UNIVERSITY OF ALBERTA

Switching Medications

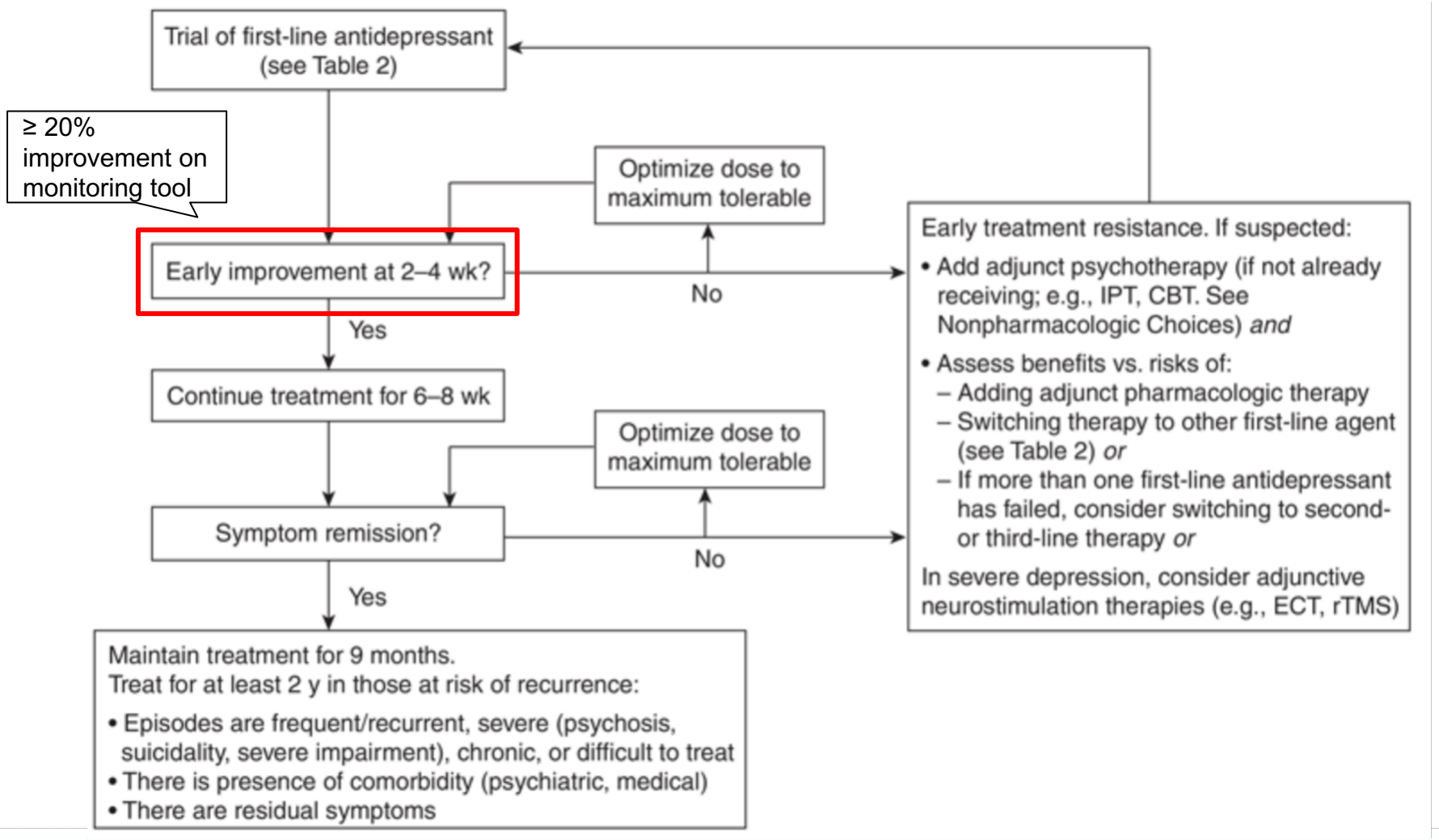
Mental Health Assessment and Prescribing by Alberta Pharmacists (MAP-AP) Study Group

REB ID Pro00093776

Learning Objectives

1. Define an adequate medication trial in Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD)
2. Define no/partial/full response to therapy for MDD and GAD
3. Describe when to add or switch pharmacotherapies for MDD and GAD
4. Describe the process of switching antidepressants
5. Discuss the pros and cons of adding adjunctive therapy

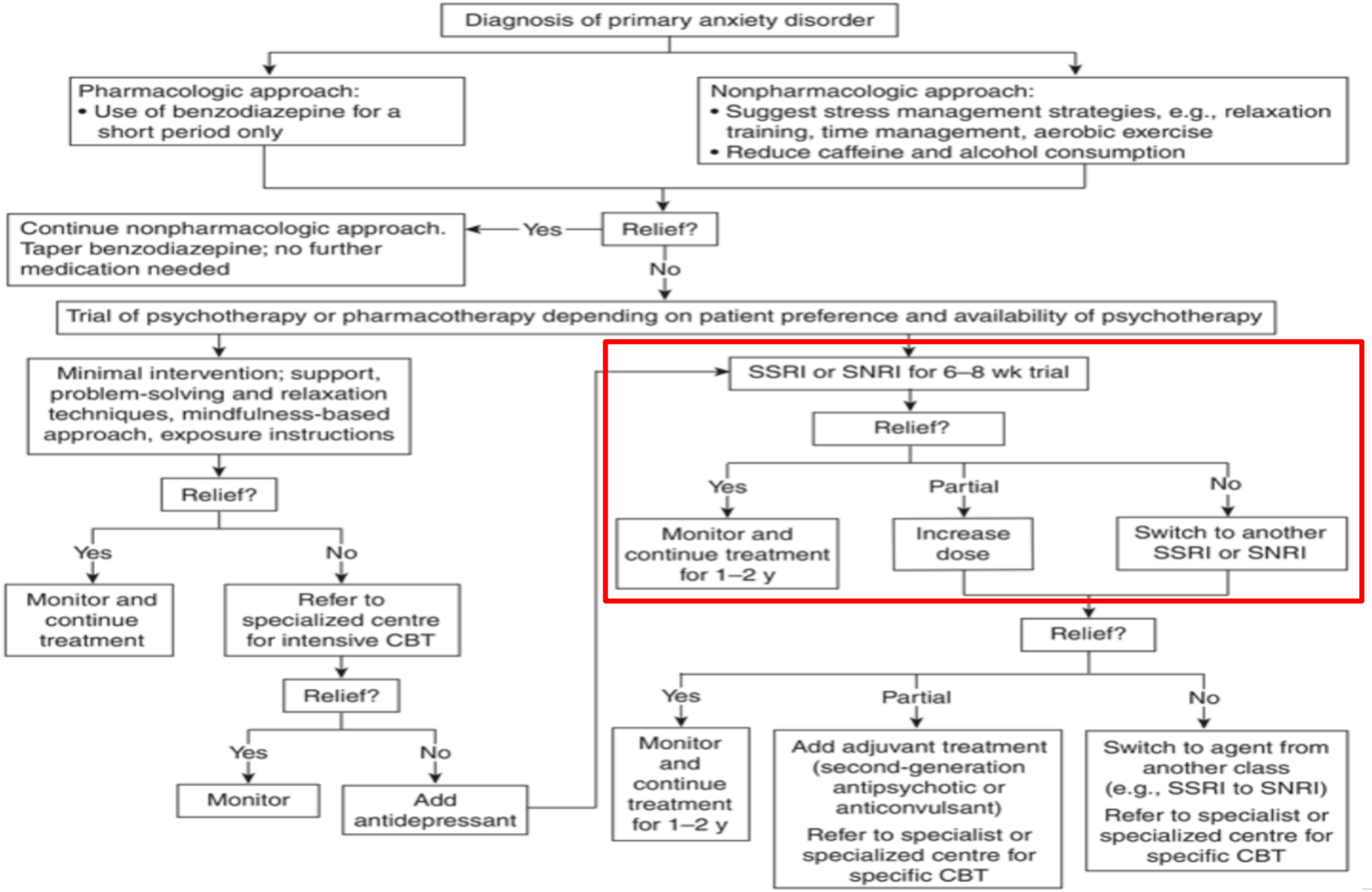
Current treatment algorithm for MDD



What defines an adequate medication trial in MDD?

- Patients should show early response to pharmacological treatment within 2-4 weeks of starting an agent[1]
- Early response is defined as ≥20% improvement in symptom score measured through a patient monitoring tool (e.g., PHQ-9)
- 2-4 weeks are benchmark points in assessing efficacy and tolerability of the initial agent chosen[1]
- ⅔ of patients will not experience full remission with the first antidepressant trial (STAR*D Trial)

Current treatment algorithm for GAD



What defines an adequate mediation trial in GAD?

- Patients should show early response to pharmacological treatment within 6-8 weeks since starting an agent[1]
- Response is defined as ≥ 50% improvement in symptom score measured through a patient monitoring tool (e.g., GAD-7)
- 6-8 weeks are benmark points in assessing efficacy and tolerability of the initial agent chosen[1]

Always consider the full picture

- Partial response can be interpreted subjectively by both patients and clinicians; therefore, the use of standardized assessment tools (e.g., PHQ-9 and GAD-7) is critical in assessing response parameters

- Consider a patient's entire mental health history, as well as patient specific factors when making decisions to add or switch pharmacotherapy
  - Severity of the psychiatric conditions
  - Adherence
  - Costs
  - Adverse effects of medications

Pharmacotherapy options: MDD

First-Line Antidepressants (As per Canadian Availability)[1]	
Medication	**Class**
Bupropion	NDRI
Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline	SSRI
Venlafaxine, desvenlafaxine, duloxetine	SNRI
Mirtazapine	NaSSA
Vortioxetine	SMS

Pharmacotherapy options: GAD

First-Line Antidepressants (As per Canadian Availability)[1]	
Medication	**Class**
Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline	SSRI
Venlafaxine	SNRI

Adverse effects of antidepressants

Class	Most Common Class Side Effects
NDRI[2]	Tachycardia, weight loss, constipation, nausea, xerostomia, insomnia, headache, migraine, dizziness, rhinitis
SSRI[3]	GI upset, anorexia, dry mouth, diaphoresis, headache, dizziness, insomnia, somnolence, anxiety, agitation, tremor. Usually resolve after 2 wk of therapy. Others: sexual dysfunction, weight gain, SIADH with hyponatremia.
SNRI [3]	Nausea, sleep disturbance, drowsiness, nervousness, dizziness, dry mouth.
NaSSA[3]	Weight gain, sedation

Switching or adding?

Consider Switch	Consider Adjunctive

• Little to no improvement with the first medication trial
• Ongoing intolerable side effects
• More time available to wait (less severe condition/ impairment)
• Patient preference on being on a single agent versus two agents
	• Two or more antidepressant trials
	• Partial response but an adjunctive agent may help in reaching remission
	  ○ 25-49% improvement for MDD
	  ○ <50% improvement for GAD
	• Initial treatment is well tolerated but an adjunctive agent may help in reaching remission
	• Patient with partial response does not want to go through the process of initiating another agent again

Switching antidepressants

- Strategies for switching antidepressants are based on their drug classes, pharmacokinetics/ pharmacodynamic profiles

- Direct switch: stop the first antidepressant abruptly and starting new antidepressant the next day
- Taper and switch immediately (sequential): gradually taper the first antidepressant, then start the new antidepressant immediately after discontinuation
- Taper and switch after a washout (sequential): gradually taper the first antidepressant, then start the new antidepressant after a washout period
- Cross-tapering (concurrent): taper the first antidepressants, and build up the dose of the new antidepressant simultaneously

Switching antidepressants

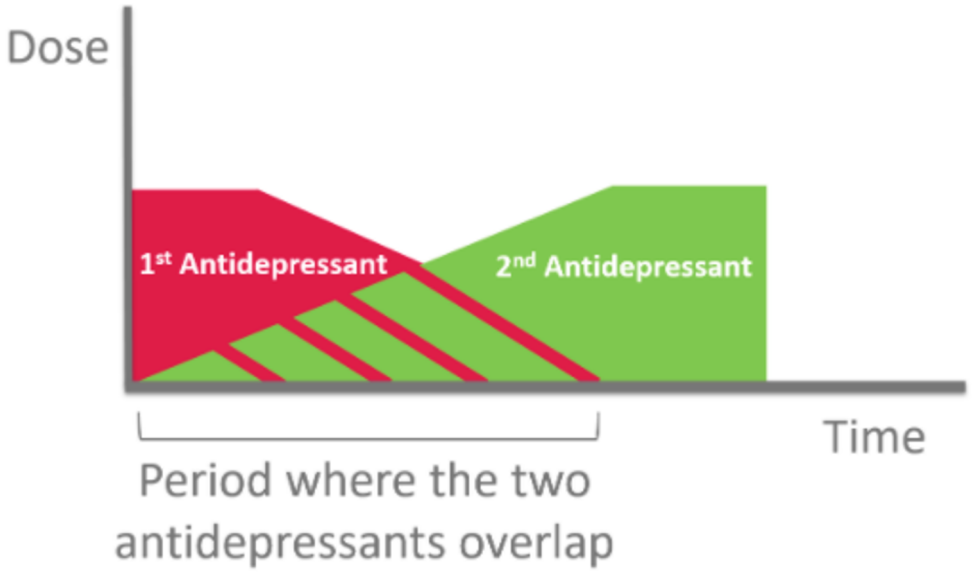
From	To	Washout Time (from complete discontinuation Washout time may be required to prevent serotonin syndrome
MAOI (irreversible)	All other agents	2 weeks (Do not combine/cross taper)
SSRI, SNRI, NaSSA, NDRI, SARI,TCA	MAOI, RIMA	5 weeks for fluoxetine* 3 weeks for vortioxetine* 2 weeks for other SSRIs,* 5-7 days NaSSA* 3-5 days NDRI* 3 days for SNRIs
SSRI, SNRI, NaSSA, NDRI, SARI, TCA	All ADs (except MAOI, RIMA)	No washout required Crossover/combine with caution. Caution with drug interactions

Resource: SwitchRx

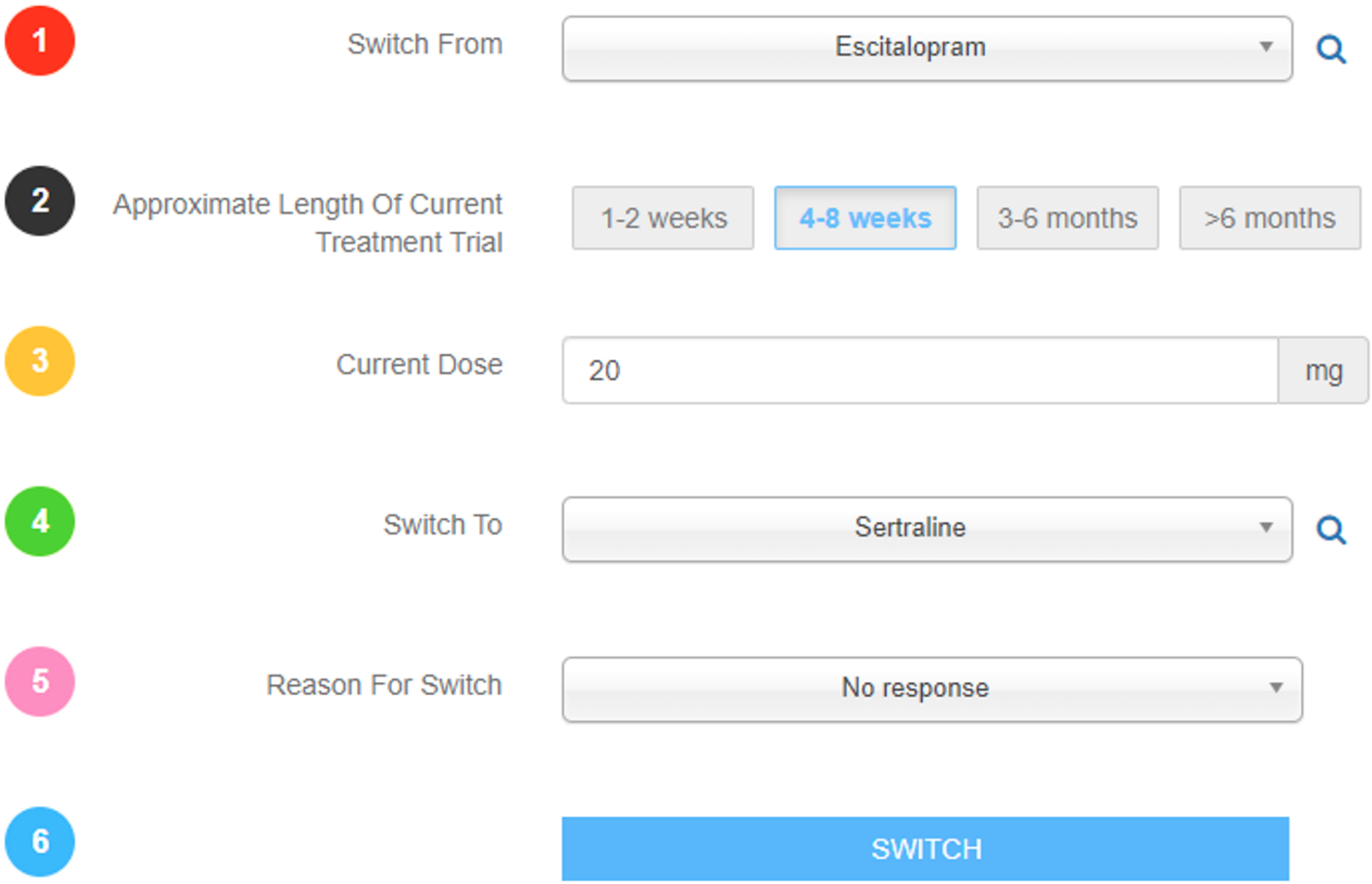
- SwitchRx
- https://www.switchrx.com/

- Provide current and useful information on adjusting patients' psychotropic treatment regimens

- Suggest an antidepressant switching schedule based on a patient's treatment regimen using the cross-taper method



Example: Switching antidepressants using SwitchRx



Example: Switching antidepressants

Timing	Escitalopram 20 mg	Sertraline
Week 1	20 mg	25 mg
Week 2	15 mg	50 mg (lowest therapeutic dose)
Week 3	10 mg	75-100 mg
Week 4	5 mg	75-100 mg
Week 5	Discontinue	100-150 mg
Week 6		150-200 mg

Adding an adjunctive therapy

- **Pros:** minimize the risk of relapse vs. switching
- **Cons:** additive side effects, regimen complexity leading to poor adherence
- Review adjunctive therapy for MDD and GAD
  - First line adjunctive agents for MDD: aripiprazole, quetiapine, risperidone
  - Second line adjunctive agent for GAD: pregabalin (BMC Psychiatry)

Resource: Canadian Quick Reference Guide to Psychiatric Medication

- Canadian quick reference guide to psychiatric medication
- http://www.mdpu.ca/documents/reference.pdf

- Summarize dose range, drug interactions, class effects, and special considerations for antidepressants, anxiolytics, and antipsychotics

References

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5. Rush AJ et al. "Acute and longer-term outcomes in depressed outpatient requiring one or several treatment steps: A STAR*D report". *The American Journal of Psychiatry*. 2006. 163(11):1905-1917.