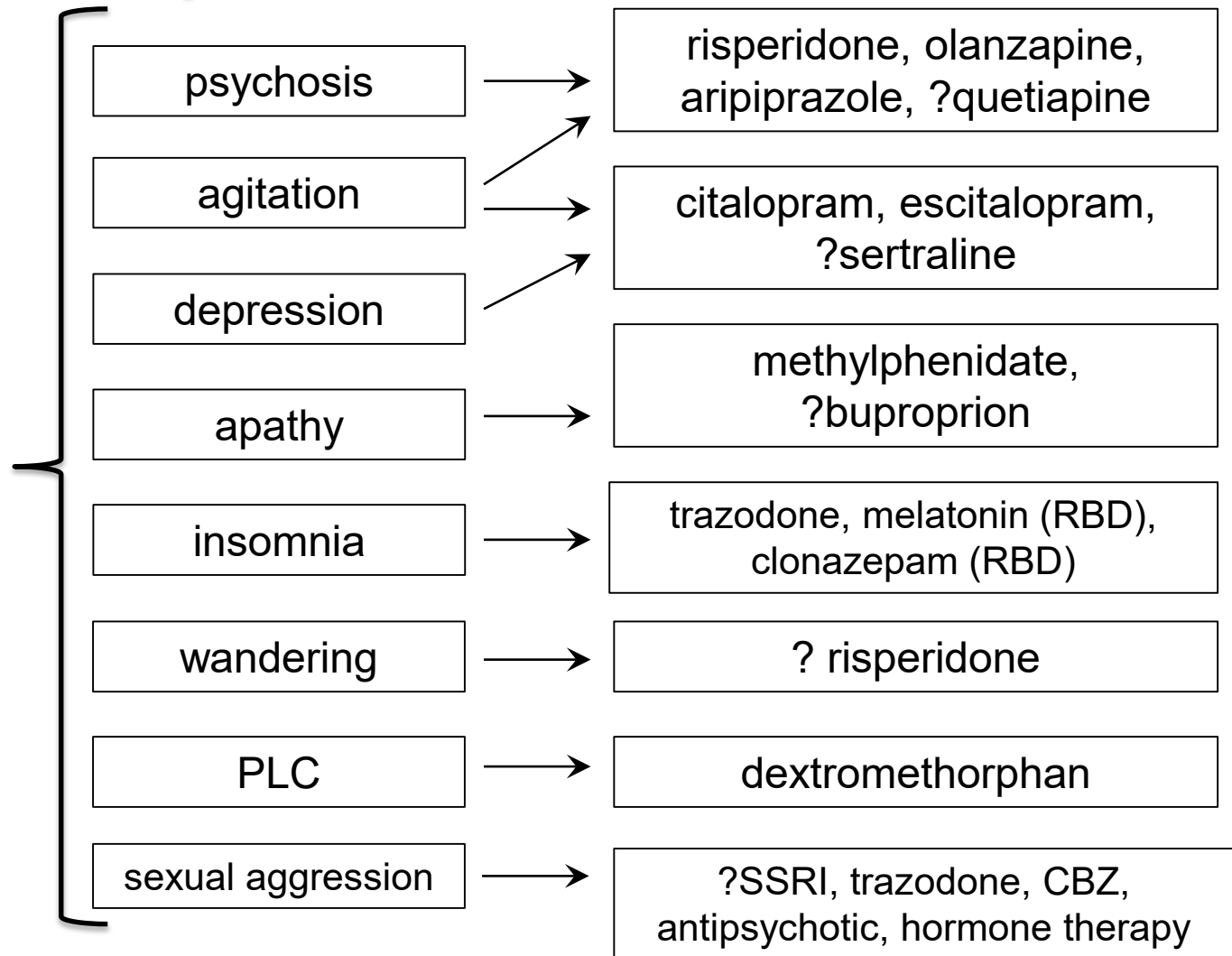
Treatment algorithm (2)



IN ALL CASES: obtain informed consent, dose appropriately, monitor outcomes, continue non-pharm interventions, consider discontinuing med

Specific BPSD

Implement caregiver, behavioral & environmental interventions first; if ineffective and BPSD dangerous or distressing...



Pharmacological options, by diagnosis

Diagnosis	Comments
Lewy body disease, including PDD & DLB	donepezil is first-line; if antipsychotic needed, consider clozapine, quetiapine or olanzapine; pimavanserin could be an option for PDD psychosis
vascular dementia	consider methylphenidate for apathy, but need to monitor blood pressure; may be more prone to vascular side effects of antipsychotics
FTD, behavioral variant	trazodone or SSRIs are first line; stimulant could be considered; avoid cognitive enhancers
intellectual/developmental disability, including Down syndrome	donepezil may help with cognitive impairment, but use low doses to improve tolerability; SSRIs may aid compulsions; use all other psychotropic medications with caution (poor tolerability)

Start low,
go slow

Antipsychotics

atypical antipsychotics

risperidone

olanzapine

aripiprazole

quetiapine

clozapine

brexpiprazole

typical antipsychotics

haloperidol

Antipsychotics: the data that led to the FDA Black Box warning

	trials N	deaths Rx	deaths placebo	OR (95% CI)
risperidone	5 1954	3.8%	2.8%	1.30 (0.76-2.23)
olanzapine	5 1662	2.6%	1.3%	1.91 (0.79-4.59)
quetiapine	3 637	5.4%	2.8%	1.67 (0.70-4.03)
aripiprazole	3 951	3.5%	1.7%	1.73 (0.70-4.30)
overall	16 5204	3.5%	2.2%	1.54 (1.06-2.23)

NNH=100 (95% CI = 53-1000)

More concerns about mortality

Medication	Case-control pairs (N)	Deaths (vs nonusers)	Risk difference	NNH
haloperidol	1921	20.7% (vs 8.4%)	3.8%	26
risperidone	6338	13.9% (vs 8.5%)	3.7%	27
olanzapine	1908	13.9% (vs 9.8%)	2.5%	40
quetiapine	4621	11.8% (vs 8.2%)	2.0%	50
antidepressant	29,704	8.3% (vs 8.0%)	0.6%	166

Atypical antipsychotics: other side effects

Side effect	Comments
sedation	antipsychotic 20% vs. placebo 8%
cognitive impairment	equivalent to one year of cognitive decline
extrapyramidal symptoms	haloperidol > risperidone > aripiprazole > olanzapine > quetiapine = clozapine
falls & fractures	1.5-2.5x increased risk
metabolic	weight gain: olanzapine > quetiapine & risperidone
stroke	risperidone 2.2% vs. placebo 1.1%; also higher risk with olanzapine
venous thrombo-embolism	evidence has not been consistent
others	risperidone: hyperprolactinemia risperidone, olanzapine: edema clozapine: neutropenia

Atypical antipsychotics: efficacy

- best evidence for risperidone, olanzapine and aripiprazole
 - mixed evidence for quetiapine
 - evidence for clozapine in very specific scenarios
 - early evidence for brexpiprazole
- overall, small effect on behavioral symptoms:
 - pooled effect size = 0.16
 - number needed to treat = 6
 - significant placebo effects (30-50% response rates)
- response usually in first 2-4 weeks
- no studies of other antipsychotics

Comparative effectiveness review

Effect on BPSD	aripiprazole	olanzapine	quetiapine	risperidone
overall	++	+	+	++
psychosis	+	+/-	+/-	++
agitation	+	++	+/-	++

++ moderate or high evidence of efficacy

+ low or very low evidence of efficacy

+/- mixed results

Starting antipsychotics

- Treatment should be initiated at a low dose and titrated up to the minimum effective dose as tolerated
- If the patient experiences a clinically significant side effect, the potential risks and benefits of the antipsychotic should be reviewed by the clinician to determine if tapering and discontinuing is indicated
- If there is no clinically significant response after a 4-week trial of an adequate dose of an antipsychotic drug, the medication should be tapered and withdrawn

Dosing of antipsychotics

	Starting dose	Maximum dose
risperidone	0.25 mg qhs	0.5 mg bid*
olanzapine	2.5 mg qhs	10 mg qhs
aripiprazole	2.5 mg qhs	10 mg qhs
quetiapine	25 mg qhs	100-200 mg/d**
clozapine	6.25-12.5 mg qhs	25-50 mg/d**
brexpiprazole	0.25-0.5 mg qhs	2 mg qhs

*Higher doses associated with EPS. **Once daily at bedtime, or twice daily

Stopping antipsychotics

- **An attempt to taper and withdraw the drug should be made within 4 months of initiation**, unless the patient experienced a recurrence of symptoms with prior attempts at tapering of antipsychotic medication
- In a patient who has shown a positive response to treatment, decision-making about possible tapering of antipsychotic medication should be accompanied by a discussion with the patient, surrogate decision maker, or other family member
- In patients with dementia whose antipsychotic medication is being tapered, assessment of symptoms should occur at least monthly during the taper and for at least 4 months after medication discontinuation to identify signs of recurrence and trigger a reassessment of the benefits and risks of antipsychotic treatment

Cochrane review of antipsychotic withdrawal

- Discontinuing antipsychotic use after only 3 months of treatment has typically not been associated with worsening BPSD, except in patients with more severe baseline

To be continued, in part 2

- Antidepressants for BPSD
- Other pharmacological options for BPSD